
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

**POST-EFFECTIVE AMENDMENT NO. 2 TO
FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

Zymeworks Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

88-3099146
(I.R.S. Employer
Identification Number)

**108 Patriot Drive, Suite A
Middletown, Delaware 19709
(302) 274-8744**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Kenneth Galbraith
Chair and Chief Executive Officer
108 Patriot Drive, Suite A
Middletown, Delaware 19709
(302) 274-8744**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

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Zymeworks Inc.
108 Patriot Drive, Suite A
Middletown, Delaware 19709
(302) 274-8744**

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this registration statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box:

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box:

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer

Non-accelerated filer

Accelerated filer

Smaller reporting company

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of Securities Act.

EXPLANATORY NOTE

Zymeworks Inc., a Delaware corporation, as successor issuer to Zymeworks BC Inc., formerly known as Zymeworks Inc., a corporation continued under the Business Corporations Act (British Columbia), or Zymeworks BC, is filing this Post-Effective Amendment No. 2 to the Registration Statement on Form S-3ASR (File No. 333-259970) filed with Securities and Exchange Commission, or the SEC, by Zymeworks BC on October 1, 2021, as amended by Post-Effective Amendment No. 1 (File No. 333-259970-01) filed with the SEC by Zymeworks on October 13, 2022, because Zymeworks expects that it will cease to be a well-known seasoned issuer (as such term is defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act) upon the filing of its Annual Report on Form 10-K for the year ended December 31, 2022. Accordingly, this Post-Effective Amendment No. 2 includes disclosure required for a registrant other than a well-known seasoned issuer.

This Post-Effective Amendment No. 2 contains:

- a base prospectus that covers the offering, issuance and sale by us of up to \$500.0 million in the aggregate of the securities identified on the cover page to the base prospectus from time to time in one or more offerings;
- a prospectus supplement covering the offering, issuance and sale by us of up to a maximum aggregate offering price of \$150.0 million of our common stock that may be issued and sold from time to time under a sales agreement with Cantor Fitzgerald & Co., or Cantor; and
- a prospectus covering the issuance from time to time of up to 2,737,836 shares of our common stock, consisting of (i) up to 658,612 shares of our common stock issuable upon the exchange of exchangeable shares, or the Exchangeable Shares, in the capital of Zymeworks ExchangeCo Ltd., a company existing under the laws of British Columbia and our indirect subsidiary, which issued the Exchangeable Shares to certain shareholders of Zymeworks BC in connection with a series of transactions, including a redomicile that closed on October 13, 2022, or the Redomicile Transactions; and (ii) up to 2,079,224 shares of common stock issuable upon the exercise of pre-funded warrants that were originally issued by Zymeworks BC and assumed by us in connection with the Redomicile Transactions.

The base prospectus immediately follows this explanatory note. The specific terms of any securities to be offered pursuant to the base prospectus will be specified in one or more prospectus supplements to the base prospectus. The sales agreement prospectus supplement immediately follows the base prospectus, and the prospectus for the shares issuable upon the outstanding Exchangeable Shares and pre-funded warrants immediately follows the sales agreement prospectus supplement. The \$150.0 million of common stock that may be offered, issued and sold under the sales agreement prospectus supplement is included in the \$500.0 million of securities that may be offered, issued and sold by us under the base prospectus. If the sales agreement with Cantor is terminated, any portion of the \$150.0 million of common stock included in the sales agreement prospectus supplement that is not sold pursuant to the sales agreement will become available for sale in other offerings pursuant to the base prospectus and a corresponding prospectus supplement, and if no shares are sold under the sales agreement, the full \$150.0 million of securities may be sold in other offerings pursuant to the base prospectus and a corresponding prospectus supplement.

PROSPECTUS



Zymeworks Inc.

\$500,000,000

Common Stock

Preferred Stock Purchase Rights

Preferred Stock

Debt Securities

Depository Shares

Warrants

Subscription Rights

Purchase Contracts

Units

We may issue securities from time to time in one or more offerings, in amounts, at prices and on terms determined at the time of offering. This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus, which will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this prospectus. You should read this prospectus and any applicable prospectus supplement before you invest. The aggregate offering price of the securities we sell pursuant to this prospectus will not exceed \$500.0 million.

The securities may be sold directly to you, through agents or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement. The price to the public of those securities and the net proceeds we expect to receive from that sale will also be set forth in a prospectus supplement.

Our common stock (together with the associated preferred stock purchase rights) is listed on the Nasdaq Global Select Market under the symbol "ZYME." Each prospectus supplement will indicate whether the securities offered thereby will be listed on any securities exchange.

Investing in our securities involves risks. Please carefully read the information under the headings "[Risk Factors](#)" beginning on page 3 of this prospectus and "Item 1A – Risk Factors" of our most recent report on Form 10-K or 10-Q that is incorporated by reference in this prospectus before you invest in our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is March 7, 2023.

TABLE OF CONTENTS

	<u>Page</u>
About this Prospectus	ii
Prospectus Summary	1
Risk Factors	3
Forward-Looking Statements	3
Use of Proceeds	3
Description of Capital Stock	3
Description of Debt Securities	4
Description of Depositary Shares	10
Description of Warrants	12
Description of Subscription Rights	13
Description of Purchase Contracts	14
Description of Units	15
Plan of Distribution	15
Legal Matters	17
Experts	17
Where You Can Find More Information	18
Incorporation by Reference	18

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the SEC using a “shelf” registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings for an aggregate offering price up to \$500.0 million.

This prospectus provides you with a general description of the securities that may be offered. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. Before you invest in our securities, you should read both this prospectus and any applicable prospectus supplement together with the additional information described in the sections titled “Where You Can Find More Information” and “Incorporation by Reference.”

We have not authorized anyone to provide you with information that is different from that contained, or incorporated by reference, in this prospectus, any applicable prospectus supplement or in any related free writing prospectus. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus and any applicable prospectus supplement or any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the applicable prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

PROSPECTUS SUMMARY

This summary highlights selected information that is presented in greater detail elsewhere, or incorporated by reference, in this prospectus. It does not contain all of the information that may be important to you and your investment decision. Before investing in our securities, you should carefully read this entire prospectus, including the matters set forth in the section titled “Risk Factors” and the financial statements and related notes and other information that we incorporate by reference herein, including our Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q. Unless the context indicates otherwise, references in this prospectus to “Zymeworks,” “we,” “our” and “us” refer, collectively, to Zymeworks Inc., a Delaware corporation, and its subsidiaries taken as a whole.

Company Overview

Zymeworks is a biotechnology company committed to the discovery, development, and commercialization of novel, multifunctional biotherapeutics. Zymeworks’ mission is to make a meaningful difference for people impacted by difficult-to-treat cancers and other serious diseases. Zymeworks’ complementary therapeutic platforms and fully integrated drug development engine provide the flexibility and compatibility to precisely engineer and develop highly differentiated antibody-based therapeutic candidates.

Corporate Information

Effective October 13, 2022, we became a Delaware corporation, following receipt of necessary shareholder, stock exchange, and court approvals (which we refer to as the Redomicile Transactions). Zymeworks Inc. was incorporated under the laws of the State of Delaware in June 2022. Our principal executive offices are located at 108 Patriot Drive, Suite A, Middletown, Delaware 19709, and our telephone number is (302) 274-8744. Our predecessor, now named Zymeworks BC Inc., was originally incorporated on September 8, 2003 under the Canada Business Corporations Act under the name “Zymeworks Inc.” On October 22, 2003, our predecessor was registered as an extra-provincial company under the Company Act (British Columbia), the predecessor to the Business Corporations Act (British Columbia), or the BCBCA. Our predecessor continued to British Columbia under the BCBCA on May 2, 2017. Our corporate website address is www.zymeworks.com.

The Securities That May Be Offered

We may offer or sell common stock (together with the associated preferred stock purchase rights), preferred stock, depositary shares, debt securities, warrants, subscription rights, purchase contracts and units in one or more offerings and in any combination. The aggregate offering price of the securities we sell pursuant to this prospectus will not exceed \$500.0 million. Each time securities are offered with this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and terms of the securities being offered and the net proceeds we expect to receive from that sale.

The securities may be sold to or through underwriters, dealers or agents or directly to purchasers or as otherwise set forth in the section titled “Plan of Distribution.” Each prospectus supplement will set forth the names of any underwriters, dealers, agents or other entities involved in the sale of securities described in that prospectus supplement and any applicable fee, commission or discount arrangements with them.

Common Stock

We may offer shares of our common stock, par value \$0.00001 per share, either alone or underlying other registered securities convertible into our common stock. Holders of our common stock are entitled to receive dividends declared by our board of directors out of funds legally available for the payment of dividends, subject to rights, if any, of preferred stockholders. We have not paid dividends in the past and have no current plans to pay dividends. Each holder of common stock is entitled to one vote per share. The holders of common stock have no preemptive rights.

Each share of common stock includes an associated right to purchase one one-thousandth of a share of our Series B Participating Preferred Stock, par value \$0.00001 per share. Until the occurrence of certain prescribed events, the preferred stock purchase rights are not exercisable and may be transferred only with our common stock. No separate consideration is payable for the preferred stock purchase rights. See the section titled “Description of Capital Stock.”

Preferred Stock

Our board of directors has the authority, subject to limitations prescribed by Delaware law, to issue preferred stock in one or more series, to establish from time to time the number of shares to be included in each series, and to fix the designation, powers, preferences and rights of the shares of each series and any of its qualifications, limitations or restrictions, in each case without further vote or action by our stockholders. Each series of preferred stock offered by us will be more fully described in the particular prospectus supplement that will accompany this prospectus, including redemption provisions, rights in the event of our liquidation, dissolution or winding up, voting rights and rights to convert into common stock.

Depository Shares

We may offer depository shares evidenced by depository receipts, with each depository share representing a fractional interest in a share of a particular series of preferred stock issued and deposited with a depository to be designated by us.

Each series of depository shares or depository receipts offered by us will be more fully described in the particular prospectus supplement that will accompany this prospectus, including redemption provisions, rights in the event of our liquidation, dissolution or winding up, voting rights and rights to convert into common stock.

Debt Securities

We may offer secured or unsecured obligations in the form of one or more series of senior or subordinated debt. The senior debt securities and the subordinated debt securities are together referred to in this prospectus as the “debt securities.” The subordinated debt securities generally will be entitled to payment only after payment of our senior debt. Senior debt generally includes all debt for money borrowed by us, except debt that is stated in the instrument governing the terms of that debt to be not senior to, or to have the same rank in right of payment as, or to be expressly junior to, the subordinated debt securities. We may offer debt securities that are convertible into shares of our common stock.

The debt securities will be issued under an indenture between us and a trustee to be identified in an accompanying prospectus supplement. We have summarized the general features of the debt securities to be governed by the indenture in this prospectus and the form of indenture has been filed as an exhibit to the registration statement of which this prospectus forms a part. We encourage you to read the indenture.

Warrants

We may offer warrants for the purchase of common stock, preferred stock or debt securities. We may offer warrants independently or together with other securities.

Subscription Rights

We may offer subscription rights to purchase our common stock, preferred stock, debt securities, depository shares, warrants or units consisting of some or all of these securities. These subscription rights may be offered independently or together with any other security offered hereby and may or may not be transferable by the stockholder receiving the subscription rights in such offering.

Purchase Contracts

We may offer purchase contracts, including contracts obligating holders or us to purchase from the other a specific or variable number of securities at a future date or dates.

Units

We may offer units comprised of one or more of the other classes of securities described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit.

RISK FACTORS

An investment in our securities involves a high degree of risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific risk factors discussed in the section of the applicable prospectus supplement titled “Risk Factors,” together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under “Part I—Item 1A—Risk Factors” of our most recent Annual Report on Form 10-K and in “Part II—Item 1A—Risk Factors” of our most recent Quarterly Report on Form 10-Q filed subsequent to such Form 10-K that are incorporated herein by reference, as may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations. Our Risk Factors are not guarantees that no such conditions exist as of the date of this report and should not be interpreted as an affirmative statement that such risks or conditions have not materialized, in whole or in part.

FORWARD-LOOKING STATEMENTS

This prospectus, each prospectus supplement and the information incorporated by reference in this prospectus and each prospectus supplement contain certain statements that constitute “forward-looking statements” within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. The words “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect,” “could,” “would,” “project,” “plan,” “potentially,” “likely,” and similar expressions and variations thereof are intended to identify forward-looking statements, but are not the exclusive means of identifying such statements. Those statements appear in this prospectus, any accompanying prospectus supplement and the documents incorporated herein and therein by reference, particularly in the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and include statements regarding the intent, belief or current expectations of our management that are subject to known and unknown risks, uncertainties and assumptions. You are cautioned that any such forward-looking statements are not guarantees of future performance and involve risks and uncertainties, and that actual results may differ materially from those projected in the forward-looking statements as a result of various factors.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely upon forward-looking statements as predictions of future events. The events and circumstances reflected in the forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, including the securities laws of the United States and the rules and regulations of the SEC, we do not plan to publicly update or revise any forward-looking statements contained herein after we distribute this prospectus, whether as a result of any new information, future events or otherwise.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

This prospectus and the documents incorporated by reference in this prospectus may contain market data that we obtain from industry sources. These sources do not guarantee the accuracy or completeness of the information. Although we believe that our industry sources are reliable, we do not independently verify the information. The market data may include projections that are based on a number of other projections. While we believe these assumptions to be reasonable and sound as of the date of this prospectus, actual results may differ from the projections.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds to us from the sale of our securities under this prospectus. Specific information about the use of proceeds from the specific issuance of any securities will be set forth in the applicable prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

The description of our capital stock, including our common stock, the preferred stock purchase rights associated with our common stock, and our preferred stock, is incorporated by reference to [Exhibit 99.1](#) to our Current Report on Form 8-K12B filed with the SEC on October 13, 2022 and in our Registration Statement on [Form 8-A](#) relating thereto, filed with the SEC on December 15, 2022.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may offer debt securities either separately or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a trustee to be identified in an accompanying prospectus supplement. We have summarized select portions of the indenture below. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement of which this prospectus forms a part and you should read the indenture for provisions that may be important to you. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture. Unless the context requires otherwise, whenever we refer to an indenture, we also are referring to any supplemental indentures or forms of debt securities that specify the terms of a particular series of debt securities.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer's certificate or by a supplemental indenture. The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered the aggregate principal amount and the following terms of the debt securities, if applicable:

- the title and ranking of the debt securities (including the terms of any subordination provisions);
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities, including the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion will be determined;
- any limit upon the aggregate principal amount of the debt securities;
- the date or dates on which the principal of the securities of the series is payable;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the right, if any, to defer payments of interest and the maximum length of such deferral period;
- the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;
- the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities, in whole or in part, at our option, and the manner in which any election by us to redeem the debt securities will be evidenced;
- any obligation we have to repurchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and the terms and conditions upon which securities of the series shall be repurchased, in whole or in part, pursuant to such obligation;

Table of Contents

- the provisions, if any, relating to conversion or exchange of any debt securities of such series, including if applicable, the conversion or exchange price, the conversion or exchange period, provisions as to whether conversion or exchange will be mandatory, at the option of the holders thereof or at our option, the events requiring an adjustment of the conversion price or exchange price and provisions affecting conversion or exchange if such series of debt securities are redeemed;
- the denominations in which the debt securities will be issued, if other than denominations of \$1,000, and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities (including the terms pertaining to the exchange of any such securities);
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made and, if other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- the manner in which the amounts of payment of principal or premium or interest, if any, on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;
- any provisions relating to any security provided for the debt securities;
- any addition to, deletion of, or change in the covenants or Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;
- if there is more than one trustee or a different trustee, the identity of the trustee and, if not the trustee, the identity of each security registrar, paying agent or authenticating agent with respect to such debt securities;
- any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and
- whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees.

We may offer debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of a clearing agency registered under the Exchange Act, which we refer to as the depositary, or a nominee of the depositary (we will refer to any debt security represented by a global debt security as a “book-entry debt security”), or a certificate issued in definitive

Table of Contents

registered form (we will refer to any debt security represented by a certificated security as a “certificated debt security”) as set forth in the applicable prospectus supplement. Except as set forth in the section titled “—Global Debt Securities and Book-Entry System,” book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities

You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange.

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

Global Debt Securities and Book-Entry System

Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the depository, and registered in the name of the depository or a nominee of the depository.

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue or series of debt securities.

No Protection in the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may provide holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person, which we refer to as a successor person, unless:

- we are the surviving corporation or the successor person (if other than us) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture; and
- immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us.

Events of Default

“Event of Default” means with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);
- default in the payment of principal of any security of that series at its maturity;
- default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee, or we and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;

Table of Contents

- certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of us; and
- any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement.

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

We will provide the trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action we are taking or propose to take in respect thereof.

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing (except an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, as described herein), then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

The indenture will provide that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in performing such duty or exercising such right or power. Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series.

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and
- the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days.

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment.

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. If a Default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall send to each securityholder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has

knowledge of such Default or Event of Default. The indenture will provide that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities.

Modification and Waiver

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

- to cure any ambiguity, defect or inconsistency;
- to comply with covenants in the indenture described in the section titled “—Consolidation, Merger and Sale of Assets”;
- to provide for uncertificated securities in addition to or in place of certificated securities;
- to add guarantees with respect to debt securities of any series or secure debt securities of any series;
- to surrender any of our rights or powers under the indenture;
- to add covenants or events of default for the benefit of the holders of debt securities of any series;
- to comply with the applicable procedures of the applicable depositary;
- to make any change that does not adversely affect the rights of any holder of debt securities;
- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;
- to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act.

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

- reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a default in the payment of the principal of, premium or interest on any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);
- make the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security;

- make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, premium and interest on those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or
- waive a redemption payment with respect to any debt security.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance

The indenture will provide that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the irrevocable deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money or U.S. government obligations in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred.

Defeasance of Certain Covenants

The indenture will provide that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

- we may omit to comply with the covenant described in the section titled “—Consolidation, Merger and Sale of Assets” and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and
- any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series.

We refer to this as covenant defeasance. The conditions include:

- depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities;
- such deposit will not result in a breach or violation of, or constitute a default under the indenture or any other agreement to which we are a party;

- no Default or Event of Default with respect to the applicable series of debt securities shall have occurred or is continuing on the date of such deposit; and
- delivering to the trustee an opinion of counsel to the effect that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred.

No Personal Liability of Directors, Officers, Employees or Stockholders

None of our past, present or future directors, officers, employees or stockholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York.

The indenture will provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture will provide that any legal suit, action or proceeding arising out of or based upon the indenture or the transactions contemplated thereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities (by their acceptance of the debt securities) irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture will further provide that service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party's address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture will further provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum.

DESCRIPTION OF DEPOSITARY SHARES

General

We may offer depositary shares representing a fractional interest in a share of a particular series of preferred stock. Unless otherwise provided in the prospectus supplement, each owner of a depositary share will be entitled, in proportion to the applicable fractional interest in a share of preferred stock represented by the depositary share, to all the rights and preferences of the preferred stock represented by the depositary share. Those rights include dividend, voting, redemption, conversion and liquidation rights.

The shares of preferred stock underlying the depositary shares will be deposited with a bank or trust company selected by us to act as depositary under a deposit agreement between us, the depositary and the holders of the depositary receipts. The depositary will be the transfer agent, registrar and dividend disbursing agent for the depositary shares.

The depositary shares will be evidenced by depositary receipts issued pursuant to the deposit agreement. Holders of depositary receipts agree to be bound by the deposit agreement, which requires holders to take certain actions such as filing proof of residence and paying certain charges.

[Table of Contents](#)

The summary of terms of the depositary shares contained in this prospectus is not complete. You should refer to the form of the deposit agreement, our certificate of incorporation and the certificate of designation for the applicable series of preferred stock that are, or will be, filed with the SEC.

Dividends and Other Distributions

The depositary will distribute all cash dividends or other cash distributions, if any, received in respect of the preferred stock underlying the depositary shares to the record holders of depositary shares in proportion to the numbers of depositary shares owned by those holders on the relevant record date. The relevant record date for depositary shares will be the same date as the record date for the underlying preferred stock.

If there is a distribution other than in cash, the depositary will distribute property (including securities) received by it to the record holders of depositary shares, unless the depositary determines that it is not feasible to make the distribution. If this occurs, the depositary may, with our approval, adopt another method for the distribution, including selling the property and distributing the net proceeds from the sale to the holders.

Liquidation Preference

If a series of preferred stock underlying the depositary shares has a liquidation preference, in the event of the voluntary or involuntary liquidation, dissolution or winding up of us, holders of depositary shares will be entitled to receive the fraction of the liquidation preference accorded each share of the applicable series of preferred stock, as set forth in the applicable prospectus supplement.

Withdrawal of Stock

Unless the related depositary shares have been previously called for redemption, upon surrender of the depositary receipts at the office of the depositary, the holder of the depositary shares will be entitled to delivery, at the office of the depositary to or upon his or her order, of the number of whole shares of the preferred stock and any money or other property represented by the depositary shares. If the depositary receipts delivered by the holder evidence a number of depositary shares in excess of the number of depositary shares representing the number of whole shares of preferred stock to be withdrawn, the depositary will deliver to the holder at the same time a new depositary receipt evidencing the excess number of depositary shares. In no event will the depositary deliver fractional shares of preferred stock upon surrender of depositary receipts. Holders of preferred stock thus withdrawn may not thereafter deposit those shares under the deposit agreement or receive depositary receipts evidencing depositary shares therefor.

Redemption of Depositary Shares

Whenever we redeem shares of preferred stock held by the depositary, the depositary will redeem as of the same redemption date the number of depositary shares representing shares of the preferred stock so redeemed, so long as we have paid in full to the depositary the redemption price of the preferred stock to be redeemed plus an amount equal to any accumulated and unpaid dividends on the preferred stock to the date fixed for redemption. The redemption price per depositary share will be equal to the redemption price and any other amounts per share payable on the preferred stock multiplied by the fraction of a share of preferred stock represented by one depositary share. If less than all the depositary shares are to be redeemed, the depositary shares to be redeemed will be selected by lot or pro rata or by any other equitable method as may be determined by the depositary.

After the date fixed for redemption, depositary shares called for redemption will no longer be deemed to be outstanding and all rights of the holders of depositary shares will cease, except the right to receive the monies payable upon redemption and any money or other property to which the holders of the depositary shares were entitled upon redemption upon surrender to the depositary of the depositary receipts evidencing the depositary shares.

Voting the Preferred Stock

Upon receipt of notice of any meeting at which the holders of the preferred stock are entitled to vote, the depositary will mail the information contained in the notice of meeting to the record holders of the depositary receipts relating to that preferred stock. The record date for the depositary receipts relating to the preferred stock will be the same date as the record date for the preferred stock. Each record holder of the depositary shares on the record date will be entitled to instruct the depositary as to the exercise of the voting rights pertaining to the number of shares of preferred stock represented by that holder's depositary shares. The depositary will endeavor, insofar as practicable, to vote the number of shares of preferred stock represented by the depositary shares in accordance with those instructions, and we will agree to take all action that may be deemed necessary by the depositary in order to enable the depositary to do so. The depositary will not vote any shares of preferred stock except to the extent that it receives specific instructions from the holders of depositary shares representing that number of shares of preferred stock.

Charges of the Depositary

We will pay all transfer and other taxes and governmental charges arising solely from the existence of the depositary arrangements. We will pay charges of the depositary in connection with the initial deposit of the preferred stock and any redemption of the preferred stock. Holders of depositary receipts will pay transfer, income and other taxes and governmental charges and such other charges (including those in connection with the receipt and distribution of dividends, the sale or exercise of rights, the withdrawal of the preferred stock and the transferring, splitting or grouping of depositary receipts) as are expressly provided in the deposit agreement to be for their accounts. If these charges have not been paid by the holders of depositary receipts, the depositary may refuse to transfer depositary shares, withhold dividends and distributions and sell the depositary shares evidenced by the depositary receipt.

Amendment and Termination of the Deposit Agreement

The form of depositary receipt evidencing the depositary shares and any provision of the deposit agreement may be amended by agreement between us and the depositary. However, any amendment that materially and adversely alters the rights of the holders of depositary shares, other than fee changes, will not be effective unless the amendment has been approved by the holders of a majority of the outstanding depositary shares. The deposit agreement may be terminated by the depositary or us only if:

- all outstanding depositary shares have been redeemed; or
- there has been a final distribution of the preferred stock in connection with our dissolution and such distribution has been made to all the holders of depositary shares.

Resignation and Removal of Depositary

The depositary may resign at any time by delivering to us notice of its election to do so, and we may remove the depositary at any time. Any resignation or removal of the depositary will take effect upon our appointment of a successor depositary and its acceptance of such appointment. The successor depositary must be appointed within 60 days after delivery of the notice of resignation or removal and must be a bank or trust company having its principal office in the United States and having the requisite combined capital and surplus as set forth in the applicable agreement.

Notices

The depositary will forward to holders of depositary receipts all notices, reports and other communications, including proxy solicitation materials received from us, that are delivered to the depositary and that we are required to furnish to the holders of the preferred stock. In addition, the depositary will make available for inspection by holders of depositary receipts at the principal office of the depositary, and at such other places as it may from time to time deem advisable, any reports and communications we deliver to the depositary as the holder of preferred stock.

Limitation of Liability

Neither we nor the depositary will be liable if either is prevented or delayed by law or any circumstance beyond its control in performing its obligations. Our obligations and those of the depositary will be limited to performance in good faith of our and its duties thereunder. We and the depositary will not be obligated to prosecute or defend any legal proceeding in respect of any depositary shares or preferred stock unless satisfactory indemnity is furnished. We and the depositary may rely upon written advice of counsel or accountants, on information provided by persons presenting preferred stock for deposit, holders of depositary receipts or other persons believed to be competent to give such information and on documents believed to be genuine and to have been signed or presented by the proper party or parties.

DESCRIPTION OF WARRANTS

We may offer warrants to purchase debt securities, preferred stock, depositary shares or common stock. We may offer warrants separately or together with one or more additional warrants, debt securities, preferred stock, depositary shares or common stock, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. If we issue warrants as part of a unit, the applicable prospectus supplement will specify whether those warrants may be separated from the other securities in the unit prior to the expiration date of the warrants. The applicable prospectus supplement will also describe the following terms of any warrants:

Table of Contents

- the specific designation and aggregate number of, and the offering price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants are to be sold separately or with other securities as parts of units;
- whether the warrants will be issued in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- the designation and terms of any equity securities purchasable upon exercise of the warrants;
- the designation, aggregate principal amount, currency and terms of any debt securities that may be purchased upon exercise of the warrants;
- if applicable, the designation and terms of the debt securities, preferred stock, depositary shares or common stock with which the warrants are issued and the number of warrants issued with each security;
- if applicable, the date from and after which any warrants issued as part of a unit and the related debt securities, preferred stock, depositary shares or common stock will be separately transferable;
- the number of shares of preferred stock, the number of depositary shares or the number of shares of common stock purchasable upon exercise of a warrant and the price at which those shares may be purchased;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the antidilution provisions, and other provisions for changes to or adjustment in the exercise price, of the warrants, if any;
- any redemption or call provisions; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange or exercise of the warrants.

DESCRIPTION OF SUBSCRIPTION RIGHTS

We may offer subscription rights to purchase our common stock, preferred stock, debt securities, depositary shares, warrants or units consisting of some or all of these securities. These subscription rights may be offered independently or together with any other security offered hereby and may or may not be transferable by the stockholder receiving the subscription rights in such offering. In connection with any offering of subscription rights, we may enter into a standby arrangement with one or more underwriters or other purchasers pursuant to which the underwriters or other purchasers may be required to purchase any securities remaining unsubscribed for after such offering.

The prospectus supplement relating to any subscription rights we offer, if any, will, to the extent applicable, include specific terms relating to the offering, including some or all of the following:

- the price, if any, for the subscription rights;

- the exercise price payable for our common stock, preferred stock, debt securities, depositary shares, warrants or units consisting of some or all of these securities upon the exercise of the subscription rights;
- the number of subscription rights to be issued to each stockholder;
- the number and terms of our common stock, preferred stock, debt securities, depositary shares, warrants or units consisting of some or all of these securities which may be purchased per each subscription right;
- the extent to which the subscription rights are transferable;
- any other terms of the subscription rights, including the terms, procedures and limitations relating to the exchange and exercise of the subscription rights;
- the date on which the right to exercise the subscription rights shall commence, and the date on which the subscription rights shall expire;
- the extent to which the subscription rights may include an over-subscription privilege with respect to unsubscribed securities or an over-allotment privilege to the extent the securities are fully subscribed; and
- if applicable, the material terms of any standby underwriting or purchase arrangement which may be entered into by us in connection with the offering of subscription rights.

The descriptions of the subscription rights in this prospectus and in any prospectus supplement are summaries of the material provisions of the applicable subscription right agreements. These descriptions do not restate those subscription right agreements in their entirety and may not contain all the information that you may find useful. We urge you to read the applicable subscription right agreements because they, and not the summaries, define your rights as holders of the subscription rights. For more information, please review the forms of the relevant subscription right agreements, which will be filed with the SEC promptly after the offering of subscription rights and will be available as described in the section titled “Where You Can Find More Information.”

DESCRIPTION OF PURCHASE CONTRACTS

The following description summarizes the general features of the purchase contracts that we may offer under this prospectus. Although the features we have summarized below will generally apply to any future purchase contracts we may offer under this prospectus, we will describe the particular terms of any purchase contracts that we may offer in more detail in the applicable prospectus supplement. The specific terms of any purchase contracts may differ from the description provided below as a result of negotiations with third parties in connection with the issuance of those purchase contracts, as well as for other reasons. Because the terms of any purchase contracts we offer under a prospectus supplement may differ from the terms we describe below, you should rely solely on information in the applicable prospectus supplement if that summary is different from the summary in this prospectus.

We will incorporate by reference into the registration statement of which this prospectus is a part the form of any purchase contract that we may offer under this prospectus before the sale of the related purchase contract. We urge you to read any applicable prospectus supplement related to specific purchase contracts being offered, as well as the complete instruments that contain the terms of the securities that are subject to those purchase contracts. Certain of those instruments, or forms of those instruments, have been filed as exhibits to the registration statement of which this prospectus is a part, and supplements to those instruments or forms may be incorporated by reference into the registration statement of which this prospectus is a part from reports we file with the SEC.

We may offer purchase contracts, including contracts obligating holders to purchase from us, and for us to sell to holders, a specific or variable number of our securities at a future date or dates. Alternatively, the purchase contracts may obligate us to purchase from holders, and obligate holders to sell to us, a specific or varying number of our securities.

If we offer any purchase contracts, certain terms of that series of purchase contracts will be described in the applicable prospectus supplement, including, without limitation, the following:

- the price of the securities or other property subject to the purchase contracts (which may be determined by reference to a specific formula described in the purchase contracts);

Table of Contents

- whether the purchase contracts are issued separately, or as a part of units each consisting of a purchase contract and one or more of our other securities, including U.S. Treasury securities, securing the holder's obligations under the purchase contract;
- any requirement for us to make periodic payments to holders or vice versa, and whether the payments are unsecured or pre-funded;
- any provisions relating to any security provided for the purchase contracts;
- whether the purchase contracts obligate the holder or us to purchase or sell, or both purchase and sell, the securities subject to purchase under the purchase contract, and the nature and amount of each of those securities, or the method of determining those amounts;
- whether the purchase contracts are to be prepaid or not;
- whether the purchase contracts are to be settled by delivery, or by reference or linkage to the value, performance or level of the securities subject to purchase under the purchase contract;
- any acceleration, cancellation, termination or other provisions relating to the settlement of the purchase contracts;
- a discussion of certain U.S. federal income tax considerations applicable to the purchase contracts;
- whether the purchase contracts will be issued in fully registered or global form; and
- any other terms of the purchase contracts and any securities subject to such purchase contracts.

DESCRIPTION OF UNITS

We may offer units comprising two or more securities described in this prospectus in any combination. For example, we might issue units consisting of a combination of debt securities and warrants to purchase common stock. The following description sets forth certain general terms and provisions of the units that we may offer pursuant to this prospectus. The particular terms of the units and the extent, if any, to which the general terms and provisions may apply to the units so offered will be described in the applicable prospectus supplement.

Each unit will be issued so that the holder of the unit also is the holder of each security included in the unit. Thus, the unit will have the rights and obligations of a holder of each included security. Units will be issued pursuant to the terms of a unit agreement, which may provide that the securities included in the unit may not be held or transferred separately at any time or at any time before a specified date. A copy of the forms of the unit agreement and the unit certificate relating to any particular issue of units will be filed with the SEC each time we issue units, and you should read those documents for provisions that may be important to you. For more information on how you can obtain copies of the forms of the unit agreement and the related unit certificate, see the section titled "Where You Can Find More Information."

The prospectus supplement relating to any particular issuance of units will describe the terms of those units, including, to the extent applicable, the following:

- the designation and terms of the units and the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provision for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- whether the units will be issued in fully registered or global form.

PLAN OF DISTRIBUTION

We may sell securities:

- through underwriters;
- through dealers;

Table of Contents

- through agents;
- directly to purchasers; or
- through a combination of any of these methods of sale.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing securityholders.

We may directly solicit offers to purchase securities or agents may be designated to solicit such offers. We will, in the prospectus supplement relating to such offering, name any agent that could be viewed as an underwriter under the Securities Act and describe any commissions that we must pay. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price or prices that may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- the public offering or purchase price;
- if applicable, the names of any selling securityholders;
- any discounts and commissions to be allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are utilized in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

If a dealer is utilized in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing securityholders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Agents, underwriters, dealers and other persons may be entitled under agreements that they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery.

The underwriters and other persons acting as agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, and/or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may over-allot in connection with the offering, creating a short position for their own accounts. In addition, to cover over-allotments or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the third business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than three scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Additional legal matters may be passed on for us, or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of Zymeworks as of December 31, 2021 and 2020, and for each of the years in the three-year period ended December 31, 2021, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2021, have been incorporated by reference herein in reliance upon the reports of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.zymeworks.com. Information accessible on or through our website is not a part of this prospectus.

This prospectus and any prospectus supplement is part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. You should review the information and exhibits in the registration statement for further information on us and our consolidated subsidiaries and the securities that we are offering. Forms of any indenture or other documents establishing the terms of the offered securities are filed as exhibits to the registration statement of which this prospectus forms a part or under cover of a Current Report on Form 8-K and incorporated in this prospectus by reference. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should read the actual documents for a more complete description of the relevant matters.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information that we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated by reference in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents furnished pursuant to Items 2.02 or 7.01 of any Current Report on Form 8-K and, except as may be noted in any such Form 8-K, exhibits filed on such form that are related to such information), until the offering of the securities under the registration statement of which this prospectus forms a part is terminated or completed:

- Zymeworks BC's [Annual Report on Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on February 24, 2022;
- Zymeworks BC's [Amendment No. 1 to Annual Report on Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on May 2, 2022;
- Zymeworks BC's Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2022 and June 30, 2022, filed with the SEC on [May 4, 2022](#) and [August 4, 2022](#), respectively;
- our Quarterly Report on [Form 10-Q](#) for the quarterly period ended September 30, 2022, filed with the SEC on November 8, 2022;
- Zymeworks BC's Current Reports on Form 8-K filed with the SEC on [January 5, 2022](#); [January 19, 2022](#); [January 27, 2022](#); [January 31, 2022](#); [February 25, 2022](#); [March 9, 2022](#); [May 2, 2022](#) (Amendment No. 1 to Form 8-K originally filed with the SEC on January 19, 2022); [May 26, 2022](#); [June 10, 2022](#); [July 15, 2022](#); [August 5, 2022](#); [August 12, 2022](#); [August 19, 2022](#); [August 26, 2022](#); [September 2, 2022](#); [September 8, 2022](#); [September 22, 2022](#); [October 11, 2022](#); [October 12, 2022](#); [October 18, 2022](#); [October 19, 2022](#) and [October 21, 2022](#);
- our Current Reports on Form 8-K filed with the SEC on [October 13, 2022](#); [October 19, 2022](#); [October 21, 2022](#); [October 28, 2022](#); [November 9, 2022](#); [November 18, 2022](#); [November 29, 2022](#); [December 5, 2022](#); [December 9, 2022](#); [December 19, 2022](#); [December 19, 2022](#); [December 21, 2022](#); [December 30, 2022](#); [January 4, 2023](#); and [January 19, 2023](#);
- our Form 8-K12B, filed with the SEC on [October 13, 2022](#); and
- the description of our common stock and the preferred stock purchase rights associated with our common stock contained in the Registration Statement on [Form 8-A](#) relating thereto, filed with the SEC on December 15, 2022, including any amendment or report filed for the purpose of updating such description.

[Table of Contents](#)

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address and telephone number:

Zymeworks Inc.
108 Patriot Drive, Suite A
Middletown, Delaware 19709
Attn: Investor Relations
(302) 274-8744

PROSPECTUS SUPPLEMENT



Zymeworks Inc.

Up to \$150,000,000

Common Stock

We have previously entered into a sales agreement, or Sales Agreement, with Cantor Fitzgerald & Co., or Cantor, dated as of November 9, 2022, relating to the sale of shares of our common stock offered by this prospectus supplement and the accompanying base shelf prospectus. In accordance with the terms of the Sales Agreement, we may offer and sell shares of our common stock, par value \$0.00001 per share, having an aggregate offering price of up to \$150,000,000 pursuant to this prospectus supplement from time to time through Cantor, acting as our sales agent.

Our common stock is listed for trading on the Nasdaq Stock Market LLC, or Nasdaq, under the symbol “ZYME.” On March 6, 2023, the last reported sale price of our common stock on Nasdaq was \$7.95 per share.

Sales of our common stock, if any, under this prospectus may be made by any method permitted that are deemed “at the market offerings” as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, or the Securities Act. Cantor is not required to sell any specific amount of our common stock, but will act as our sales agent using commercially reasonable efforts, consistent with its normal trading and sales practices on mutually agreed terms between Cantor and us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Cantor will be entitled to compensation from us at a commission rate of up to 3.0% of the gross sales price of any shares of common stock sold through it under the Sales Agreement. In connection with the sale of common stock on our behalf, Cantor will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Cantor will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Cantor with respect to certain liabilities, including civil liabilities under the Securities Act and the Securities Exchange Act of 1934, as amended, or the Exchange Act. See “Plan of Distribution” beginning on page S-74 for additional information regarding the compensation to be paid to Cantor.

An investment in our securities involves a high degree of risk. Please read “[Risk Factors](#)” on page S-13 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement before investing in our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

CANTOR

The date of this prospectus supplement is March 7, 2023.

TABLE OF CONTENTS

Prospectus Supplement

ABOUT THIS PROSPECTUS SUPPLEMENT	S-1
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS	S-3
PROSPECTUS SUPPLEMENT SUMMARY	S-8
THE OFFERING	S-11
RISK FACTORS	S-13
USE OF PROCEEDS	S-71
DILUTION	S-72
PLAN OF DISTRIBUTION	S-74
LEGAL MATTERS	S-75
EXPERTS	S-75
WHERE YOU CAN FIND MORE INFORMATION	S-76
INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE	S-77

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and the securities offered hereby, and also adds to and updates information contained in the accompanying base shelf prospectus and the documents incorporated into each by reference. The second part, the accompanying base shelf prospectus, gives more general information and disclosure. This prospectus supplement is deemed to be incorporated by reference into the accompanying base shelf prospectus solely for the purpose of this offering. When we refer only to the “prospectus,” we are referring to both parts combined.

If there is any inconsistency between information in or incorporated by reference into the accompanying base shelf prospectus and information in or incorporated by reference into this prospectus supplement, you should rely only on the information contained in or incorporated by reference into this prospectus supplement. This prospectus supplement, the accompanying base shelf prospectus and the documents incorporated into each by reference include important information about us, the common stock being offered and other information you should know before investing. Before you invest in our common stock, you should read this prospectus supplement and the accompanying base shelf prospectus together with the additional information described in the sections titled “Where You Can Find More Information” and “Incorporation by Reference.”

Neither we nor Cantor have authorized anyone to provide any information or to make any representations other than those contained in this prospectus supplement and the accompanying base shelf prospectus, the documents incorporated by reference herein or therein or in any free writing prospectuses prepared by us or on our behalf or to which we have referred you. We are not, and Cantor is not, making an offer to sell these securities in any jurisdiction where the offer or sale thereof is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying base shelf prospectus and the documents incorporated into each by reference is accurate only as of the respective dates of the applicable documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

Market data and certain industry forecasts used in this prospectus supplement, the accompanying base shelf prospectus and the documents incorporated by reference herein or therein were obtained from market research, publicly available information and industry publications. We believe that these sources are generally reliable, but the accuracy and completeness of this information is not guaranteed. We have not independently verified such information, and we do not make any representation as to the accuracy of such information.

Unless otherwise indicated in this prospectus supplement and the accompanying base shelf prospectus, all dollar amounts and references to “\$” or “US\$” are to U.S. dollars and references to “C\$” are to Canadian dollars. This prospectus supplement, the accompanying base shelf prospectus and the documents incorporated by reference herein and therein contain translations of some Canadian dollar amounts into U.S. dollars solely for your convenience.

In this prospectus supplement, unless the context otherwise requires or otherwise expressly states, all references to “we,” “us,” “our” or similar terms, as well as references to “Zymeworks” or the “Company,” (i) for periods until the completion of the Redomicile Transactions (as defined below), refer to Zymeworks BC Inc. (formerly known as “Zymeworks Inc.”), or Zymeworks BC, either alone or together with its wholly owned subsidiaries, Zymeworks Biopharmaceuticals Inc., Zymeworks Pharmaceuticals Limited, Zymeworks Inc. (formerly known as Zymeworks Delaware Inc.), Zymeworks CallCo ULC, or CallCo, Zymeworks ExchangeCo Ltd., or ExchangeCo, and Zymeworks Management Inc. and (ii) for periods after the completion of the Redomicile Transactions, refer to Zymeworks Inc., either alone or together with its subsidiaries, including, as applicable, Zymeworks BC, Zymeworks Biopharmaceuticals Inc., Zymeworks Pharmaceuticals Limited, CallCo, ExchangeCo, Zymeworks Management Inc., Zymeworks Zanidatamab Inc., and Zymeworks Lifesciences Pte. Ltd. In the accompanying base shelf prospectus, unless the context otherwise requires, references to “we,” “us,” “our” or similar terms, as well as references to “Zymeworks” or the “Company,” refer to Zymeworks BC Inc., either alone or together with its wholly-owned subsidiary as of the date of the base shelf prospectus, Zymeworks Biopharmaceuticals Inc.

Furthermore, except as otherwise indicated, references to “Merck,” “BMS,” “GSK,” “Daiichi Sankyo,” “Janssen,” “LEO,” “BeiGene,” “Iconic,” “Pfizer,” “Atreca” and “Jazz” refer to Merck Sharp & Dohme Research GmbH, Celgene Corporation and Celgene Alpine Investment Co. LLC (now a Bristol-Myers Squibb company), GlaxoSmithKline Intellectual Property Development Limited, Daiichi Sankyo Co., Ltd., Janssen Biotech, Inc., LEO Pharma A/S, BeiGene Ltd., Iconic Therapeutics, Inc., Pfizer Inc., Atreca, Inc. and Jazz Pharmaceuticals Ireland Limited, respectively.

[Table of Contents](#)

We own or have rights to trademarks, service marks or trade names that we use in connection with the operation of our business. In addition, our names, logos and website names and addresses are our service marks or trademarks. Our registered trademarks include Azymetric, Zymeworks, ZymeCAD, EFECT, ZymeLink and the phrase “Building Better Biologics”. The other trademarks, trade names and service marks appearing in this prospectus supplement, the accompanying base shelf prospectus and documents incorporated by reference herein and therein are the property of their respective owners. Solely for convenience, the trademarks, service marks, tradenames and copyrights referred to in this prospectus supplement are listed without the ©, ® and TM symbols, but we will assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensors to these trademarks, service marks and tradenames.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying base shelf prospectus, including the documents incorporated by reference herein or therein, contain “forward-looking statements” or information within the meaning of applicable securities legislation, including Section 27A of the Securities Act, and Section 21E of the Exchange Act. Forward-looking statements include statements that may relate to our plans, objectives, goals, strategies, future events, future revenue or performance, capital expenditures, financing needs and other information that is not historical information. Forward-looking statements can often be identified by the use of terminology such as “subject to,” “believe,” “anticipate,” “plan,” “expect,” “intend,” “estimate,” “project,” “may,” “will,” “should,” “would,” “could,” “can,” the negatives thereof, variations thereon and similar expressions, or by discussions of strategy. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. In particular, forward-looking statements in this prospectus supplement, the accompanying base shelf prospectus and the documents incorporated by reference herein and therein include, but are not limited to, statements about:

- the size of our addressable markets and our ability to commercialize product candidates;
- the achievement of advances in and expansion of our therapeutic platforms and antibody engineering expertise;
- the likelihood of product candidate development and clinical trial progression, initiation or success;
- our ability to predict and manage government regulation;
- the impact of the COVID-19 pandemic on our business and operations; and
- the expected benefits and other impacts of the Redomicile Transactions.

All forward-looking statements, including, without limitation, those related to our examination of historical operating trends, are based upon our current expectations and various assumptions. Certain assumptions made in preparing the forward-looking statements include:

- our ability to manage our growth effectively;
- the absence of material adverse changes in our industry or the global economy;
- our ability to understand and predict trends in our industry and markets;
- our ability to enter into and maintain good business relationships with strategic partners;
- our ability to comply with current and future regulatory standards;
- our ability to protect our intellectual property rights;
- our continued compliance with third-party license terms and the non-infringement of third-party intellectual property rights;
- our ability to manage and integrate any acquisitions we may pursue;
- our ability to retain key personnel; and
- our ability to raise sufficient debt or equity financing to support our continued growth.

We believe there is a reasonable basis for our expectations and beliefs, but they are inherently uncertain. We may not realize our expectations, and our beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements. The following uncertainties and factors, among others

Table of Contents

(including those referred to in the section titled “Risk Factors” in this prospectus supplement, the accompanying base shelf prospectus and in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2022), could affect future performance and cause actual results to differ materially from those matters expressed in or implied by forward-looking statements:

- our or our partners’ ability to obtain regulatory approval for product candidates without significant delays;
- the predictive value of our current or planned clinical trials;
- delays with respect to the development and commercialization of our product candidates, which may cause increased costs or delay receipt of product revenue;
- our or any of our partners’ ability to enroll subjects in clinical trials and thereby complete trials on a timely basis;
- the design or our execution of clinical trials may not support regulatory approval, including where clinical trials are conducted outside the United States;
- our ability to achieve milestones and receive associated milestone payments pursuant to the terms of our collaboration agreements, including the Jazz Collaboration Agreement (as defined below);
- the extent to which our business may be adversely affected by the COVID-19 pandemic;
- global economic and political conditions, including as a result of the Russian invasion of Ukraine, as well as social and political unrest in the locations where our clinical trials are held, and the related impact on our business and the markets generally;
- expected benefits of the Redomicile Transactions may not materialize as expected or at all;
- unanticipated tax consequences in connection with the Redomicile Transactions;
- the Fast Track and Breakthrough Therapy designations for any of our product candidates may not expedite regulatory review or approval;
- the U.S. Food and Drug Administration, or the FDA, may not accept data from trials we conduct outside the United States;
- disruptions at the FDA and other government agencies caused by funding shortages or global health concerns;
- our discretion to discontinue or reprioritize the development of any of our product candidates;
- the potential for our product candidates to have undesirable side effects;
- no regulatory agency has made a determination that any of our product candidates are safe or effective for use by the general public or for any indication;
- our ability to face significant competition, including biosimilar products;
- the likelihood of broad market acceptance of our product candidates;
- our ability to obtain Orphan Drug Designation or exclusivity for some or all of our product candidates;
- our ability to commercialize products outside of the United States;
- the outcome of reimbursement decisions by third-party payors relating to our products;

Table of Contents

- our expectations with respect to the market opportunities for any product that we or our strategic partners develop;
- our ability to pursue product candidates that may be profitable or have a high likelihood of success;
- our ability to use and expand our therapeutic platforms to build a pipeline of product candidates;
- our ability to meet the requirements of ongoing regulatory review;
- the threat of product liability lawsuits against us or any of our strategic partners;
- changes in product candidate manufacturing or formulation that may result in additional costs or delay;
- the potential disruption of our business and dilution of our shareholdings associated with acquisitions and joint ventures;
- the potential for foreign governments to impose strict price controls;
- the risk of security breaches or data loss, which could compromise sensitive business or health information;
- current and future legislation that may increase the difficulty and cost of commercializing our product candidates;
- economic, political, regulatory and other risks associated with international operations;
- our exposure to legal and reputational penalties as a result of any of our current and future relationships with various third parties;
- our ability to comply with export control and import laws and regulations;
- our history of significant losses since inception;
- our ability to generate revenue from product sales and achieve profitability;
- our requirement for substantial additional funding;
- the potential dilution to our stockholders associated with future financings;
- restrictions on our ability to seek financing, which may be imposed by future debt;
- unstable market and economic conditions;
- currency fluctuations and changes in foreign currency exchange rates;
- our ability to maintain existing and future strategic partnerships;
- our ability to realize the anticipated benefits of our strategic partnerships;
- our ability to secure future strategic partners;
- our reliance on third-party manufacturers to produce our product candidate supplies and on other third parties to store, monitor and transport bulk drug substance and drug product;
- risk related to the manufacture of product candidates and difficulties in production;
- our reliance on third parties to oversee clinical trials of our product candidates and, in some cases, maintain regulatory files for those product candidates;

Table of Contents

- our reliance on the performance of independent clinical investigators and contract research organizations, or CROs;
- our reliance on third parties for various operational and administrative aspects of our business including our reliance on third parties' cloud-based software platforms;
- our ability to operate without infringing the patents and other proprietary rights of third parties;
- our ability to obtain and enforce patent protection for our product candidates and related technology;
- our patents could be found invalid or unenforceable if challenged;
- our intellectual property rights may not necessarily provide us with competitive advantages;
- we may become involved in expensive and time-consuming patent lawsuits;
- the risk that the duration of our patents will not adequately protect our competitive position;
- our ability to obtain protection under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments, and similar foreign legislation;
- we may be unable to protect the confidentiality of our proprietary information;
- our ability to comply with procedural and administrative requirements relating to our patents;
- the risk of claims challenging the inventorship of our patents and other intellectual property;
- our intellectual property rights for some of our product candidates are dependent on the abilities of third parties to assert and defend such rights;
- patent reform legislation and court decisions can diminish the value of patents in general, thereby impairing our ability to protect our products;
- we may not be able to protect our intellectual property rights throughout the world;
- we will require FDA approval for any proposed product candidate names and any failure or delay associated with such approval may adversely affect our business;
- our election to rely on certain reduced reporting and disclosure requirements available to smaller reporting companies may make our common stock less attractive to investors;
- the risk of employee misconduct including noncompliance with regulatory standards and insider trading;
- our ability to market our products in a manner that does not violate the law and subject us to civil or criminal penalties;
- if we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected;
- our ability to retain key executives and attract and retain qualified personnel;
- our ability to manage organizational growth;
- our exposure to potential securities class action litigation; and
- if securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

[Table of Contents](#)

Consequently, forward-looking statements should be regarded solely as our current plans, estimates and beliefs. You should not place undue reliance on forward-looking statements. We cannot guarantee future results, events, levels of activity, performance or achievements. We do not undertake and specifically decline any obligation to update, republish or revise forward-looking statements to reflect future events or circumstances or to reflect the occurrences of unanticipated events, except as required by law. Our Risk Factors are not guarantees that no such conditions exist as of the date of this prospectus supplement and should not be interpreted as an affirmative statement that such risks or conditions have not materialized, in whole or in part.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus supplement, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights key aspects of this offering and certain information contained elsewhere in this prospectus supplement and the documents incorporated by reference. This summary is not complete and does not contain all of the information that may be important to you or that you should consider before investing in our common stock. You should read carefully the other information included and incorporated by reference in this prospectus supplement and the accompanying base shelf prospectus before investing in our common stock. You should pay special attention to the risks and uncertainties identified in the sections titled “Risk Factors” and “Cautionary Note Regarding Forward-Looking Statements” and elsewhere in this prospectus supplement, the accompanying base shelf prospectus and the documents incorporated by reference herein or therein, including our Quarterly Report on Form 10-Q for the three months ended September 30, 2022, when determining whether an investment in our common stock is appropriate for you.

Company Overview

Zymeworks is a biotechnology company committed to the discovery, development, and commercialization of novel, multifunctional biotherapeutics. Zymeworks’ mission is to make a meaningful difference for people impacted by difficult-to-treat cancers and other serious diseases. Zymeworks’ complementary therapeutic platforms and fully integrated drug development engine provide the flexibility and compatibility to precisely engineer and develop highly differentiated antibody-based therapeutic candidates.

Risk Factors Summary

Our business is subject to numerous risks and uncertainties, including those highlighted in the section of this prospectus supplement titled “Risk Factors.” The following is a summary of the principal risks we face:

- We have a limited number of product candidates, all which are still in preclinical or clinical development. If we do not obtain regulatory approval of one or more of our product candidates, or experience significant delays in doing so, our business will be materially adversely affected.
- Clinical trials are expensive, time consuming, difficult to design and implement, and involve uncertain outcomes. Furthermore, the results of previous preclinical studies and clinical trials may not be predictive of future results, and the results of our current and planned clinical trials may not satisfy the requirements of the FDA or comparable regulatory authorities outside the United States.
- Our long-term prospects depend in part upon discovering, developing and commercializing additional product candidates, which may fail in development or suffer delays that adversely affect their commercial viability.
- Our product candidates may have undesirable side effects that may delay or prevent marketing approval or, if approval is received, require them to be taken off the market, require them to include safety warnings or otherwise limit their sales; no regulatory agency has made any determination that any of our product candidates are safe or effective for use by the general public for any indication.
- We face significant competition, and if our competitors develop and market products that are more effective, safer or less expensive than our product candidates, our commercial opportunities will be negatively impacted.
- If any of our product candidates receive regulatory approval, the approved products may not achieve broad market acceptance among physicians, patients, the medical community and third-party payors, in which case revenue generated from their sales would be limited.
- We may not be successful in our efforts to use our therapeutic platforms to build a pipeline of product candidates.

- If any product liability lawsuits are successfully brought against us or any of our strategic partners, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.
- Security breaches and incidents, loss of data and other disruptions could compromise sensitive information related to our business or protected health information or prevent us from accessing critical information and expose us to liability, which could adversely affect our business and our reputation.
- Current and future legislation may increase the difficulty and cost for us to commercialize any products that we or our strategic partners develop and affect the prices we may obtain.
- We have incurred significant losses since inception and anticipate that we will continue to incur losses for the foreseeable future. We have no products approved for commercial sale, and to date we have not generated any revenue or profit from product sales. We may never achieve or sustain profitability.
- We will require substantial additional funding, which may not be available to us on acceptable terms, or at all, and, if not available, may require us to delay, scale back, or cease our product development programs or operations.
- We will depend on our collaborative relationship with Jazz to further develop and commercialize zanidatamab, and if our relationship is not successful or is terminated, we may be delayed in or unable to effectively develop and/or commercialize zanidatamab, which could have a material adverse effect on our business.
- Our existing strategic partnerships are important to our business, and future strategic partnerships will likely also be important to us. If we are unable to maintain our strategic partnerships, or if these strategic partnerships are not successful, our business could be adversely affected.
- We rely on third-party manufacturers to produce our product candidates and on other third parties to provide supplies and store, monitor and transport bulk drug substance and drug product. We and our third-party partners may encounter difficulties with respect to these activities that could delay or impair our ability to initiate or complete our clinical trials or commercialize approved products.
- We rely on third parties to monitor, support, conduct and oversee clinical trials of the product candidates that we are developing and, in some cases, to maintain regulatory files for those product candidates. We may not be able to obtain regulatory approval for our product candidates or commercialize any products that may result from our development efforts if we are not able to maintain or secure agreements with such third parties on acceptable terms, if these third parties do not perform their services as required, or if these third parties fail to timely transfer any regulatory information held by them to us.
- If we are unable to obtain, maintain and enforce patent and trade secret protection for our product candidates and related technology, our business could be materially harmed.
- If we are unable to protect the confidentiality of our proprietary information, the value of our technology and products could be adversely affected.
- Our effective tax rate may change in the future.
- Our stock price is likely to be volatile and the market price of our common stock may drop below the price paid by stockholders.
- Delaware law and provisions in our amended and restated certificate of incorporation and amended and restated bylaws might delay, discourage or prevent a change in control of Zymeworks or changes in our management, thereby depressing the market price of our common stock.

Company Information

Effective October 13, 2022, we became a Delaware corporation, following receipt of necessary shareholder, stock exchange, and court approvals (which we refer to as the Redomicile Transactions). Zymeworks Inc. was incorporated under the laws of the State of Delaware in June 2022. Our principal executive offices are located at 108 Patriot Drive, Suite A, Middletown, Delaware 19709, and our telephone number is (302) 274-8744. Our predecessor, now named Zymeworks BC Inc., was originally incorporated on September 8, 2003 under the Canada Business Corporations Act under the name “Zymeworks Inc.” On October 22, 2003, our predecessor was registered as an extra-provincial company under the Company Act (British Columbia), the predecessor to the Business Corporations Act (British Columbia), or the BCBCA. Our predecessor continued to British Columbia under the BCBCA on May 2, 2017. Our corporate website address is www.zymeworks.com. The references to www.zymeworks.com in this prospectus supplement, the accompanying base shelf prospectus and the documents incorporated by reference herein or therein are inactive textual references only, and the information found on our internet website is not incorporated by reference into, and should not be considered part of, this prospectus supplement, the accompanying base shelf prospectus or the documents incorporated by reference herein or therein. Investors should not rely on any such information in deciding whether to invest in our common stock. In addition, in response to the COVID-19 pandemic, we implemented and expect to continue implementing remote working arrangements. Our executive officers and directors are located in several jurisdictions, including the United States, Canada and the United Kingdom.

THE OFFERING

Common stock offered by us:	Shares of our common stock having an aggregate offering price of up to \$150,000,000.
Common stock to be outstanding following the offering:	Up to 81,927,425 shares of our common stock, based on 63,059,501 shares of common stock outstanding as of December 31, 2022 and assuming sales of 18,867,924 shares of our common stock in this offering at an offering price of \$7.95 per share, which was the last reported sale price of our common stock on Nasdaq on March 6, 2023. The actual number of shares issued will vary depending on the sale price under this offering.
Plan of Distribution:	“At-the-market offering” that may be made from time to time through our sales agent, Cantor. See “Plan of Distribution.”
Use of Proceeds:	We intend to use the net proceeds from the sale of our common stock pursuant to this offering, if any, together with our existing cash and cash equivalents, (i) to continue research and development relating to zanidatamab zovodotin and our other preclinical and discovery-stage programs and (ii) for general corporate purposes. See “Use of Proceeds” on page S-71.
Risk Factors:	Investing in our common stock involves risks. See “Risk Factors” beginning on page S-13 of this prospectus supplement and on page 3 of the accompanying base shelf prospectus, as well as those risks and uncertainties identified in the documents incorporated by reference herein or therein, including our Quarterly Report on Form 10-Q for the three months ended September 30, 2022.
Nasdaq symbol:	“ZYME”

The number of shares of our common stock to be outstanding after this offering is based on 63,059,501 shares of common stock outstanding as of December 31, 2022, and excludes:

- 1,374,601 shares of common stock issuable upon the exercise of fully-vested outstanding options to purchase shares of common stock, at a weighted average exercise price of C\$20.23 per share, and 2,553,862 shares of common stock issuable upon the exercise of fully-vested outstanding options to purchase shares of common stock, at a weighted average exercise price of \$20.86 per share, in each case as of December 31, 2022;
- 772,540 shares of common stock issuable upon the exercise of unvested outstanding options to purchase shares of common stock, at a weighted average exercise price of C\$16.86 per share, and 2,311,283 shares of common stock issuable upon the exercise of unvested outstanding options to purchase shares of common stock, at a weighted average exercise price of \$14.38 per share, in each case as of December 31, 2022;
- 700,000 shares of common stock issuable upon the exercise of unvested outstanding options to purchase shares of common stock, as of December 31, 2022, at a weighted average exercise price of \$12.36 per share;
- 227,223 shares of common stock issuable upon vesting of outstanding restricted stock units outstanding as of December 31, 2022;

- 3,205,132 shares of common stock reserved for future issuance under our stock option plan and 1,722,239 shares of common stock reserved for future issuance under our employee stock purchase plan, in each case as of December 31, 2022;
- 50,000 shares of common stock reserved for future issuance under our Inducement Stock Option and Equity Compensation Plan as of December 31, 2022;
- 1,424,533 shares of common stock issuable upon the exchange of the Exchangeable Shares as of December 31, 2022; and
- 2,079,224 shares of common stock issuable upon the exercise of pre-funded warrants as of December 31, 2022.

On October 12, 2022, we entered into a Preferred Stock Rights Agreement, or the Rights Agreement, with Computershare Trust Company, N.A., pursuant to which we declared a dividend for each share of common stock consisting of one right, or a Right, to purchase one one-thousandth of a share of our Series B Participating Preferred Stock, par value \$0.0001 per share, at an exercise price of \$74.00 per one one-thousandth of a share. Pursuant to the terms of the Rights Agreement, one Right will accompany any new share of common stock that is issued pursuant to this offering prior to the earlier of the Distribution Date (as defined in the Rights Agreement) and the termination of the Rights Agreement. For additional information, see our Form 8-K12B filed with the Securities and Exchange Commission on October 13, 2022.

RISK FACTORS

Investing in our common stock is speculative and involves a high degree of risk. The following risk factors, as well as risks currently unknown to us, could materially adversely affect our future business, operations and financial condition and could cause them to differ materially from the estimates described in forward-looking information relating to us, or our business, property or financial results, each of which could cause purchasers of our common stock to lose part or all of their investment. In addition to the other information contained in this prospectus supplement, the accompanying base shelf prospectus and the documents incorporated by reference herein and therein, prospective investors should carefully consider the factors described in the section titled “Risk Factors” in the accompanying base shelf prospectus and our Quarterly Report on Form 10-Q for the three months ended September 30, 2022 and the factors set out below in evaluating Zymeworks and its business before making an investment in our common stock. Our Risk Factors are not guarantees that no such conditions exist as of the date of this report and should not be interpreted as an affirmative statement that such risks or conditions have not materialized, in whole or in part.

Risks Related to Our Business and the Development and Commercialization of Our Product Candidates

We have a limited number of product candidates, all which are still in preclinical or clinical development. If we do not obtain regulatory approval of one or more of our product candidates, or experience significant delays in doing so, our business will be materially adversely affected.

We currently have no products approved for sale or marketing in any country, and may never be able to obtain regulatory approval for any of our product candidates. As a result, we are not currently permitted to market any of our product candidates in the United States or in any other country until we obtain regulatory approval from the FDA or comparable regulatory authorities outside the United States. Our product candidates are in preclinical or clinical development and we have not submitted an application, or received marketing approval, for any of our product candidates. Obtaining regulatory approval of our product candidates will depend on many factors, including:

- completing clinical trials that demonstrate the efficacy and safety of our product candidates;
- preparation and submission to the appropriate regulatory authorities of an application for marketing approval that includes substantial evidence of safety, purity and potency from results of nonclinical testing and clinical trials;
- establishing and maintaining adequate commercial manufacturing arrangements or establishing our own commercial manufacturing capabilities or reliable arrangements with third-party contract manufacturers;
- potential pre-approval audits of nonclinical sites, clinical trial sites, and third-party manufacturing sites that generated the data and product in support of the marketing application; and
- launching commercial sales, marketing and distribution operations.

Many of these factors are wholly or partially beyond our control, including clinical advancement, the regulatory submission process and changes in the competitive landscape. If we do not achieve one or more of these factors in a timely manner, we could experience significant delays or an inability to develop our product candidates at all.

Clinical trials are expensive, time consuming, difficult to design and implement, and involve uncertain outcomes. Furthermore, the results of previous preclinical studies and clinical trials may not be predictive of future results, and the results of our current and planned clinical trials may not satisfy the requirements of the FDA or comparable regulatory authorities outside the United States.

We have not previously submitted a Biologics License Application, or BLA, to the FDA or similar marketing applications to foreign health authorities. A BLA must include extensive preclinical and clinical data and supporting information to establish the product candidate’s safety, purity and efficacy for each desired indication. The BLA must also include significant information regarding the manufacturing controls for the product. The novel nature of our product candidates may introduce uncertain, complex, expensive and lengthy challenges that could impact regulatory approval. Even if we eventually complete clinical testing and receive approval of any regulatory filing for our product candidates, the FDA or foreign health authorities may approve our product candidates for a more limited indication or a narrower patient population than we originally requested.

There is typically an extremely high rate of attrition from the failure of product candidates proceeding through preclinical studies and clinical trials. Positive or timely results from preclinical or early-stage trials do not ensure positive or timely results in late-stage clinical trials or product approval by the FDA or comparable regulatory authorities outside the United States. We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective for use in a diverse population before we can seek regulatory approvals for their commercial sale. Our clinical trials may produce negative or inconclusive results, and we or any of our current and future strategic partners may decide, or regulators may require us, to conduct additional clinical or preclinical testing. In some instances, there can be significant variability in safety or efficacy results between different preclinical studies and clinical trials of the same product candidate due to numerous factors, including changes in clinical trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. Moreover, success in preclinical studies or early-stage clinical trials does not mean that future clinical trials or registrational clinical trials will be successful because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and comparable regulatory authorities outside the United States, despite having progressed through preclinical studies and initial clinical trials. Product candidates that have shown promising results in early clinical trials may suffer significant setbacks in subsequent clinical trials or registrational clinical trials. For example, a number of companies in the pharmaceutical industry have suffered significant setbacks in late-stage clinical trials, even after obtaining promising results in earlier-stage clinical trials. Similarly, interim results of a clinical trial do not necessarily predict final results.

There is a high failure rate for biopharmaceutical products proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development. For example, the FDA's Oncology Center of Excellence initiated Project Optimus to reform the dose optimization and dose selection paradigm in oncology drug development and Project FrontRunner to help develop and implement strategies to support approvals in the early clinical setting, among other goals. How the FDA plans to implement those goals and their impact on specific clinical programs and the industry are unclear.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the FDA or foreign health authorities may disagree with the design, implementation or data analyses of our clinical trials;
- the FDA or foreign health authorities may determine that our product candidate(s) do not have adequate risk-benefit ratio or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- the FDA or foreign health authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a BLA or other submission or to obtain regulatory approval in the United States or elsewhere;

Table of Contents

- the FDA or foreign health authorities may fail to approve the manufacturing processes, test procedures and specifications or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or foreign health authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Additionally, we have conducted, and may in the future conduct, clinical trials outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA and its determination that the trials also complied with all applicable U.S. laws and regulations. If the FDA does not accept the data from any clinical trials we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or halt our development of any future product candidates.

If clinical trials for our product candidates are prolonged, delayed or stopped, we may be unable to obtain regulatory approval and commercialize our product candidates on a timely basis, or at all, which would require us to incur additional costs and delay our receipt of any product revenue.

We are currently evaluating zanidatamab in Phase 1, Phase 2, and Phase 3 clinical trials, including certain ongoing pivotal clinical trials, and zanidatamab zovodotin in a Phase 1 clinical trial in patients with recurrent or metastatic HER2-expressing solid tumors. We may experience delays in our ongoing or future preclinical studies or clinical trials, and we do not know whether future preclinical studies or clinical trials will begin on time, need to be redesigned, enroll an adequate number of patients on time or be completed on schedule, if at all. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during clinical development, and, because our product candidates are in an early stage of development, there is a high risk of failure and we may never succeed in developing marketable products. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials, particularly because early trials have smaller numbers of subjects tested. In addition, it is not uncommon for product candidates to exhibit unforeseen safety or efficacy issues, such as immunogenicity, when tested in humans despite promising results in preclinical animal models.

Any clinical trials that we may conduct may not demonstrate the safety and efficacy profiles necessary to obtain regulatory approval to market our product candidates. As we continue developing our product candidates, serious adverse events, undesirable side effects, or unexpected characteristics may emerge, causing us to abandon these product candidates or limit their development to more narrow uses or subpopulations in which the risk-benefit ratio is more acceptable.

Patients treated with our product candidates may experience side effects or adverse events that are unrelated to our product candidates but may still impact the success of our clinical trials. The inclusion of patients with significant co-morbidities in our clinical trials may result in deaths or other adverse medical events due to an underlying condition or other therapies or medications that such patients may be using. Any of these events could prevent us from obtaining regulatory approval or achieving or maintaining market acceptance and impair our ability to commercialize our product candidates. In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to a variety of factors, including, but not limited to, changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants.

The commencement or completion of these planned clinical trials could be substantially delayed or prevented by many factors, including:

- further discussions with the FDA or other regulatory agencies regarding the scope or design of our clinical trials;
- the limited number of, and competition for, suitable sites to conduct our clinical trials, many of which may already be engaged in other clinical trial programs, including some that may be for the same indication as our product candidates;

Table of Contents

- any delay or failure to obtain approval or agreement to commence a clinical trial in any of the countries where enrollment is planned;
- inability to obtain sufficient funds required for a clinical trial;
- clinical holds on, or other regulatory objections to, a new or ongoing clinical trial;
- delay or failure to manufacture sufficient supplies of the product candidate for our clinical trials;
- delay or failure to reach agreement on acceptable clinical trial agreement terms or clinical trial protocols with prospective sites or contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different sites or CROs;
- delay or failure to obtain an institutional review board, or IRB, approval to conduct a clinical trial at a prospective site;
- slower than expected rates of patient recruitment and enrollment;
- failure of patients to complete the clinical trial;
- the inability to enroll a sufficient number of patients in studies to ensure adequate statistical power to detect statistically significant treatment effects;
- unforeseen safety issues, including severe or unexpected drug-related adverse effects experienced by patients, including possible deaths;
- lack of efficacy during clinical trials;
- termination of our clinical trials by one or more clinical trial sites;
- inability or unwillingness of patients or clinical investigators to follow our clinical trial protocols;
- inability to monitor patients adequately during or after treatment by us or our CROs;
- our CROs or clinical study sites failing to comply with the trial protocol or regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, deviating from the protocol or dropping out of a study;
- the inability to address any noncompliance with regulatory requirements or safety concerns that arise during the course of a clinical trial;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or foreign health authorities for violations of applicable regulatory requirements;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical trial sites, including due to a facility manufacturing any of our product candidates or any of their components being ordered by the FDA or foreign health authorities to temporarily or permanently shut down due to violations of current good manufacturing processes, or cGMP, regulations or other applicable requirements, or cross-contaminations of product candidates in the manufacturing process;
- the need to repeat or terminate clinical trials as a result of inconclusive or negative results or unforeseen complications in testing;
- our clinical trials may be suspended or terminated upon a breach or pursuant to the terms of any agreement with, or for any other reason by, current or future strategic partners that have responsibility for the clinical development of any of our product candidates; and
- receiving untimely or unfavorable feedback from applicable regulatory authorities regarding the trial or requests from regulatory authorities to modify the design of a trial.

We could also experience delays in physicians enrolling patients in clinical trials of our product candidates in lieu of prescribing existing treatments or other clinical trials. Furthermore, a clinical trial may be suspended or terminated by us, the IRBs for the institutions in which such trials are being conducted, the Data Monitoring Committee for such trial, or by the FDA or foreign health authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial

operations or trial site by the FDA or foreign health authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience termination of, or delays in the completion of, any clinical trial of our product candidates, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenue will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenue.

Securing regulatory approval also requires the submission of information about the manufacturing processes and inspection of manufacturing facilities by the relevant regulatory authority. The FDA or foreign health authorities may fail to approve our manufacturing processes or facilities, whether run by us or our contract manufacturing organizations. In addition, if we make manufacturing changes to our product candidates in the future, we may need to conduct additional preclinical and/or clinical studies to bridge our modified product candidates to earlier versions.

Changes in regulatory requirements, policies and guidelines may also occur and we may need to significantly amend clinical trial protocols to reflect these changes with appropriate regulatory authorities. These changes may require us to renegotiate terms with CROs or resubmit clinical trial protocols to IRBs for re-examination, which may impact the costs, timing or successful completion of a clinical trial. Our clinical trials may be suspended or terminated at any time by the FDA, other regulatory authorities, the IRB overseeing the clinical trial at issue, any of our clinical trial sites with respect to that site, or us.

Any failure or significant delay in commencing or completing clinical trials for our product candidates would adversely affect our ability to obtain regulatory approval, and our commercial prospects and ability to generate product revenue will be diminished.

In addition, even if the trials are successfully completed, clinical data are often susceptible to varying interpretations and analyses, and we cannot guarantee that the FDA or foreign health authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. We cannot guarantee that the FDA or foreign health authorities will view any of our product candidates as having adequate safety and efficacy profiles even if favorable results are observed in these clinical trials, and we may receive unexpected or unfavorable feedback from the FDA or foreign health authorities regarding satisfaction of safety, purity and potency (including clinical efficacy), amongst other factors. To the extent that the results of the trials are not satisfactory to the FDA or foreign health authorities for support of a marketing application, approval of our product candidates may be significantly delayed, or we may be required to expend significant additional resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates.

Our long-term prospects depend in part upon discovering, developing and commercializing additional product candidates, which may fail in development or suffer delays that adversely affect their commercial viability.

Our future operating results are dependent in part on our ability to successfully discover, develop, obtain regulatory approval for and commercialize product candidates beyond those we currently have in clinical development. A product candidate can unexpectedly fail at any stage of preclinical and clinical development. Our investments in our early-stage research and development efforts may not yield any promising product candidates. Even if our research and development efforts yield product candidates that advance into clinical studies, the historical failure rate for product candidates is high due to risks relating to safety, efficacy, clinical execution, changing standards of medical care and other unpredictable variables. The results from preclinical testing or early clinical trials of a product candidate may not be predictive of the results that will be obtained in later stage clinical trials of the product candidate.

The success of other product candidates we may develop will depend on many factors, including the following:

- generating sufficient data to support the initiation or continuation of clinical trials;
- obtaining regulatory permission to initiate clinical trials;
- contracting with the necessary parties to conduct clinical trials;

- successful enrollment of patients in, and the completion of, clinical trials on a timely basis;
- the timely manufacture of sufficient quantities of the product candidate for use in clinical trials; and
- adverse events in the clinical trials.

Even if we successfully advance any other product candidates into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in this “Risk Factors” section. Accordingly, we cannot assure you that we will ever be able to discover, develop, obtain regulatory approval of, commercialize or generate significant revenue from our other product candidates.

If we, or any of our partners, are unable to enroll patients in clinical trials, we will be unable to complete these trials on a timely basis or at all.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of subjects to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, ability to obtain and maintain patient consents, risk that enrolled subjects will drop out before completion, competing clinical trials and clinicians’ and patients’ perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. In particular, we are developing certain of our product candidates for the treatment of rare diseases, which have limited pools of patients from which to draw for clinical testing. If we, or any of our strategic partners that perform clinical tests for our product candidates, are unable to enroll a sufficient number of patients to complete clinical testing, we will be unable to gain marketing approval for such product candidates and our business will be harmed.

In addition, the U.S. federal Right to Try Act, among other things, provides a federal framework for patients to access certain investigational new drug products that have completed a Phase 1 clinical trial. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA approval under the FDA expanded access program. While there is no obligation to make product candidates available to eligible patients as a result of the Right to Try Act, new and emerging legislation regarding expanded access to unapproved drugs could negatively impact enrollment in our clinical trials and our business in the future.

The design or our execution of clinical trials may not support regulatory approval.

The design or execution of a clinical trial can determine whether its results will support regulatory approval, and flaws in the design or execution of a clinical trial may not become apparent until the clinical trial is well advanced. In some instances, there can be significant variability in safety or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We do not know whether any Phase 2, Phase 3 or other clinical trials we or any of our strategic partners may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates.

Further, the FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and in determining when or whether regulatory approval will be obtained for any of our product candidates. Our product candidates may not be approved even if they achieve their primary endpoints in any Phase 3 clinical trials or registration trials. The FDA or other non-U.S. regulatory authorities may disagree with our trial design and our interpretation of data from preclinical studies and clinical trials. In addition, any of these regulatory authorities may change requirements for the approval of a product candidate even after reviewing and providing comments or advice on a protocol for a pivotal Phase 3 clinical trial that has the potential to result in FDA or other agencies’ approval. In addition, any of these regulatory authorities may also approve a product candidate for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-marketing clinical trials. The FDA or other non-U.S. regulatory authorities may not approve the labeling claims that we believe would be necessary or desirable for the successful commercialization of our product candidates.

Interim, preliminary or top-line data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim, preliminary or top-line data from clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary or top-line data previously published. As a result, interim, preliminary and top-line data should be viewed with caution until the final data are available. Adverse differences between interim, preliminary or top-line data and final data could significantly harm our reputation and business prospects. Moreover, preliminary, interim and top-line data are subject to the risk that one or more of the clinical outcomes may materially change as more patient data become available when patients mature on study, patient enrollment continues or as other ongoing or future clinical trials with a product candidate further develop. Past results of clinical trials may not be predictive of future results.

In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically more extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. Similarly, even if we are able to complete our planned and ongoing preclinical studies and clinical trials of our product candidates according to our current development timeline, the positive results from such preclinical studies and clinical trials of our product candidates may not be replicated in subsequent preclinical studies or clinical trial results.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical and other nonclinical findings made while clinical trials were underway or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical, nonclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or other regulatory approval.

The Fast Track and Breakthrough Therapy designations we have received for zanidatamab may not result in faster development, regulatory review or approval process.

The FDA has granted Fast Track designations to zanidatamab for the first-line treatment of patients with HER2-overexpressing GEA in combination with standard of care chemotherapy and for previously treated or recurrent gene-amplified biliary tract cancers, or BTC. These Fast Track designations do not ensure that we will experience a faster development, regulatory review or approval process compared to conventional FDA procedures or that we will ultimately obtain regulatory approval. Additionally, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. The FDA also granted Breakthrough Therapy designation for zanidatamab for treatment of patients with previously treated HER2 gene-amplified locally advanced/unresectable or metastatic BTC. While we anticipate meeting with the FDA in 2023 to discuss the data readout from the HERIZON-BTC-01 study in support of submitting a BLA for zanidatamab in patients with previously treated HER2 gene-amplified BTC, the receipt of a Breakthrough Therapy designation for a product candidate may not ultimately result in a faster development process or review, and it does not in any way assure approval of a product candidate by the FDA. In addition, designation as a Breakthrough Therapy is within the discretion of the FDA and the FDA may decide to rescind a Breakthrough Therapy designation if it believes that a designated product candidate no longer meets the conditions for qualification of this program. If our clinical development program is suspended, terminated, or put on clinical hold due to unexpected adverse events or other issues, including clinical supply issues, we may not realize all the benefits associated with the Fast Track designation. Furthermore, Fast Track designation does not change the standards for approval, and the designation alone does not guarantee qualification for the FDA's priority review procedures.

Zanidatamab has also been granted Breakthrough Therapy designation from the Center for Drug Evaluation in China for treating patients with BTC who have failed prior systemic therapies.

Development of product candidates in combination with other therapies could expose us to additional risks.

Even if any of our product candidates were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA, the European Medicines Agency, or EMA, or other comparable foreign regulatory authorities could revoke approval of the therapy used in combination with any of our product candidates, or safety, efficacy, manufacturing or supply issues could arise with these existing therapies. In addition, it is possible that existing therapies with which our product candidates are approved for use could themselves fall out of favor or be relegated to later lines of treatment. This could result in the need to identify other combination therapies for our product candidates or our own products being removed from the market or being less successful commercially. We may also evaluate our product candidates in combination with one or more other cancer therapies that have not yet been approved for marketing by the FDA, EMA or comparable foreign regulatory authorities. We will not be able to market and sell any product candidate in combination with any such unapproved cancer therapies that do not ultimately obtain marketing approval. If the FDA, EMA or other comparable foreign regulatory authorities do not approve or revoke their approval of these other therapies, or if safety, efficacy, commercial adoption, manufacturing or supply issues arise with the therapies we choose to evaluate in combination with any other product candidate, we may be unable to obtain approval of or successfully market any one or all of the product candidates we develop.

Additionally, if the third-party providers of therapies or therapies in development used in combination with our product candidates are unable to produce sufficient quantities for clinical trials or for commercialization of our product candidates, or if the cost of combination therapies are prohibitive, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified product candidates from being developed, or approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA to review and clear or approve new product candidates can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, including delays or disruptions due to the COVID-19 pandemic, travel restrictions, staffing shortages, government shutdowns and furloughs, may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In response to the COVID-19 pandemic and travel restrictions, the FDA has issued industry guidance regarding plans to employ remote interactive evaluations and risk management methods, among other considerations, to meet user fee commitments and goal dates as well as plans toward resuming standard operational levels. Recently, President Biden announced that the administration intends to end the COVID-19 national and public health emergencies on May 11, 2023. The full impact of this termination of the public health emergencies on the FDA and other regulatory policies and operations are unclear. However, if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, or if the FDA and other agencies experience other delays, backlogs or disruptions, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Successful development of our current and future product candidates is uncertain and we may discontinue or reprioritize the development of any of our product candidates at any time, at our discretion.

Before obtaining regulatory approval for the commercial distribution of our product candidates, we must conduct, at our own expense, extensive preclinical tests and clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Preclinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. Additionally, the results from nonclinical testing or early clinical trials of a product candidate may not predict the results that will be obtained in subsequent human clinical trials of that product candidate. There is a high failure rate for drugs proceeding through clinical studies. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in any future clinical development could have a material adverse effect on our business and operating results. Alternatively, management may elect to discontinue development of certain product candidates to accommodate a shift in corporate strategy, despite positive clinical results. Based on our operating results and business strategy, among other factors, we may discontinue the development of any of our product candidates under development or reprioritize our focus on other product candidates at any time and at our discretion.

Additionally, because we have limited financial and managerial resources, we focus on research programs, therapeutic platforms and product candidates that we identify for specific indications. As a result, we may forgo or delay pursuit of opportunities with other therapeutic platforms or product candidates or for other indications that later prove to have greater commercial potential. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights.

Our product candidates may have undesirable side effects that may delay or prevent marketing approval or, if approval is received, require them to be taken off the market, require them to include safety warnings or otherwise limit their sales; no regulatory agency has made any determination that any of our product candidates are safe or effective for use by the general public for any indication.

All of our product candidates are still in preclinical or clinical development. Consequently, all of our product candidates are required to undergo ongoing safety testing in humans as part of clinical trials. Unforeseen side effects from any of our product candidates could arise either during clinical development or, if approved by regulatory authorities, after the approved product has been marketed. Zanidatamab and zanidatamab zovodotin continue to be evaluated in clinical trials, and the results of these and future clinical trials may show that zanidatamab, zanidatamab zovodotin or our other product candidates cause undesirable or unacceptable side effects, which could interrupt, delay or halt clinical trials, and result in delay of, or failure to obtain, marketing approval from the FDA and other regulatory authorities, or result in marketing approval from the FDA and other regulatory authorities with restrictive label warnings, limited patient populations or potential product liability claims. Even if we believe that our clinical trials and preclinical studies demonstrate the safety and efficacy of our product candidates, only the FDA and other comparable regulatory agencies may ultimately make such determination. No regulatory agency has made any such determination that any of our product candidates are safe or effective for use by the general public for any indication.

If any of our product candidates receive marketing approval and we or others later identify undesirable or unacceptable side effects caused by such products:

- regulatory authorities may require us to take our approved product off the market;
- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies, or impose a risk evaluation and mitigation strategy that includes restrictions and conditions on product distribution, prescribing and/or dispensing;
- we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product;
- we may be subject to limitations on how we may promote the product;
- sales of the product may decrease significantly;
- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Any of these events could prevent us or our current or future strategic partners from achieving or maintaining market acceptance of the affected product or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating revenue from the sale of any future products.

We face significant competition, and if our competitors develop and market products that are more effective, safer or less expensive than our product candidates, our commercial opportunities will be negatively impacted.

The life sciences industry is highly competitive and subject to rapid and significant technological change. We are currently developing biotherapeutics that will compete with other drugs and therapies that currently exist or are being developed. Products we may develop in the future are also likely to face competition from other drugs and therapies, some of which we may not currently be aware. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, universities and other research institutions. Many of our competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and in manufacturing pharmaceutical products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development and collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we develop obsolete. As a result of all of these factors, our competitors may succeed in obtaining patent protection or FDA approval or discovering, developing and commercializing products in our field before we do.

Specifically, there are a large number of companies developing or marketing treatments for cancer and autoimmune disorders, including many major pharmaceutical and biotechnology companies. These treatments consist both of small-molecule drug products, as well as biologics that work by using various antibody therapeutic platforms to address specific cancer targets. For additional information relating to the competitive environment we operate in, see Item 1. “Business – Competition.”

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, more convenient or less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for our product candidates, which could result in our competitors establishing a strong market position before we are able to enter the market.

Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. In addition, the biopharmaceutical industry is characterized by rapid technological change. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical.

In addition, we expect to compete with biosimilar versions of already approved products like trastuzumab or pertuzumab, and even if our product candidates achieve marketing approval, they may be challenged to achieve a price premium over competitive biosimilar products and will compete for market share with them.

The Biologics Price Competition and Innovation Act of 2009, which is included in the Patient Protection and Affordable Care Act, or PPACA, authorized the FDA to approve similar versions of innovative biologics, commonly known as biosimilars. Under the PPACA, a manufacturer may submit an application for licensure of a biologic product that is “biosimilar to” or “interchangeable with” a previously approved biologic product or “reference product.” Manufacturers may not submit an application for a biosimilar to the FDA until four years following

approval of the reference product, and the FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if our product candidates, if approved, are deemed to be reference products eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. Additionally, from time to time, there are proposals to repeal or modify the PPACA, including proposals that could significantly shorten the exclusivity period for biologics.

If any of our product candidates receive regulatory approval, the approved products may not achieve broad market acceptance among physicians, patients, the medical community and third-party payors, in which case revenue generated from their sales would be limited.

The commercial success of our product candidates will depend upon their acceptance among physicians, patients and the medical community. The degree of market acceptance of our product candidates will depend on a number of factors, including:

- limitations or warnings contained in the approved labeling for a product candidate;
- changes in the standard of care for the targeted indications for any of our product candidates;
- limitations in the approved clinical indications for our product candidates;
- demonstrated clinical safety and efficacy compared to other products;
- sales, marketing and distribution support;
- availability of coverage and extent of reimbursement from managed care plans and other third-party payors;
- timing of market introduction and perceived effectiveness of competitive products;
- availability of alternative therapies at similar or lower cost, including generic, biosimilar and over-the-counter products;
- the extent to which the product candidate is approved for inclusion on formularies of hospitals and managed care organizations;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy for particular diseases;
- whether the product can be used effectively with other therapies to achieve higher response rates;
- adverse publicity about our product candidates or favorable publicity about competitive products;
- convenience and ease of administration of our products; and
- potential product liability claims.

If any of our product candidates are approved, but do not achieve an adequate level of acceptance by physicians, patients and the medical community, we may not generate sufficient revenue from these products, and we may not become or remain profitable. In addition, efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful.

We may be unable to obtain orphan drug exclusivity in specific indications for zanidatamab or in future product candidates that we may develop. If our competitors are able to obtain orphan product exclusivity for their products in specific indications, we may not be able to have competing products approved in those indications by the applicable regulatory authority for a significant period of time.

The FDA has granted Orphan Drug Designation to zanidatamab for the treatment of BTC and gastric cancer, including cancer of the gastroesophageal junction, the EMA has granted Orphan Drug Designation to zanidatamab for the treatment of gastric cancer and BTC, and we may seek Orphan Drug Designation for additional indications in the future. Orphan Drug Designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

Generally, if a product candidate with an Orphan Drug Designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same drug for the same indication for that time period. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for Orphan Drug Designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. The loss of Orphan Drug Designation could have a negative effect on our ability to successfully commercialize our product candidates, earn revenues and achieve profitability.

Even if orphan drug exclusivity for zanidatamab is obtained, or is obtained for any other product candidates that receive an Orphan Drug Designation in the future, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Further, in the United States, even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition submitted by a competitor if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. If we are unable to manufacture sufficient supply of our product to meet the needs of patients, the FDA can withdraw our orphan exclusive marketing rights or approve another marketing application for the same drug product before the expiration of the exclusivity period.

Further, in *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299 (11th Cir. 2021), the court disagreed with the FDA's longstanding position that the orphan drug exclusivity only applies to the approved use or indication within an eligible disease, and not to all uses or indications within the entire disease or condition. In particular, the circuit court held that the orphan drug exclusivity for Catalyst's drug blocked the FDA's approval of another drug for all uses or indications within the same orphan-designated disease, Lambert-Eaton myasthenic syndrome, or LEMS, even though Catalyst's drug was approved at that time only for use in the treatment of LEMS in adults. Accordingly, the court ordered the FDA to set aside the approval of a drug indicated for LEMS in children. This decision created uncertainty in the application of the orphan drug exclusivity. On January 24, 2023, the FDA published a notice in the Federal Register to clarify that while the agency complies with the court's order in Catalyst, the FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the Catalyst order – that is, the agency will continue tying the scope of orphan drug exclusivity to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan designated disease or condition that have not yet been approved. It is unclear how future litigation, legislation, agency decisions, and administrative actions will impact the scope of the orphan drug exclusivity.

Even if we obtain FDA approval of any of our product candidates, we may never obtain approval or commercialize such products outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials, which would be costly and time consuming. Regulatory requirements can vary widely from country to country and region to region and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any product

[Table of Contents](#)

candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our target market will be reduced and our ability to realize the full market potential of our products will be harmed.

Our ability to eventually generate significant revenues from product sales will depend on a number of factors, including:

- successful completion of preclinical studies;
- submission of INDs or other regulatory applications for our planned clinical trials or future clinical trials and authorizations from regulators to initiate clinical studies;
- successful enrollment in, and completion of, clinical trials;
- achieving favorable results from clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing and maintaining sufficient manufacturing capabilities, whether internally or with third parties, for clinical and commercial supply;
- obtaining pricing, reimbursement, and hospital formulary access;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in combination with other products;
- sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials and commercialization activities;
- effectively competing with other therapies;
- developing and implementing successful marketing and reimbursement strategies;
- obtaining and maintaining patent, trade secret and other intellectual property protection and regulatory exclusivity for our product candidates; and
- maintaining a continued acceptable safety profile of any product following approval, if any.

If we do not achieve one or more of these requirements in a timely manner, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

We cannot be certain that our clinical trials will be initiated and completed on time, if at all, or whether our planned clinical strategy will be acceptable to the FDA or foreign health authorities. To become and remain profitable, we must develop, obtain approval for and eventually commercialize products, if approved, that generate significant revenue. In addition, it is not uncommon for product candidates to exhibit unforeseen safety issues or inadequate efficacy when tested in humans despite promising results in preclinical animal models or earlier trials, and we may ultimately be unable to demonstrate adequate safety and efficacy of our product candidates to obtain marketing approval. Even if we obtain approval and begin commercializing one or more of our product candidates, we may never generate revenue that is significant or large enough to achieve profitability.

Even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development, manufacturing and other expenditures to develop and market additional product candidates. Our failure to become or remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations.

Reimbursement decisions by third-party payors may have an adverse effect on pricing and market acceptance. If there is not sufficient reimbursement for our products, it is less likely that our products will be widely used.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. Many countries require approval of the sale price of a drug before it can be marketed. The pricing review period begins after marketing or product licensing approval is granted in most cases. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product and negatively impact the revenues we are able to generate from the sale of the product in that country.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other third-party payors. In many jurisdictions, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our products. If we are not currently capturing the scientific and clinical data that will be required for reimbursement approval, we may be required to conduct additional trials, which may delay or suspend reimbursement approval. Additionally, in the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of a product candidate that receives regulatory approval to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

Even if our product candidates are approved for sale by the appropriate regulatory authorities, market acceptance and sales of these products will depend on reimbursement policies and may be affected by future healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will reimburse and establish payment levels. We cannot be certain that reimbursement will be available for any products that we develop. If reimbursement is not available or is available on a limited basis, we may not be able to successfully commercialize any of our approved products.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, also called the Medicare Modernization Act, or MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation established Medicare Part D, which expanded Medicare coverage for outpatient prescription drug purchases by the elderly but provided authority for limiting the number of drugs that will be covered in any therapeutic class. The MMA also introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. We expect to experience pricing pressures in connection with the sale of any products that we develop, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals. In August 2022, Congress passed the Inflation Reduction Act of 2022, which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single-source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. The impact of these legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is unclear. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA, EMA or other regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses.

Interim reimbursement levels for new drugs, if applicable, may also be insufficient to cover our and any collaborator's costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that currently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our or any collaborator's inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products that we or our strategic partners develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize product candidates and our overall financial condition.

If the market opportunities for any product that we or our strategic partners develop are smaller than we believe they are, our revenue may be adversely affected and our business may suffer.

We intend to initially focus our independent product candidate development on treatments for oncology. Our projections of addressable patient populations that have the potential to benefit from treatment with our product candidates are based on estimates. If our projections are inaccurate, the market opportunities for any of our product candidates could be significantly diminished and have an adverse material impact on our business.

We may not be successful in our efforts to use our therapeutic platforms to build a pipeline of product candidates.

We intend to use our therapeutic platforms to build a pipeline of product candidates and progress these product candidates through clinical development for the treatment of a variety of diseases. Although our research and development efforts to date have resulted in a pipeline of product candidates directed at various cancers, we may not be able to develop product candidates that are safe and effective. In addition, although we expect that our therapeutic platforms will allow us to develop further product candidates, they may not prove to be successful at doing so. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. If we do not continue to successfully develop and begin to commercialize product candidates, we will face difficulty in obtaining product revenue in future periods, which could result in significant harm to our financial position and adversely affect our stock price.

Even if we receive regulatory approval to commercialize any of the product candidates that we develop, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or subject to certain conditions of approval, and may contain requirements for potentially costly post-approval trials, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the marketed product.

For any approved product, we will be subject to ongoing regulatory obligations and extensive oversight by regulatory authorities, including with respect to manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product. These requirements include submissions of safety and other post-approval information and reports, as well as continued compliance with cGMP and good clinical practice, or GCP, for any clinical trials that we or our strategic partners conduct after approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product;
- withdrawal of the product from the market or voluntary or mandatory product recalls;

- fines, warning letters or holds on clinical trials;
- refusal by the FDA, EMA or another applicable regulatory authority to approve pending applications or supplements to approved applications filed by us or our strategic partners, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

Occurrence of any of the foregoing could have a material and adverse effect on our business and results of operations. Further, the FDA's or other ex-U.S. regulators' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

The FDA strictly regulates manufacturers' promotional claims of drug products. In particular, a drug product may not be promoted by manufacturers for uses that are not approved by the FDA, as reflected in the FDA-approved labeling, although healthcare professionals are permitted to use drug products for off-label uses. The FDA, the Department of Justice, the Inspector General of the Department of Health and Human Services, among other government agencies, actively enforce the laws and regulations prohibiting manufacturers' promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including large civil and criminal fines, penalties, and enforcement actions. The FDA has also imposed consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed for companies that engaged in such prohibited activities. If we cannot successfully manage the promotion of our approved product candidates, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

If any product liability lawsuits are successfully brought against us or any of our strategic partners, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability lawsuits related to the testing of our product candidates in seriously ill patients, and will face an even greater risk if product candidates are approved by regulatory authorities and introduced commercially. Product liability claims may be brought against us or our strategic partners by participants enrolled in our clinical trials, patients, health care providers or others using, administering or selling any of our future approved products. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities. Regardless of their merit or eventual outcome, liability claims may result in:

- decreased demand for any future approved products;
- injury to our reputation;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- increased regulatory scrutiny;
- significant litigation costs;
- substantial monetary awards to, or costly settlement with, patients or other claimants;
- product recalls or a change in the indications for which they may be used;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize our product candidates.

We may need to have in place increased product liability coverage when we begin the commercialization of our product candidates. Insurance coverage is becoming increasingly expensive. As a result, we may be unable to maintain or obtain sufficient insurance at a reasonable cost to protect us against losses that could have a material adverse effect on our business. A successful product liability claim or series of claims brought against us, particularly if judgments exceed any insurance coverage we may have, could decrease our cash resources and adversely affect our business, financial condition and results of operation.

Patients with cancer and other diseases targeted by our product candidates are often already in severe and advanced stages of disease and have both known and unknown significant pre-existing and potentially life-threatening health risks. During the course of treatment, patients may suffer adverse events, including death, for reasons that may be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our product candidates, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which we do not believe that an adverse event is related to our product candidates, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may interrupt our sales efforts, delay our regulatory approval process in other countries, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations.

If we or any of our third-party manufacturers encounter manufacturing difficulties, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or prevented.

The manufacture of biological drug products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques, process and quality controls. Manufacturers of biologic products often encounter difficulties in production and sourcing, particularly in scaling up or out, validating the production process and assuring high reliability of the manufacturing processes (including the absence of contamination), in light of variations and supply constraints of key components. These problems include logistics and shipping, difficulties with production costs and yields, quality control, including consistency, stability, purity and efficacy of the product, product testing, operator error and availability of qualified personnel, as well as compliance with applicable federal, state and foreign regulations. If contaminants are discovered in our supply of our product candidates or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure you that any stability, purity, and efficacy failures, deficiencies, or other issues relating to the manufacture of our product candidates will not occur in the future. Our research and development activities also involve the controlled use of potentially hazardous substances, including chemical and biological materials, by our third-party manufacturers. While we currently outsource all manufacturing to third parties, we and our manufacturers are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury, and any related liability, resulting from medical or hazardous materials.

Material modifications in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates are developed through preclinical to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability, or our strategic partners' ability, to commence product sales and generate revenue.

Strategic transactions could disrupt our business, cause dilution to our stockholders and otherwise harm our business.

We actively evaluate various strategic transactions on an ongoing basis. For example, we may acquire other businesses, products or technologies as well as pursue strategic alliances, joint ventures, investments in complementary businesses, out-licensing agreements, divestitures or other transactions. Any of these transactions could be material to our financial condition and operating results and expose us to many risks, including:

- disruption in our relationships with existing strategic partners or suppliers as a result of such a transaction;
- unanticipated liabilities related to acquired companies;
- difficulties integrating acquired personnel, technologies and operations into our existing business;
- retention of key employees;
- diversion of management time and focus from operating our business to management of strategic alliances or joint ventures or acquisition integration challenges;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and marketing approvals;
- increases in our expenses and reductions in our cash available for operations and other uses; and
- possible write-offs or impairment charges relating to acquired businesses.

Also, the anticipated benefit of any strategic transaction may not materialize or such strategic transaction may be prohibited. Additionally, future acquisitions or dispositions could result in potentially dilutive issuances of our equity securities, the incurrence of debt, contingent liabilities or amortization expenses or write-offs of goodwill, any of which could harm our financial condition. We cannot predict the number, timing or size of any future strategic alliances, joint ventures, investments, acquisitions, divestitures or other strategic transactions, or the effect that any such transactions might have on our operating results.

Many governments impose strict price controls, which may adversely affect our future profitability.

In many countries, particularly in those in the EU, prescription drug pricing and reimbursement is subject to governmental control. In those countries that impose price controls, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our strategic partners may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies.

Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we or our strategic partners might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay commercial launch of the product candidate, possibly for lengthy time periods, and negatively impact the revenue that is generated from the sale of the product in that country. If reimbursement of such product candidates is unavailable or limited in scope or amount, if pricing is set at unsatisfactory levels, or if there is competition from lower priced cross-border sales, our profitability will be negatively affected.

Security breaches and incidents, loss of data and other disruptions could compromise sensitive information related to our business or protected health information or prevent us from accessing critical information and expose us to liability, which could adversely affect our business and our reputation.

In the ordinary course of our business, we and our CROs and other service providers collect, store and otherwise process petabytes of sensitive data, including legally protected health information, personal information, intellectual property and proprietary business information owned or controlled by ourselves or our strategic partners. We manage and maintain our applications and data by utilizing a combination of on-site systems, managed data center systems and cloud-based data center systems. These applications and data encompass a wide variety of business-critical information, including research and development information, commercial information and business and financial information. We face four primary risks relative to protecting this critical information: loss of access risk, inappropriate disclosure risk, inappropriate modification risk and the risk of being unable to adequately monitor our controls over the first three risks.

Although we take measures designed to protect sensitive information from unauthorized access or disclosure, our information technology and infrastructure and those of our CROs and our other third-party service providers may utilize may be vulnerable to attacks by hackers or viruses or breached, interrupted or compromised due to inadvertent or intentional actions by our employees, contractors, business partners, and/or other third parties, or from cyber-attacks by malicious third parties (including supply chain cyber-attacks or the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information). Any such breach, incident, or interruption could compromise systems and networks used in our business and lead to the loss, destruction, alteration, prevention of access to, disclosure, or dissemination of, or damage or unauthorized access to, our data (including trade secrets or other confidential information, intellectual property, proprietary business information, and personal information) or data that is processed or maintained on our behalf, or other assets, which could result in financial, legal, business and reputational harm to us. Any such event could result in legal claims, demands and litigation or governmental investigations or other proceedings, liability under laws that protect the privacy of personal information, such as the Health Insurance Portability and Accountability Act of 1996, or “HIPAA”, and regulatory penalties and other liabilities. Although we have implemented security measures and a formal enterprise security program designed to prevent unauthorized access to sensitive data, there is no guarantee that we or our third-party service providers can protect our systems or networks or other systems or networks used in our business from security breaches, incidents, or compromises. Any loss, destruction, alteration, prevention of access to, disclosure, or dissemination of, or damage or unauthorized access to, our data or other data that is processed or maintained on our behalf could also disrupt our operations (including our ability to conduct our analyses, pay providers, conduct research and development activities, collect, process and prepare company financial information, provide information about any future products, and manage the administrative aspects of our business) and damage our reputation, any of which could adversely affect our business.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, impose certain requirements relating to the privacy, security, transmission and breach reporting of individually identifiable health information upon entities subject to the law, such as health plans, healthcare clearinghouses and healthcare providers and their respective business associates and subcontractors that perform services for them that involve individually identifiable health information. Mandatory penalties for HIPAA violations can be significant, and criminal and monetary penalties, as well as injunctive relief, may be imposed for HIPAA violations. Although most drug manufacturers are not directly subject to HIPAA, prosecutors are increasingly using HIPAA-related theories of liability against drug manufacturers and their agents and we also could be subject to criminal penalties if we knowingly obtain individually identifiable health information from a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

Furthermore, in the event of a breach as defined by HIPAA, HIPAA regulations impose specific reporting requirements to regulators, individuals impacted by the breach and, in some cases, the media. Issuing such notifications can be costly, time and resource intensive, and can generate significant negative publicity. Breaches of HIPAA may also constitute contractual violations that could lead to contractual damages or terminations. In addition to HIPAA, other applicable data privacy and security obligations, including U.S. state data breach notification laws, may require us to notify relevant stakeholders of any security breaches or incidents that result in the unauthorized disclosure, or dissemination of, personal information. Such disclosures are costly, and the disclosures or the failure to comply with such requirements, could lead to adverse impacts.

Furthermore, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on other third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business.

In addition, we may face increased cybersecurity risks due to our reliance on internet technology given that we have employees at three office locations (Vancouver, Seattle, and Dublin) and a significant number of employees who work remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities.

We are subject to stringent and changing obligations related to privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation, fines and penalties, disruptions of our business operations, reputational harm and other adverse business consequences.

U.S. states have enacted and are considering enacting laws relating to the protection of personal information (including health and other data of patients, research subjects, and other individuals), which may be more rigorous than, or impose additional requirements beyond those required by, HIPAA. For example, the California Consumer Privacy Act, or CCPA, which became effective on January 1, 2020, gives California consumers expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used. The CCPA allows for statutory fines for noncompliance (up to \$7,500 per violation) as well as a limited private right of action for data breaches, which may increase the volume of data breach litigation. In addition, the California Privacy Rights Act of 2020, or CPRA, which went into effect on January 1, 2023, expands the CCPA by, among other things, giving California residents the ability to limit use of certain sensitive personal information, establishing restrictions on personal information retention, expanding the types of data breaches subject to the CCPA's private right of action, and establishing a new California Privacy Protection Agency to implement and enforce the new law. While limited CCPA exemptions may apply to portions of our business, the recency of the CCPA's implementing regulations and the California Attorney General's enforcement activity means obligations under the CCPA, as modified by the CPRA, could evolve in the future, which may increase our compliance costs and potential liability. Many similar privacy and security laws have been proposed at the federal level and in other states, certain of which have been enacted, including such laws in Colorado, Connecticut, Utah and Virginia. These or other proposed or enacted laws relating to privacy and security could similarly increase our compliance obligations and costs in the future.

We may also become subject to laws and regulations in non-U.S. countries covering privacy and security and the protection of health-related and other personal information. In particular, the European Economic Area, or EEA has adopted privacy and security protection laws and regulations that impose significant compliance obligations. Laws and regulations in these jurisdictions apply broadly to the collection, use, storage, disclosure, processing and security of information that identifies or may be used to identify an individual, such as names, contact information, and sensitive personal information such as health data. These laws and regulations are subject to frequent revisions and differing interpretations, and have generally become more stringent over time.

The General Data Protection Regulation 2016/679, or GDPR, applies to the processing of personal information and imposes many requirements for controllers and processors of personal information, including, for example, higher standards for obtaining consent from individuals to process their personal information, more robust disclosures to individuals and a strengthened individual data rights regime, shortened timelines for data breach notifications, limitations on retention and secondary use of information, increased requirements pertaining to health data and pseudonymized (i.e., key-coded) data and additional obligations when contracting third-party processors in connection with the processing of the personal information. The GDPR allows EEA countries to make additional laws and regulations further limiting the processing of genetic, biometric or health data. Failure to comply with the requirements of the GDPR and the applicable national privacy and security laws of EEA countries may result in fines of up to €20,000,000 or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, and other administrative penalties; we may also be liable should any individual who has suffered financial or non-financial damage arising from our infringement of the GDPR exercise their right to receive compensation against us. Furthermore, adverse publicity relating to our failure to comply with the GDPR could cause a loss of goodwill, which could have an adverse effect on our reputation, brand, business and financial condition. Additionally, the United Kingdom, or UK, has implemented legislation similar to the GDPR, referred to as the UK GDPR, which provides for fines of up to the greater of £17.5 million or 4% of global turnover.

Certain jurisdictions, including the EEA, have enacted data localization laws and cross-border personal information transfer laws. For example, absent appropriate safeguards or other circumstances, the GDPR generally restricts the transfer of personal information to countries outside the EEA, such as the United States, which the European Commission does not consider to provide an adequate level of personal information protection. On July 16, 2020, the Court of Justice of the European Union, or CJEU, invalidated the European Union-U.S. Privacy Shield, or Privacy Shield, as a data transfer mechanism for transferring personal information from the EEA to the United States. While the European Union, or EU, standard contractual clauses, or EU SCCs, remain a valid mechanism to transfer personal information to third countries outside the EEA, the CJEU's ruling has also imposed enhanced due diligence obligations on data exporters and importers to ensure that the laws of the country to which the personal information is transferred offer a level of data protection that is essentially equivalent to the EEA. Also, the EU has issued updated EU SCCs, and the UK has issued its own standard contractual clauses, or UK SCCs, that are required to be implemented over time. Although we do not transfer personal data from the EEA to the United States via the Privacy Shield, the CJEU's decision means that the status of transfers of personal information from the EEA and other regions, including the UK, to the United States is subject to significant regulatory uncertainty. To the extent we transfer personal information from other jurisdictions to the United States, we may not be able to implement or maintain an appropriate data transfer mechanism to continue such international transfers of data. Additionally, the CJEU's invalidation of the Privacy Shield, the revised EU SCCs and new UK SCCs, regulatory guidance and opinions, and other developments relating to cross-border data transfer may require us to implement additional contractual and technical safeguards for any personal information transferred out of the EEA, UK, or other regions, which may increase compliance costs, lead to increased regulatory scrutiny or liability, and may require additional contractual negotiations, which may adversely impact our business, financial condition, and operating results.

Separate from, and in addition to, requirements under the GDPR and UK GDPR, certification requirements for the hosting of health data will vary by jurisdiction. To the extent we operate in various EEA countries or the UK, there might be other national healthcare regulations or regulatory requirements with which we will be required to comply. For example, France requires hosts of health data to obtain a prior certification with the competent certification body.

The interpretation and application of consumer, health-related and privacy and security laws in the United States, the EEA, and elsewhere are often uncertain, contradictory and in flux. Any failure or perceived failure to comply with federal, state or foreign laws or regulations, contractual or other legal obligations related to privacy or security may result in claims, warnings, communications, requests or investigations from individuals, supervisory authorities or other legal or regulatory authorities in relation to our processing of personal information, and regulatory investigations or other proceedings. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. If so, this could result in government-imposed fines or orders requiring that we change our practices, which could adversely affect our business. In addition, these privacy regulations vary between states, may differ from country to country, and may vary based on whether testing is performed in the United States or in the local country. Complying with these various laws could cause us to incur substantial costs or require us to change our business practices and compliance procedures in a manner adverse to our business.

Current and future legislation may increase the difficulty and cost for us to commercialize any products that we or our strategic partners develop and affect the prices we may obtain.

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change healthcare systems in ways that could affect our ability to sell any of our product candidates profitably, if such product candidates are approved for sale. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

In March 2010, the PPACA became law in the United States. The PPACA may affect the operational results of companies in the pharmaceutical industry, including us, by imposing on them additional costs. For example, effective January 1, 2010, PPACA increased the minimum Medicaid drug rebates for pharmaceutical companies and imposed an annual fee on certain branded prescription drugs and biologics. Since the enactment of PPACA, there have been executive, judicial and Congressional challenges to certain aspects of the PPACA, including judicial challenges in the Fifth Circuit Court and the United States Supreme Court. In June 2021, the United States Supreme

Court held that Texas and other challengers had no legal standing to challenge the PPACA, dismissing the case without specifically ruling on the constitutionality of the PPACA. Accordingly, the PPACA remains in effect in its current form. It is unclear how future litigation or healthcare measures promulgated by the Biden administration will impact our business, financial condition and results of operations. Complying with any new legislation or changes in healthcare regulation could be time-intensive and expensive, resulting in a material adverse effect on our business.

Other legislative changes have been proposed and adopted since the PPACA was enacted. For example, the Bipartisan Budget Act of 2018, among other things, amended the PPACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans. The Budget Control Act of 2011, which calls for aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, began in 2013 and, due to subsequent legislative amendments, will remain in effect through 2031, with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on potential customers for our product candidates, if approved, and, accordingly, our future financial operations. We are unable to predict the future course of federal or state health care legislation or foreign regulations relating to the marketing, pricing and reimbursement of pharmaceutical products.

There have been U.S. Congressional inquiries, presidential executive orders, and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. Additionally, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. As discussed above, Congress passed the Inflation Reduction Act of 2022, which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single-source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. The implementation of cost containment measures, including the prescription drug provisions under the Inflation Reduction Act, as well as other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved. Complying with any new legislation and regulatory changes could be time-intensive and expensive, resulting in a material adverse effect on our business.

Further, many states have proposed or enacted legislation that seeks to indirectly or directly regulate pharmaceutical drug pricing, such as by requiring biopharmaceutical manufacturers to publicly report proprietary pricing information or to place a maximum price ceiling on pharmaceutical products purchased by state agencies. For example, a number of states are considering or have enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our products candidates. We cannot be sure to what extent these and future legislative and regulatory efforts, whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform

measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate, if approved, is prescribed or used.

In the EU similar political, economic and regulatory developments may affect our ability to profitably commercialize any future products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. Our future products, if any, might not be considered medically reasonable and necessary for a specific indication or cost-effective by third-party payors, an adequate level of reimbursement might not be available for such products, and third-party payors' reimbursement policies might adversely affect our or our strategic partners' ability to sell any future products profitably.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-approval testing and other requirements.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or elsewhere. If we or our strategic partners are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our strategic partners are not able to maintain regulatory compliance, our product candidates may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

Unstable or unfavorable global market and economic conditions may have adverse consequences on our business, financial condition and stock price.

Global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, increases in the rate of inflation and uncertainty about economic stability. We cannot assure you that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our business, financial condition, and stock price may be adversely affected by any such economic downturn, volatile business environment, or large-scale unpredictable or unstable market conditions, including a prolonged government shutdown, geopolitical events such as the conflict between Russia and Ukraine, or a global pandemic such as the COVID-19 pandemic.

If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

Our business may become subject to economic, political, regulatory and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. We have physical operations and personnel in Canada, the United States, and Ireland, and maintain offices in these three countries. We have recently established a subsidiary in Singapore, and intend to hire personnel and establish an office there. In addition, some of our suppliers and collaborative and clinical trial relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

Table of Contents

- economic instability or weakness, including inflation, reduced growth, diminished credit availability, weakened consumer confidence or increased unemployment;
- instability in the international geopolitical environment, including as a result of the Russian invasion of Ukraine;
- sociopolitical instability in particular foreign economies and markets;
- differing regulatory requirements for drug approvals in foreign countries;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers, including any changes that China may impose as a result of political tensions between Canada and China or the United States and China;
- regulatory changes and economic conditions following the UK's withdrawal from the EU and uncertainty related to the terms of the withdrawal;
- changes in non-U.S. currency exchange rates and currency controls;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- differing reimbursement regimes, including price controls;
- negative consequences from changes in tax laws;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities outside the United States;
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires; and
- supply and other disruptions resulting from the impact of public health epidemics, including the COVID-19 pandemic, on our strategic partners, third-party manufacturers, suppliers and other third parties upon which we rely.

Our business has been and may continue to be adversely affected by the COVID-19 pandemic.

The COVID-19 pandemic has had a broad adverse impact on the global economy across many industries and has resulted in significant governmental measures being implemented to control the spread of the virus, including quarantines, travel restrictions and business shutdowns, as well as significant volatility in global financial markets. Recently, President Biden announced that the administration intends to end the COVID-19 national and public health emergencies on May 11, 2023. The full impact of this termination of the public health emergencies on the FDA and other regulatory policies and operations are unclear.

Certain clinical trial activities, including patient enrollment and site activations, may be delayed or otherwise impacted by COVID-19 or another pandemic or epidemic, or emergence of other infectious diseases. Although we do not currently anticipate any further material impacts to our business from COVID-19 or another pandemic or epidemic, these and similar, and perhaps more severe, disruptions in our operations could negatively impact our business and financial condition in the future, but the extent of such impact will depend on future developments, which are highly uncertain and cannot be predicted, such as the location, duration and severity of outbreaks (including future potential waves or cycles), travel restrictions and social distancing, business closures or disruptions, and the effectiveness of actions taken to contain and treat the disease and to address its impact, including on financial markets.

If a resurgence of COVID-19, the emergence of another pandemic or epidemic, or the emergence of other infectious diseases were to occur, a lack of coordinated response on risk mitigation and global vaccination deployment could result in significant increases to the duration and severity of such event and could have a corresponding negative impact on our business. For example, insufficient vaccine availability, reduced effectiveness of vaccines over time or against new variants, or resistance to vaccination by certain persons may result in increasing infection and hospitalization rates, which have been and could be further complicated by the emergence of more virulent or infectious variants of the virus or other diseases.

If the COVID-19 pandemic, another pandemic or epidemic, or other infectious diseases surge, worsen or continue for a prolonged period of time, particularly in regions where we or our strategic partners and suppliers do business, we could experience disruptions that could significantly impact our current and planned clinical trials, preclinical research and other business activities, including:

- disruption to and delays in preclinical research activities due to extended closure or reduced capacity of lab facilities;
- further delays or difficulties in enrolling patients in our ongoing and planned clinical trials;
- patients discontinuing their treatment or follow-up visits;
- further delays or difficulties in clinical site initiation, including limitations on access to sites, limitations to site initiation activities that can be carried out remotely, and limitations on the number of clinical site staff on site from time to time;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- shortages, disruptions in supply, logistics or other activities related to the procurement of materials and other supplies, which could have a negative impact on our ability to conduct preclinical research, initiate or complete our clinical trials or commercialize our product candidates;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of clinical trials;
- interruption of key business activities due to illness and/or quarantine of key individuals and delays associated with recruiting, hiring and training new temporary or permanent replacements for such key individuals, both internally and at our third-party service providers and strategic partners;
- limitations in resources that would otherwise be focused on the conduct of our business or our current or planned clinical trials or preclinical research, including because of sickness, the desire to avoid contact with large groups of people, restrictions on travel, or prolonged stay-at-home or similar working arrangements;
- delays in receiving approvals from regulatory authorities to initiate our planned clinical trials;
- changes in regulations as part of a response to the COVID-19 pandemic, another pandemic or epidemic, or other infectious diseases, which may require us to change the ways in which our clinical trials are conducted and incur unexpected costs, or require us to discontinue clinical trials altogether;
- delays in necessary interactions with regulators (including the FDA), ethics committees and other important agencies and contractors due to limitations in employee resources or furlough of government or contractor personnel;
- disruptions to our strategic partners' operations, which could delay the development of our product candidates in certain geographical regions and thereby affect the timing of development and commercial milestone payments and royalties on potential future product sales we may receive; and
- limitations on our ability to recruit any necessary preclinical research, clinical, regulatory and other professional staff on the timeframe required to support our research and development programs.

In addition, COVID-19, another pandemic or epidemic, or other infectious diseases could disrupt the global financial markets, reducing our ability to access capital, which could negatively affect our liquidity. If a resurgence of COVID-19, the emergence of another pandemic or epidemic, or the emergence of other infectious diseases were to occur, the volatility of the financial market may be heightened, which could adversely impact the value of our common stock.

Our business and current and future relationships with customers and third-party payors in the United States and elsewhere will be subject, directly or indirectly, to applicable federal and state anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens, and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors in the United States and elsewhere play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval.

Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers, and third-party payors and other entities may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, including the federal Anti-Kickback Statute and the federal False Claims Act, that may constrain the business or financial arrangements and relationships through which we conduct clinical research on product candidates and market, sell and distribute any products for which we obtain marketing approval. In addition, we may be subject to transparency laws and patient privacy regulation by the federal government and by the U.S. states and foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, impose criminal or civil penalties, as applicable, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government (including the Medicare and Medicaid programs) or other third-party payor claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- HIPAA established the federal offense of health care fraud, which among other things, imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g. public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services relating to healthcare matters;
- HIPAA, as amended by HITECH, and its implementing regulations, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without the appropriate authorization by entities subject to the law, such as health plans, healthcare clearinghouses and healthcare providers and their respective business associates and their covered subcontractors;
- the federal Open Payments program under the Physician Payments Sunshine Act, created under Section 6002 of the PPACA and its implementing regulations, requires applicable group purchasing organizations and manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to HHS information related to "payments or other transfers of value" made in the previous year to covered recipients, including physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors, other health care professionals (such as nurse practitioners and physician assistants) and teaching hospitals, and information regarding ownership and investment interests held by physicians (as defined above) or their immediate family members; and

- analogous and similar state and foreign laws and regulations, including: state anti-kickback and false claims laws that may apply to our business practices (including research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by state governmental and non-governmental third-party payors, including private insurers); state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government; state laws that require drug manufacturers to track gifts and other remuneration and items of value provided to healthcare professionals and entities and file reports relating to pricing and marketing information; and state and foreign laws that govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of any available statutory exceptions and safe harbors, it is possible that some of our current and future business activities could be subject to challenge under one or more of such laws.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. Any failure or perceived failure by us to comply with such laws, regulations, or case law may result in governmental investigations or enforcement actions, litigation, claims and other proceedings, harm our reputation, and could result in significant liability. Additionally, if our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including damages, fines, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws and the curtailment or restructuring of our operations, which could have a material adverse effect on our business. If any of the physicians or other providers or entities with whom we expect to do business, including our strategic partners, is found not to be in compliance with applicable laws, it may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which could also materially affect our business.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations that can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, the United Kingdom Bribery Act 2010, the Proceeds of Crime Act 2002, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other partners from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We currently engage third parties for clinical trials outside of the United States and we may in the future engage third parties to sell our products outside of the United States once we enter a commercialization phase, or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violation of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

Third-party manufacturers may not be able to comply with U.S. export control regulations, cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in a necessity to replace current third parties, resulting in the possibility of supply delays, clinical holds on our trials, sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business, financial condition, results of operations and growth prospects.

We have received an unsolicited, non-binding proposal from an existing investor to purchase our Company.

In April 2022, All Blue Falcons FZE, or All Blue Falcons, an existing stockholder, submitted an unsolicited, non-binding proposal to purchase our Company for \$10.50 per share in cash. Our board of directors carefully reviewed the proposal and, in May 2022, unanimously determined that the unsolicited, non-binding proposal substantially undervalued our Company and was not in the best interest of the Company and its stockholders. While All Blue Falcons has not submitted a follow-up proposal and we have not had subsequent engagement with All Blue Falcons following our rejection of the non-binding proposal, reviewing this matter has in the past and may in the future divert management's and our board of directors' attention and has and may require us to incur significant costs related to our engagement of advisors. Any further actions by All Blue Falcons or others may disrupt our business and operations by causing uncertainty among and potentially loss of current and prospective employees, partners, suppliers and other constituencies important to our success or delay certain initiatives, transactions or the like that we are pursuing. Any of the foregoing could materially and negatively impact our business and financial results. The price of our common stock could be subject to price fluctuations due to the uncertainty associated with any such matter.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since inception and anticipate that we will continue to incur losses for the foreseeable future. We have no products approved for commercial sale, and to date we have not generated any revenue or profit from product sales. We may never achieve or sustain profitability.

We are a clinical-stage biopharmaceutical company. We have incurred significant losses since our inception. Our net income for the year ended December 31, 2022 was \$124.3 million, while our net loss for the years ended December 31, 2021 and 2020 was \$211.8 million and \$180.6 million, respectively. As of December 31, 2022, our accumulated deficit was \$558.8 million. We expect to continue to incur losses for the foreseeable future as we continue our research and development of, and seek regulatory approvals for, our product candidates, prepare for and begin to commercialize any approved product candidates and add infrastructure, which may include personnel, to support our product development efforts. In addition, inflationary pressure could adversely impact our financial results. The net losses and negative cash flows incurred to date, together with expected future losses, have had, and likely will continue to have, an adverse effect on our stockholders' deficit and working capital. The amount of future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability.

To become and remain profitable, we must succeed in developing and commercializing product candidates with significant market potential. This will require us to be successful in a range of challenging activities for which we are only in the preliminary stages, including developing product candidates, obtaining regulatory approval for such product candidates, and manufacturing, marketing and selling those product candidates for which we may obtain regulatory approval. We may never succeed in these activities and may never generate revenue from product sales that is significant enough to achieve profitability. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to become or remain profitable would depress our market value and could impair our ability to raise capital, expand our business, develop other product candidates, or continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of uncertainty. We have never generated any revenue from product sales and may never be profitable.

We have devoted substantially all of our financial resources and efforts to developing our proprietary therapeutic platforms, identifying potential product candidates and conducting preclinical studies and clinical trials. We and our partners are still developing our product candidates, and we have not completed development of any products. Our revenue to date has been primarily revenue from the license of our proprietary therapeutic platforms for the development of product candidates by others or revenue from our strategic partners. Our ability to generate revenue and achieve profitability depends in large part on our ability, alone or with our strategic partners, to achieve milestones and to successfully complete the development of, obtain the necessary regulatory approvals for, and commercialize, product candidates. We do not anticipate generating revenue from sales of products in the near term.

We will require substantial additional funding, which may not be available to us on acceptable terms, or at all, and, if not available, may require us to delay, scale back, or cease our product development programs or operations.

We are currently advancing two of our product candidates through clinical development as well as other potential product candidates through discovery and preclinical development. Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. In order to obtain regulatory approval, we will be required to conduct clinical trials for each indication for each of our product candidates. Although our collaboration agreements with Jazz and BeiGene provide for the future funding requirements for our lead asset, zanidatamab, we will continue to require additional funding to complete the development and commercialization of zanidatamab zovodotin, and to continue to advance the development of our other product candidates, and such funding may not be available on acceptable terms or at all. If sufficient funds on acceptable terms are not available when needed, or at all, we could be forced to significantly reduce operating expenses and delay, scale back or eliminate one or more of our development programs or our business operations. For example, in January 2022, we began implementing a Company-wide reduction in workforce to help achieve a more cost-efficient organization, which we believe will enhance our ability to execute on our key priorities. While we completed the reduction in workforce by the end of 2022, the full impact of the reduction in workforce is not yet known.

Our future funding requirements will depend on many factors, including:

- the number and characteristics of other product candidates that we pursue;
- the scope, progress, timing, cost and results of research, preclinical development, and clinical trials;
- the costs, timing and outcome of seeking and obtaining FDA and non-U.S. regulatory approvals;
- the costs associated with manufacturing our product candidates and establishing sales, marketing and distribution capabilities;
- our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make in connection with the licensing, filing, defense and enforcement of any patents or other intellectual property rights;
- our ability to achieve the anticipated cost reductions from the reduction in workforce implemented in 2022;
- our ability to hire when needed additional management, scientific and medical personnel;
- the effect of competing products that may limit market penetration of our product candidates;
- our need to implement additional internal systems and infrastructure, including financial and reporting systems; and
- the economic and other terms, timing of and success of our existing strategic partnerships, and any collaboration, asset monetization, licensing, or other arrangements into which we may enter in the future, including the timing of receipt of any milestone or royalty payments under these agreements.

Until we can generate a sufficient amount of product revenue to finance our cash requirements, which we may never do, we expect to finance future cash needs primarily through a combination of public and private equity offerings, debt financings, asset monetization, strategic partnerships and grant funding.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish substantial rights.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these new securities may include liquidation or other preferences that adversely affect our stockholders' rights as common stockholders. Debt financing, if available at all, may involve agreements that include covenants limiting or restricting our ability to take specific actions such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise additional funds through partnerships, collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, product candidates, or future revenue streams, or grant licenses on terms that are not favorable to us. We cannot assure that we will be able to obtain additional funding if and when necessary. If we are unable to obtain adequate financing on a timely basis, we could be required to delay, scale back or eliminate one or more of our development programs or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to Our Dependence on Third Parties

We will depend on our collaborative relationship with Jazz to further develop and commercialize zanidatamab, and if our relationship is not successful or is terminated, we may be delayed in or unable to effectively develop and/or commercialize zanidatamab, which could have a material adverse effect on our business.

In October 2022, Zymeworks BC entered into the Jazz Collaboration Agreement with Jazz. Pursuant to the terms of the agreement, we received a \$50 million upfront payment following receipt of HSR Clearance and delivery of licenses and technology transfer to Jazz and a further payment of \$325 million following Jazz's decision to continue the collaboration after readout of the top-line clinical data from HERIZON-BTC-01. We are also eligible to receive additional milestone payments upon achievement of certain regulatory and commercial milestones, as well as tiered royalties on Jazz's net sales of licensed products. We will depend on Jazz to collaborate with us to develop and commercialize zanidatamab in the territories covered by the Jazz Collaboration Agreement and, as a result, the eventual success or commercial viability of zanidatamab is largely beyond our control. Following receipt of the initial payments totaling \$375 million, any future financial returns to us depend in large part on achievement of regulatory and commercialization milestones, plus a share of any revenue from sales. Therefore, our success, and any associated financial returns to us and our investors, will depend in significant part on Jazz's performance under the Jazz Collaboration Agreement.

We are subject to a number of additional specific risks associated with our dependence on our collaborative relationship with Jazz, including:

- adverse decisions by Jazz regarding the development and commercialization of zanidatamab;
- possible disagreements as to the timing, nature and extent of development plans, including clinical trials or regulatory approval strategy;
- loss of significant rights if we fail to meet our obligations under the agreement;
- changes in key management personnel at Jazz; and
- possible disagreements with Jazz regarding the agreement, for example, with regard to ownership of intellectual property rights.

If either we or Jazz fail to perform our respective obligations, any clinical trial, regulatory approval or development progress could be significantly delayed or halted, could result in costly or time-consuming litigation or arbitration and could have a material adverse effect on our business.

Decisions by Jazz to emphasize other drug candidates currently in its portfolio ahead of zanidatamab, or to add competitive agents to its portfolio could result in a decision to terminate the agreement, in which event, among other things, we may be responsible for paying any remaining costs of ongoing or future clinical trials. If Jazz decides to terminate the Jazz Collaboration Agreement, we may be delayed in or unable to effectively develop and/or commercialize zanidatamab, which could have a material adverse effect on our business.

Any of the above discussed scenarios could adversely affect the timing and extent of the development and commercialization activities related to zanidatamab, which could materially and adversely impact our business.

Our existing strategic partnerships are important to our business, and future strategic partnerships will likely also be important to us. If we are unable to maintain our strategic partnerships, or if these strategic partnerships are not successful, our business could be adversely affected.

We have limited capabilities for drug development and commercialization of our product candidates, if approved. Accordingly, we have entered into strategic partnerships with other companies that we believe can provide such capabilities, including our collaboration and license agreements with Jazz, BeiGene, BMS, GSK, Daiichi Sankyo, Janssen, LEO, Iconic, Merck and Atreca. These relationships also have provided us with non-dilutive funding for our wholly owned pipeline and therapeutic platforms and we expect to receive additional funding under these strategic partnerships in the future. Our existing strategic partnerships, and any future strategic partnerships we enter into, may pose a number of risks, including the following:

- strategic partners have significant discretion in determining the efforts and resources that they will apply to these partnerships;
- strategic partners may not perform their obligations as expected;
- strategic partners may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the partners' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- strategic partners may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- strategic partners could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the strategic partners believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than our product candidates;
- product candidates discovered in collaboration with us may be viewed by our strategic partners as competitive with their own product candidates or products, which may cause strategic partners to cease to devote resources to the commercialization of our product candidates;
- a strategic partner with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product candidates;
- disagreements with strategic partners, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- strategic partners may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- strategic partners may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;

- strategic partnerships may be terminated for the convenience of the partner and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates. For example, each of our collaboration and license agreements with Jazz, BeiGene, BMS, GSK, Daiichi Sankyo, Janssen, LEO, Iconic, Merck and Atreca may be terminated for convenience upon the completion of a specified notice period;
- we may elect to enter into additional licensing or collaboration agreements to partner our product candidates in territories we currently retain, and in the event we grant exclusive rights to such partners, we would be precluded from potential commercialization of our product candidates within the territories in which we have a partner; and
- strategic partners may not have the ability or the development capabilities to perform their obligations as expected, including as a result of the impact of the COVID-19 pandemic or the emergence of another pandemic or epidemic on our strategic partners' operations or business.

If our strategic partnerships do not result in the successful development and commercialization of product candidates or if one of our partners terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under our strategic partnership agreements, our development of our therapeutic platforms and product candidates could be delayed and we may need additional resources to develop product candidates and our therapeutic platforms.

We face significant competition in seeking new strategic partners.

For some of our product candidates, we may in the future determine to collaborate with additional pharmaceutical and biotechnology companies for development and potential commercialization of therapeutic products. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the strategic partner's resources and expertise, the terms and conditions of the proposed collaboration and the proposed strategic partner's evaluation of a number of factors. These factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The strategic partner may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate.

Strategic partnerships are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future strategic partners. If we are unable to reach agreements with suitable strategic partners on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay one or more of our other development programs, delay potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into strategic partnerships and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our therapeutic platforms and our business may be materially and adversely affected.

We rely on third-party manufacturers to produce our product candidates and on other third parties to provide supplies and store, monitor and transport bulk drug substance and drug product. We and our third-party partners may encounter difficulties with respect to these activities that could delay or impair our ability to initiate or complete our clinical trials or commercialize approved products.

We do not currently own or operate any manufacturing facilities. We rely on our strategic partners to manufacture product candidates licensed to them or work with multiple third-party contract manufacturers to produce sufficient quantities of materials required for the manufacture of our product candidates for preclinical testing and clinical trials, in compliance with applicable regulatory and quality standards, and intend to do so for the commercial manufacture of our products. If we are unable to arrange for such third-party manufacturing sources, or fail to do so on commercially reasonable terms, we may not be able to successfully produce sufficient supply of product candidate or we may be delayed in doing so. Such failure or substantial delay could materially harm our business.

The manufacture of biopharmaceutical products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. The process of manufacturing our product candidates is susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our product candidates or in the third-party manufacturing facilities in which our product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. All of our engineered antibodies are manufactured by utilizing cells that are stored in a cell bank. We have one master cell bank and one working cell bank utilized for each antibody manufactured in accordance with cGMP. While we believe we would have adequate back up at a secondary storage location, should any cell bank be lost in a catastrophic event, it is possible that we could lose part of a cell bank and have our manufacturing potentially impacted by the need to replace the cell bank. Any adverse developments affecting manufacturing operations for our product candidates, if any are approved, may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our products. We may also have to take inventory write-offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives.

Furthermore, reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates ourselves, including reliance on the third party for regulatory compliance and quality control and assurance, volume production, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control (including a failure to manufacture our product candidates in accordance with our product specifications) and the possibility of termination or nonrenewal of the agreement by the third party at a time that is costly or damaging to us. In addition, the FDA, EMA and other regulatory authorities require that our product candidates be manufactured according to cGMP and similar foreign standards. Pharmaceutical manufacturers and their subcontractors are required to register their facilities or products manufactured at the time of submission of the marketing application and then annually thereafter with the FDA and certain state and foreign agencies. They are also subject to periodic unannounced inspections by the FDA, state and other foreign authorities. Any subsequent discovery of problems with a product, or a manufacturing or laboratory facility used by us or our strategic partners, may result in restrictions on the product or on the manufacturing or laboratory facility, including marketed product recall, suspension of manufacturing, product seizure, or a voluntary withdrawal of the drug from the market. We may have little to no control regarding the occurrence of third-party manufacturer incidents. Any failure by our third-party manufacturers to comply with cGMP or failure to scale up manufacturing processes, including any failure to deliver sufficient quantities of product candidates in a timely manner, could lead to a delay in, or failure to obtain, regulatory approval of any of our product candidates.

In addition to third-party manufacturers, we rely on other third parties to store, monitor and transport bulk drug substance and drug product. If we are unable to arrange for such third-party sources, or fail to do so on commercially reasonable terms, we may not be able to successfully supply sufficient product candidate or we may be delayed in doing so. Such failure or substantial delay could materially harm our business.

In addition, disruptions to ports and other shipping infrastructure, as were experienced during the COVID-19 pandemic, may result in shortages or delays impacting the availability of materials and other supplies, which could negatively impact our manufacturers, suppliers and other third parties on whom we rely. While we have not yet suffered any direct, material negative impacts from these ongoing supply chain disruptions, we cannot be certain that we will not be impacted, which could increase our costs or negatively impact our development timelines.

We rely on third parties to monitor, support, conduct and oversee clinical trials of the product candidates that we are developing and, in some cases, to maintain regulatory files for those product candidates. We may not be able to obtain regulatory approval for our product candidates or commercialize any products that may result from our development efforts if we are not able to maintain or secure agreements with such third parties on acceptable terms, if these third parties do not perform their services as required, or if these third parties fail to timely transfer any regulatory information held by them to us.

We rely on entities outside of our control, which may include academic institutions, CROs, hospitals, clinics and other third-party strategic partners, to monitor, support, conduct and oversee preclinical studies and clinical trials of our current and future product candidates. We also rely on third parties to perform clinical trials on our current and future product candidates when they reach that stage. As a result, we have less control over the timing and cost of these studies and the ability to recruit trial subjects than if we conducted these trials with our own personnel.

If we are unable to maintain or enter into agreements with these third parties on acceptable terms, or if any such engagement is terminated prematurely, we may be unable to enroll patients on a timely basis or otherwise conduct our trials in the manner we anticipate. In addition, there is no guarantee that these third parties will devote adequate time and resources to our studies or perform as required by our contract or in accordance with regulatory requirements, including maintenance of clinical trial information regarding our product candidates. These third parties, in turn, may face their own constraints in obtaining the resources and personnel needed to perform the work for which we engage them. If these third parties fail to meet expected deadlines, fail to transfer to us any regulatory information in a timely manner, fail to adhere to protocols or fail to act in accordance with regulatory requirements or our agreements with them, or if they otherwise perform in a substandard manner or in a way that compromises the quality or accuracy of their activities or the data they obtain, then clinical trials of our product candidates may be extended or delayed with additional costs incurred, or our data may be rejected by the FDA, EMA or other regulatory agencies.

Ultimately, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities.

We and our CROs are required to comply with GCP regulations and guidelines enforced by the FDA, the competent authorities of the member states of the EU and comparable foreign regulatory authorities for products in clinical development. Regulatory authorities enforce these GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and clinical trial sites. If we or any of our CROs fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and our submission of marketing applications may be delayed or the FDA may require us to perform additional clinical trials before approving our marketing applications. Upon inspection, the FDA could determine that any of our clinical trials fail or have failed to comply with applicable GCP regulations. In addition, our clinical trials must be conducted with product produced under the cGMP regulations enforced by the FDA, and our clinical trials may require a large number of test subjects. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and increase our costs. Moreover, our business may be implicated if any of our CROs violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

If any of our clinical trial sites terminate for any reason, we may experience the loss of follow-up information on patients enrolled in our ongoing clinical trials unless we are able to transfer the care of those patients to another qualified clinical trial site. Further, if our relationship with any of our CROs is terminated, we may be unable to enter into arrangements with alternative CROs on commercially reasonable terms, or at all.

Switching or adding CROs or other suppliers can involve substantial cost and require extensive management time and focus. In addition, there is a natural transition period when a new CRO or supplier commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. If we are required to seek alternative supply arrangements, the resulting delays and potential inability to find a suitable replacement could materially and adversely impact our business.

We rely on third parties for various operational and administrative aspects of our business, including for certain cloud-based software platforms, which impact our financial, operational and research activities. If any of these third parties fail to provide timely, accurate and ongoing service or if the cloud-based platforms suffer outages that we are unable to mitigate, our business may be adversely affected.

We currently rely upon third-party consultants and contractors to provide certain operational and administrative services, including external financial, legal, clinical and research consultation. The failure of any of these third parties to provide accurate and timely service may adversely impact our business operations. In addition, if such third-party service providers were to cease operations, temporarily or permanently, face financial distress or other business disruption, or increase their fees, or if our relationships with these providers deteriorate, we could suffer increased costs until an equivalent provider could be found, if at all, or we could develop internal capabilities, if ever.

In addition, if we are unsuccessful in choosing or finding high-quality partners, if we fail to negotiate cost-effective relationships with them, or if we ineffectively manage these relationships, it could have an adverse impact on our business and financial performance.

Further, our operations depend on the continuing and efficient operation of our information technology and communications systems and infrastructure, and specifically on “cloud-based” platforms. These platforms are vulnerable to damage or interruption from earthquakes, vandalism, sabotage, terrorist attacks, floods, fires, power outages, telecommunications failures, and computer viruses or other deliberate attempts to harm the systems. The occurrence of a natural or intentional disaster, any decision to close a facility we are using without adequate notice, or particularly an unanticipated problem at our cloud-based virtual server facility, could result in harmful interruptions in our service, resulting in adverse effects to our business.

Risks Related to Our Intellectual Property

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our future approved products or impair our competitive position. For example, certain patents and patent applications held by third parties cover Fab and Fc region engineering methods for bispecific antibodies, and antibodies having mutations in Fab heavy and light chain regions and Fc regions to generate correctly paired bispecific antibodies. If our products or our strategic partners’ products incorporate any Fab or Fc region mutations covered by any claims of these patents or patents that may issue from these applications, and if licenses for them are not available on commercially reasonable terms or at all, and we are unable to invalidate or render unenforceable those patents, our business could be materially harmed.

We are also aware of third-party patents and patent applications containing claims directed to compositions and methods for treating various forms of cancer with antibodies targeting HER2, alone or in combination with other anti-cancer agents, which patents and applications could potentially be construed to cover our product candidates and the use thereof to treat cancer. If our products or our strategic partners’ products were found to infringe any such patents, and if licenses for them are not available on commercially reasonable terms, or at all, and we were unable to invalidate or render unenforceable those patents, our business could be materially harmed. These patents may not expire before we receive marketing authorization for our product candidates, and could delay the commercial launch of one or more future products. There is also no assurance that there are not third-party patents or patent applications of which we are aware, but which we do not believe are relevant to our business, which may, nonetheless, ultimately be found to limit our ability to make, use, sell, offer for sale or import our future approved products or impair our competitive position.

Patents that we may ultimately be found to infringe could be issued to third parties. Third parties may have or obtain valid and enforceable patents or proprietary rights that could block us from developing product candidates using our technology. Our failure to obtain a license to any patent covering any technology that we require may materially harm our business, financial condition and results of operations. Moreover, our failure to maintain a license to any patent covering any technology that we require may also materially harm our business, financial condition and results of operations. Furthermore, we would be exposed to a threat of litigation.

In the pharmaceutical industry, significant litigation and other proceedings regarding patents, patent applications, trademarks and other intellectual property rights are commonplace. Any such lawsuits and proceedings could be costly and could affect our results of operations and divert the attention of our management and scientific personnel. Some of our competitors may be able to sustain the cost of such litigation and proceedings more effectively than we can because of their substantially greater resources. There is a risk that a court would decide that we or our strategic partners are infringing a third party's patents and would order us or our strategic partners to stop the activities or stop the manufacture, use, or sale of any product covered by the patents. In that event, we or our strategic partners may not have a viable alternative to the technology protected by the patent and may need to halt work on the affected product candidate or cease commercialization of an approved product. In addition, there is a risk that a court would order us or our strategic partners to pay third-party damages or some other monetary award, depending upon the jurisdiction. An adverse outcome in any litigation or other proceeding could subject us to significant liabilities to third parties, potentially including treble damages and attorneys' fees if we are found to have willfully infringed, and we may be required to cease using the technology that is at issue or to license the technology from third parties. We may not be able to obtain any required licenses on commercially acceptable terms or at all. Any of these outcomes could have a material adverse effect on our business.

If we are unable to obtain, maintain and enforce patent and trade secret protection for our product candidates and related technology, our business could be materially harmed.

Our strategy depends on our ability to identify and seek patent protection for our discoveries. This process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we have licensed from third parties. Therefore, our owned or in-licensed patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Our patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our current and future product candidates in the United States or in other countries.

Moreover, the patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has been the subject of much litigation. The issuance of a patent does not ensure that it is valid or enforceable. Third parties may challenge the validity, enforceability or scope of our issued patents, and such patents may be narrowed, invalidated, circumvented, or deemed unenforceable. In addition, changes in law may introduce uncertainty in the enforceability or scope of patents owned by biotechnology companies. If our patents are narrowed, invalidated or held unenforceable, third parties may be able to commercialize our technology or products and compete directly with us without payment to us. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, and such prior art could potentially invalidate one or more of our patents or prevent a patent from issuing from one or more of our pending patent applications. There is also no assurance that there is not prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our patents and patent applications, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim.

Furthermore, even if our patents are unchallenged, they may not adequately protect our intellectual property, provide exclusivity for our product candidates, prevent others from designing around our claims or provide us with a competitive advantage. The legal systems of certain countries do not favor the aggressive enforcement of patents, and the laws of other countries may not allow us to protect our inventions with patents to the same extent as the laws of the United States. Because patent applications in the United States and many other jurisdictions are typically not

published until 18 months after filing, or in some cases not at all, and because publications of discoveries in scientific literature lag behind actual discoveries, we cannot be certain that we were the first to make the inventions claimed in our issued patents or pending patent applications, or that we were the first to file for protection of the inventions set forth in our patents or patent applications. As a result, we may not be able to obtain or maintain protection for certain inventions. Therefore, the issuance, validity, enforceability, scope and commercial value of our patents in the United States and in other countries cannot be predicted with certainty and, as a result, any patents that we own or license may not provide sufficient protection against competitors. We may not be able to obtain or maintain patent protection from our pending patent applications, from those we may file in the future, or from those we may license from third parties. Moreover, even if we are able to obtain patent protection, such patent protection may be of insufficient scope to achieve our business objectives. In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our own patented product and practicing our own patented technology.

Our patents covering one or more of our products or product candidates could be found invalid or unenforceable if challenged.

Any of our intellectual property rights could be challenged or invalidated despite measures we take to obtain patent and other intellectual property protection with respect to our product candidates and proprietary technology. For example, if we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the United States and in some other jurisdictions, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld material information from the U.S. Patent and Trademark Office, or USPTO, or the applicable foreign counterpart, or made a misleading statement, during prosecution. A litigant or the USPTO itself could challenge our patents on this basis even if we believe that we have conducted our patent prosecution in accordance with the duty of candor and in good faith. The outcome following such a challenge is unpredictable.

With respect to challenges to the validity of our patents, for example, there might be invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on a product candidate. Even if a defendant does not prevail on a legal assertion of invalidity and/or unenforceability, our patent claims may be construed in a manner that would limit our ability to enforce such claims against the defendant and others. The cost of defending such a challenge, and any resulting loss of patent protection, could have a material adverse impact on one or more of our product candidates and our business.

Enforcing our intellectual property rights against third parties may also cause such third parties to file other counterclaims against us, which could be costly to defend and could require us to pay substantial damages, cease the use, manufacture, or sale of certain products or enter into a license agreement and pay royalties (which may not be possible on commercially reasonable terms or at all). Any efforts to enforce our intellectual property rights are also likely to be costly and may divert the efforts of our scientific and management personnel.

Our intellectual property rights will not necessarily provide us with competitive advantages.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we or our strategic partners own or have exclusively licensed;
- others may independently develop similar or alternative technologies without infringing our intellectual property rights;

- issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- we may obtain patents for certain compounds many years before we obtain marketing approval for products containing such compounds, and because patents have a limited life, which may begin to run prior to the commercial sale of the related product, the commercial value of our patents may be limited;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may fail to develop additional proprietary technologies that are patentable;
- the laws of certain countries may not protect our intellectual property rights to the same extent as the laws of the United States, or we may fail to apply for or obtain adequate intellectual property protection in all the jurisdictions in which we operate; and
- the patents of others may have an adverse effect on our business, for example by preventing us from marketing one or more of our product candidates for one or more indications.

Any of the aforementioned threats to our competitive advantage could have a material adverse effect on our business.

We may become involved in lawsuits to protect or enforce our patents and trade secrets, which could be expensive, time consuming and unsuccessful.

Third parties may seek to market biosimilar versions of any approved products. Alternatively, third parties may seek approval to market their own products similar to or otherwise competitive with our product candidates. In these circumstances, we may need to defend or assert our patents, including by filing lawsuits alleging patent infringement. The outcome following legal assertions of invalidity and unenforceability is unpredictable. In any of these types of proceedings, a court or agency with jurisdiction may find our patents invalid or unenforceable. Even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

Even after they have issued, our patents and any patents that we license may be challenged, narrowed, invalidated or circumvented. If our patents are invalidated or otherwise limited or will expire prior to the commercialization of our product candidates, other companies may be better able to develop products that compete with ours, which could adversely affect our competitive business position, business prospects and financial condition. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

The following are examples of litigation and other adversarial proceedings or disputes that we could become a party to involving our patents or patents licensed to us:

- we or our strategic partners may initiate litigation or other proceedings against third parties to enforce our patent or trade secret rights;
- third parties may initiate litigation or other proceedings seeking to invalidate patents owned by or licensed to us or to obtain a declaratory judgment that their product or technology does not infringe our patents or patents licensed to us;
- third parties may initiate opposition or reexamination proceedings challenging the validity or scope of our patent rights, requiring us or our strategic partners and/or licensors to participate in such proceedings to defend the validity and scope of our patents;
- there may be a challenge or dispute regarding inventorship or ownership of patents or trade secrets currently identified as being solely or co-owned by us or by a licensor who has granted a license to us;

- the USPTO may initiate an interference between patents or patent applications owned by or licensed to us and those of our competitors, requiring us or our strategic partners and/or licensors to participate in an interference proceeding to determine the priority of invention, which could jeopardize our patent rights; or
- third parties may seek approval to market biosimilar versions of our future approved products prior to expiration of relevant patents owned by or licensed to us, requiring us to defend our patents, including by filing lawsuits alleging patent infringement.

These lawsuits and proceedings would be costly and could affect our results of operations and divert the attention of our managerial and scientific personnel. Adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our licensors can. There is a risk that a court or administrative body would decide that our patents are invalid, unenforceable or not infringed or trade secrets not misappropriated by a third party's activities, or that the scope of certain issued claims must be further limited. An adverse outcome in a litigation or proceeding involving our own patents or trade secrets could limit our ability to assert our patents or trade secrets against these or other competitors, affect our ability to receive royalties or other licensing consideration from our licensees, and may curtail or preclude our ability to exclude third parties from making, using and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition.

We may not be able to prevent, alone or with our licensors or licensees, infringement or misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have an adverse effect on the price of our common stock.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to develop a platform that is similar to, or better than, ours in a way that is not covered by the claims of our patents;
- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of our patents;
- we might not have been the first to make the inventions covered by patents or pending patent applications;
- we might not have been the first to file patent applications for these inventions;
- any patents that we obtain may not provide us with any competitive advantages or may ultimately be found invalid or unenforceable; or
- we may not develop additional proprietary technologies that are patentable or that afford meaningful trade secret protection.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain protection under the Hatch-Waxman Amendments and similar legislation in other countries for extending the term of patents covering each of our product candidates, our business may be materially harmed.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced, possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

If we are unable to protect the confidentiality of our proprietary information, the value of our technology and products could be adversely affected.

In addition to patent protection, we also rely on other proprietary rights, including protection of trade secrets, and other proprietary information. For example, we treat our confidential and proprietary computational technologies, including unpatented know-how and other proprietary information, as trade secrets. We enter into confidentiality agreements with our employees, consultants, strategic partners and others upon the commencement of their relationships with us. These agreements provide that all confidential information developed by the individual or made known to the individual by us during the course of the individual's relationship with us be kept confidential and not disclosed to third parties. Our agreements with employees and our personnel policies also provide that any inventions conceived by the individual in the course of rendering services to us shall be our exclusive property. However, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. We cannot guarantee that we have entered into such agreements with each party that has or may have had access to, or houses or hosts, our trade secrets or proprietary information or that has been involved in the development of intellectual property. Further, despite such agreements, such inventions or confidential information may become disclosed or assigned to third parties. Monitoring unauthorized uses and disclosures is difficult and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. To the extent that our employees, consultants or contractors use technology or know-how owned by third parties in their work for us, disputes may arise between us and those third parties as to the rights in such technology or know-how or in related inventions. To the extent that an individual who is not obligated to assign rights in intellectual property to us is rightfully an inventor of intellectual property, we may need to obtain an assignment or a license to that intellectual property from that individual, or a third party or from that individual's assignee. Such assignment or license may not be available on commercially reasonable terms or at all.

We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems and cloud storage sources, but such security measures may be breached, including through cyber-hacking or cyberattacks, and we may not have adequate remedies for any breach.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. The disclosure of our trade secrets would impair our competitive position and may materially harm our business, financial condition and results of operations. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to maintain trade secret protection could adversely affect our competitive business position. In addition, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, or if we otherwise lose protection for our trade secrets or proprietary know-how, the value of this information may be greatly reduced and our business and competitive position could be harmed. Adequate remedies may not exist in the event of unauthorized use or disclosure of our proprietary information.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously or concurrently employed at research institutions and/or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, or we, have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers, or that patents and applications we have filed to protect inventions of these employees, even those related to one or more of our product candidates, are rightfully owned by their former or concurrent employer. Litigation may be necessary to defend against these claims. Such trade secrets or other proprietary information could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by regulations and governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents or applications will be due to the USPTO and various foreign patent offices at various points over the lifetime of our patents or applications. We have systems in place to remind us to pay these fees, and we rely on our outside patent annuity service to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

Although we are not currently experiencing any claims challenging the inventorship or ownership of our patents, we may in the future be subject to claims that former employees, strategic partners or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. While it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. For example, the assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, or we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Patent protection and patent prosecution for some of our product candidates may be dependent on, and the ability to assert patents and defend them against claims of invalidity may be maintained by, third parties.

There may be times in the future when certain patents that relate to our product candidates or any approved products are controlled by our licensees or licensors. Although we may, under such arrangements, have rights to consult with our strategic partners on actions taken as well as back-up rights of prosecution and enforcement, we have in the past and may in the future relinquish rights to prosecute and maintain patents and patent applications within our portfolio as well as the ability to assert such patents against infringers.

If any current or future licensee or licensor with rights to prosecute, assert or defend patents related to our product candidates fails to appropriately prosecute and maintain patent protection for patents covering any of our product candidates, or if patents covering any of our product candidates are asserted against infringers or defended against claims of invalidity or unenforceability in a manner that adversely affects such coverage, our ability to develop and commercialize any such product candidate may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products.

Changes in patent laws or patent jurisprudence could diminish the value of patents in general, thereby impairing our ability to protect our products.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. We cannot predict the breadth of claims that may be allowed or found to be enforceable in our patents, in our strategic partners' patents or in third-party patents. Recent U.S. Supreme Court rulings have either narrowed the scope of patent protection available in certain circumstances or weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this has created uncertainty with respect to the validity, scope and value of patents, once obtained.

For our U.S. patent applications containing a priority claim after March 16, 2013, there is a greater level of uncertainty in the patent law. In September 2011, the Leahy-Smith America Invents Act, also known as the America Invents Act, or AIA, was signed into law. The AIA includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation.

The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have an adverse effect on our business. An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties disclosing or claiming the same invention. A third party that has filed, or files a patent application in the USPTO after March 16, 2013, but before us, could be awarded a patent covering a given invention, even if we had made the invention before it was made by the third party. This requires us to be cognizant of the time from invention to filing of a patent application.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal court necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action.

Depending on decisions by the U.S. Congress, the U.S. federal courts, the USPTO or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that may weaken our and our licensors' ability to obtain new patents or to enforce existing patents we and our licensors or partners may obtain in the future.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some countries do not protect intellectual property rights to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our current or future products, if any, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Recent U.S. Supreme Court cases have narrowed the scope of what is considered patentable subject matter, for example, in the areas of software and diagnostic methods involving the association between treatment outcome and biomarkers. This could impact our ability to patent certain aspects of our technology in the United States.

Many companies have encountered significant problems in protecting and defending intellectual property rights in jurisdictions other than the United States. The legal systems of certain countries do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Additionally, the requirements for patentability may differ in certain countries. For example, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In India, unlike the United States, there is no link between regulatory approval of a drug and its patent status. In addition to India, certain countries in Europe and developing countries, including China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

Geo-political actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors or licensees and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors or licensees. For example, the United States, Canadian, and foreign government actions related to Russia's invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees that have citizenship or nationality in, are registered in, or have a predominately primary place of business or profit-making activities in the United States and other countries that Russia has deemed unfriendly without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

As another example, the complexity and uncertainty of European patent laws have increased in recent years. In Europe, a new unitary patent system will likely be introduced by the end of 2023, which would significantly impact European patents, including those granted before the introduction of such a system. Under the unitary patent system, European applications will soon have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court, or UPC. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. Patents granted before the implementation of the UPC will have the option of opting out of the jurisdiction of the UPC and remaining as national patents in the UPC countries. Patents that remain under the jurisdiction of the UPC will be potentially vulnerable to a single UPC-based revocation challenge that, if successful, could invalidate the patent in all countries who are signatories to the UPC. We cannot predict with certainty the long-term effects of any potential changes.

We use open source software in connection with our internal research and development programs, which could negatively affect our ability to develop products and subject us to litigation or other actions.

We use open source software in connection with our internal research and development programs. The terms of many open source licenses have not been interpreted by U.S. courts or courts outside of the U.S., and there is a risk that these licenses could be construed in a way that could impose unanticipated conditions or restrictions on our ability to use this software. As a result, we could be subject to lawsuits by parties claiming ownership of what we believe to be open source software, or claiming that software we developed using such open source software is a derivative work of open source software and demanding the release of portions of our source code, or otherwise seeking to enforce the terms of the applicable open source license. Litigation could be costly for us to defend, have a negative effect on our financial condition and results of operations or require us to devote additional research and development resources to change our platform and offerings.

If we were to combine our proprietary software with open source software in a certain manner, we could, under certain open source licenses, be required to release the source code of our proprietary software to the public. While we monitor our use of open source software and try to ensure that none is used in a manner that would require us to disclose our proprietary source code or that would otherwise breach the terms of an open source agreement, such use could inadvertently occur, or could be claimed to have occurred, in part because open source license terms are often ambiguous. If we inappropriately use open source software, or if the license terms for open source software that we use change, we may be required to re-engineer our platform, incur additional costs, discontinue the use of some or all of our platform or take other remedial actions.

In addition to risks related to license requirements, usage of open source software can lead to greater risks than use of third-party commercial software, because open source licensors generally do not provide warranties or assurance of title or controls on origin of the software. In addition, many of the risks associated with usage of open source software, such as the lack of warranties or assurances of title, cannot be eliminated, and could, if not properly addressed, negatively affect our business. We have established processes to help alleviate these risks, including a review process for the use of open source software, but we cannot be sure that all of our use of open source software is in a manner that is consistent with our current policies and procedures, or will not subject us to liability. Any of these risks could be difficult to eliminate or manage and, if not addressed, could have an adverse effect on our business, financial condition and results of operations.

We will need to obtain FDA approval for any proposed product candidate names, and any failure or delay associated with such approval may adversely affect our business.

Any proprietary name or trademark we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the USPTO. The FDA typically conducts a review of proposed product candidate names, including an evaluation of the potential for confusion with other product names. The FDA may also object to a product name if it believes the name inappropriately implies certain medical claims or contributes to an overstatement of efficacy. If the FDA objects to any product candidate names we propose, we may be required to adopt an alternative name for our product candidates. If we adopt an alternative name, we would lose the benefit of any existing trademark applications for such product candidate and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product candidates.

Risks Related to the Redomicile Transactions

We may fail to realize certain benefits of the Redomicile Transactions, including as a result of the shares of our common stock not being included in a U.S. stock market index.

We believe that the Redomicile Transactions will enhance stockholder value over the long-term and raise the profile and marketability of our capital stock in the United States through, among other things, the ability to attract deeper and growing pools of passive investment capital in the United States, particularly if shares of our common stock are included in certain U.S. stock market indices and other investment vehicles that only include securities of U.S.-incorporated companies. However, if shares of our common stock are not included in such U.S. stock market indices, this could result in increased selling pressure and/or decreased demand for our common stock that would increase stock price volatility or cause the market price of the shares of our common stock to fall. Initial inclusion and continued inclusion in a stock market index or fund is not guaranteed and is subject to numerous factors which can be applied subjectively by the entity managing the index or fund. There are no assurances that we will be included in any U.S. stock market indices or funds in a timely manner, or at all. Even if we are included in a U.S. stock market index or fund, the entities managing such indices or funds may change their inclusion criteria, resulting in the future exclusion from such index or fund.

In addition, we incurred a number of non-recurring costs associated with the Redomicile Transactions, including legal fees, accountants' fees, proxy solicitor fees, filing fees, mailing expenses and financial printing expenses. The completion of the Redomicile Transactions and the associated reorganization of our corporate structure may result in additional and unforeseen expenses in the future. While it is expected that benefits of the Redomicile Transactions will offset these transaction costs over time, this net benefit may not be achieved in the short-term or at all. These combined factors could adversely affect our business and overall financial condition. The success of the Redomicile Transactions will depend, in part, on our ability to realize the anticipated benefits associated with the Redomicile Transactions and associated reorganization of our corporate structure, and we may not be able to realize such benefits on a timely basis or at all.

The Redomicile Transactions may result in sales of shares of our common stock by certain retail and institutional stockholders or investment funds that are not permitted to hold shares of our common stock under their internal guidelines.

The Redomicile Transactions may result in sales of shares of our common stock by certain retail and institutional stockholders or investment funds (including Canadian-focused funds) that are not permitted to hold shares of our common stock under their internal guidelines, or are limited in the size of any such investments. Such sales could result in increased selling pressure and/or decreased demand for shares of our common stock, which could increase stock price volatility or cause the market price of the shares of our common stock to fall. As a result of the foregoing, certain of these investors may be required under their internal guidelines to sell their shares at times when, or at prices for which, they would otherwise not have sold. If an investor sells its shares at a time when the market price is lower than their cost basis in the shares, the investor will suffer a loss that could be significant to such investor.

Our business may be impacted by the uncertainty associated with the Redomicile Transactions.

Following completion of the Redomicile Transactions, our principal executive offices are located in Middletown, Delaware. We have physical operations and personnel in Canada, the United States, and Ireland, and maintain offices in these three countries. Our executive officers and directors are located in several jurisdictions, including the United States, Canada and the United Kingdom.

Certain relationships, including with employees, suppliers, CROs, partners, collaborators, governments and other stakeholders, may be subject to disruption due to uncertainty associated with the Redomicile Transactions. Specifically, certain stakeholders may be reluctant to engage in business with us following the completion of the Redomicile Transactions or may impose additional conditions on or apply less favorable terms to transactions involving us. This could have an adverse effect on our business and operations.

In connection with the completion of the Redomicile Transactions we may need to enter into certain new arrangements which may not be on terms as favorable as arrangements entered into by Zymeworks BC.

In connection with completion of the Redomicile Transactions we may need to enter into new arrangements as the ultimate parent company to Zymeworks BC and its subsidiaries. While we anticipate such terms will be materially consistent with existing arrangements, there is no assurance that such arrangement will not impose additional operating or financial restrictions on us, or that such arrangements will be on commercially reasonable terms or terms that are acceptable to us.

In addition, the completion of the Redomicile Transactions may have triggered certain technical change in control, right of first offer, notice, consent, assignment or other provisions in agreements to which Zymeworks BC or our other subsidiaries are a party. If we are unable to assert that such provisions should not apply, or we are unable to comply with or negotiate waivers of those provisions, the counterparties may exercise their rights and remedies under the agreements, including potentially terminating such agreements or seeking monetary damages. Even if we are able to negotiate waivers, the counterparties may require a fee for such waivers or seek to renegotiate the agreements on terms less favorable to us.

Negative publicity resulting from the Redomicile Transactions could adversely affect our business and the market price of our common stock.

Transactions similar to the Redomicile Transactions that have been undertaken by other companies have in some cases generated significant news coverage, some of which has been negative. Negative publicity generated by the Redomicile Transactions could cause certain persons with whom we have a business relationship to be more reluctant to do business with us. In addition, negative publicity could cause certain of our employees, particularly those in Canada, to perceive uncertainty regarding future opportunities available to them. Either of these events could have a significant adverse impact on our business. Negative publicity could also cause some of our stockholders to sell their shares or decrease the demand for new investors to purchase such shares, which could have an adverse impact on the price of our common stock.

Our current organizational structure may result in certain tax and operational inefficiencies that may adversely affect our business, financial condition and results of operations.

On October 13, 2022, the Redomicile Transactions were completed, which were governed by a transaction agreement dated July 14, 2022, as restated and amended on August 18, 2022, or the “Restated and Amended Transaction Agreement,” by and among Zymeworks BC, us, CallCo and ExchangeCo. Pursuant to the terms of the Restated and Amended Transaction Agreement, we, Zymeworks BC, CallCo and ExchangeCo agreed, among other things, to use reasonable efforts to take certain corporate steps and actions, as may be necessary or desirable, to effect and implement certain post-arrangement transactions following the implementation of the arrangement under the BCBCA, or the “Post-Arrangement Transactions,” including the movement of certain subsidiaries of Zymeworks BC so that they become our directly, wholly-owned subsidiaries. Following Zymeworks BC’s entry into the Jazz Collaboration Agreement, we reevaluated the potential impacts of completing the Post-Arrangement Transactions and have determined that completing the Post-Arrangement Transactions as contemplated in the Restated and Amended Transaction Agreement would result in negative tax consequences. As a result, we are evaluating alternatives to the previously contemplated Post-Arrangement Transactions with our advisors. We cannot be certain that we will be able to identify and implement an alternative set of post-arrangement transactions. Even if we do identify an alternative set of post-arrangement transactions, we cannot be certain that such alternative will result in a more tax-efficient or operationally-efficient organizational structure. While we are evaluating alternative approaches, our current organizational structure may result in certain tax and operational inefficiencies that may adversely affect our business, financial condition and results of operations.

Our effective tax rate may change in the future.

We are subject to U.S. federal income taxes on our earnings and the earnings of our non-U.S. subsidiaries in a manner that may adversely impact our effective tax rate. For example, we may have to include additional amounts in income under the so-called “global intangible low-taxed income” regime or as a result of the application of “controlled foreign corporation” rules. In addition, the United States has enacted the Inflation Reduction Act, which, among other changes, imposes a 1% excise tax on certain stock buybacks and an alternative minimum tax on adjusted financial statement income. In addition, our Canadian tax attributes (including net operating loss and tax credit carryforwards and deductible Scientific Research and Experimental Development Expenditure carryforwards) will generally not be available to offset U.S. income and may be subject to limitation.

Further, our future operations and business structure may result in increased tax burden. For example, changes in our clinical development plans and business or commercialization strategies may result in an increased effective tax rate. Taxation of international business operations and intercompany transactions, including transactions between us and non-U.S. subsidiaries, is complicated. Any changes in the U.S. or non-U.S. taxation of such activities may increase our worldwide effective tax rate and harm our business, financial condition, and results of operations.

Enforcement of rights against us in Canada may be limited.

Following the Redomicile Transactions, our principal executive offices are located in Middletown, Delaware and the majority of our directors, officers and experts reside outside of Canada. Accordingly, it may not be possible for our stockholders to effect service of process within Canada upon us or the majority of our directors, officers or experts, or to enforce judgments obtained in Canadian courts against us or the majority of our directors, officers or experts.

Risks Related to the Exchangeable Shares

The Exchangeable Shares will not be listed on any stock exchange.

Pursuant to the Redomicile Transactions, holders of Zymeworks BC common shares exchanged their Zymeworks BC common shares for shares of our common stock or, at their election with respect to all or a portion of their Zymeworks BC common shares and subject to applicable eligibility criteria and an overall cap, exchangeable shares (the “Exchangeable Shares”) in the capital of ExchangeCo. The Exchangeable Shares will not be listed on any stock exchange. Although Exchangeable Shares are exchangeable at the option of the holder for shares of our common stock, there is no market through which the Exchangeable Shares may be sold, and holders may not be able to sell their Exchangeable Shares.

Holders of Exchangeable Shares may experience a delay in receiving shares of our common stock from the date they request an exchange, which may affect the value of the shares the holder receives in such exchange.

Holders of Exchangeable Shares who request an exchange may not receive shares of our common stock until a period of time after the applicable request is received. During this period, the market price of our common stock may increase or decrease. Any such increase or decrease would affect the value of the consideration to be received by such a holder of Exchangeable Shares upon a subsequent sale of shares of our common stock received in the exchange.

There may be a taxable event for a holder of Exchangeable Shares beyond such holder’s control.

A holder of Exchangeable Shares will be considered to have disposed of Exchangeable Shares (i) on a redemption (including pursuant to a retraction request) of such Exchangeable Shares by holders of Exchangeable Shares or ExchangeCo, and (ii) on an acquisition of such Exchangeable Shares by us or CallCo. Although each is a taxable event, the Canadian federal income tax consequences of the disposition will be different depending on whether the event giving rise to the disposition is a redemption or an acquisition.

Prior to the sunset date of the Exchangeable Shares, ExchangeCo may redeem Exchangeable Shares in limited circumstances, and ExchangeCo shall redeem the Exchangeable Shares on the sunset date. Accordingly, an Eligible Holder may have a taxable event in a transaction beyond their control.

The tax treatment of Exchangeable Shares for non-Canadian tax purposes is uncertain.

The tax treatment of Exchangeable Shares for non-Canadian tax purposes, including U.S. federal income tax purposes, is uncertain. Holders of Exchangeable Shares who are subject to taxation in jurisdictions other than Canada should consult with their tax advisors regarding the tax treatment of Exchangeable Shares under non-Canadian tax laws and regulations.

Risks Related to Additional Legal and Compliance Matters

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, insider trading, and noncompliance with our policies and procedures.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with federal and state health care fraud and abuse laws and regulations, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Conduct and Business Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions. In addition, employees may become subject of allegations of gender discrimination and other misconduct that are not in compliance with our policies and procedures, which, regardless of the ultimate outcome, may result in adverse publicity that could materially harm our brand, reputation and business.

If we or our contractors or agents market products in a manner that violates healthcare fraud and abuse laws, or if we violate government price reporting laws and transparency laws, we may be subject to civil or criminal penalties.

In addition to FDA restrictions on the marketing of pharmaceutical products, federal and state healthcare laws restrict certain business practices in the biopharmaceutical industry. Although we currently do not have any products on the market, we may be subject, and if our product candidates are approved and we begin commercialization will be subject, to additional healthcare laws and regulations enforced by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. These state and federal healthcare laws, commonly referred to as “fraud and abuse” laws, have been applied to restrict certain marketing practices in the pharmaceutical industry, and include anti-kickback, false claims, data privacy and security and transparency statutes and regulations.

Federal false claims laws prohibit, among other things, any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, or causing to be made, a false statement to get a false claim paid. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. Most states also have statutes or regulations similar to the federal anti-kickback law and federal false claims laws, which may apply to items such as pharmaceutical products and services reimbursed by private insurers. Administrative, civil and criminal sanctions may be imposed under these federal and state laws.

The federal civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

HIPAA created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, including private third-party payors, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of, or payment for, healthcare benefits, items or services.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by HITECH, and its implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates-independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, and newly empowered state attorneys general with the authority to enforce HIPAA. In January 2013, the Office for Civil Rights of the U.S. Department of Health and Human Services issued the Final Omnibus Rule under HIPAA pursuant to HITECH that makes significant changes to the privacy, security and breach notification requirements and penalties. The Final Omnibus Rule generally took effect in September 2013 and enhances certain privacy and security protections, and strengthens the government's ability to enforce HIPAA. The Final Omnibus Rule also enhanced requirements for both covered entities and business associates regarding notification of breaches of unsecured protected health information. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways. These state laws may not have the same effect and often are not preempted by HIPAA, thus complicating compliance efforts.

Additionally, the PPACA also included the federal Physician Payments Sunshine Act, which requires applicable group purchasing organizations and manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually information related to certain payments or other transfers of value made in the previous year to covered recipients, including physicians, as defined by law, and teaching hospitals and, effective for data reported in 2022, expanded to include nurse practitioners, physician assistants, clinical nurse specialists, certified registered nurse anesthetists and anesthesiologist assistants, and certified nurse-midwives, including certain ownership and investment interests held by physicians or their immediate family members. Failure to comply with the required reporting requirements could subject applicable reporting entities such as manufacturers to substantial civil monetary penalties.

Also, many states have similar healthcare statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Certain states require pharmaceutical companies to implement a comprehensive compliance program that includes a limit or outright ban on expenditures for, or payments to, individual medical or health professionals and/or require pharmaceutical companies to track and report gifts and other payments made to physicians and other healthcare providers.

If our operations are found to be in violation of any of the healthcare laws or regulations described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion of products from reimbursement under government programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings or the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products will be sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

If we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.

Our research and development involves, and may in the future involve, the use of potentially hazardous materials and chemicals. Our operations may produce hazardous waste products. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards mandated by local, state and federal laws and regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations and fire and building codes, including those governing laboratory procedures, exposure to blood-borne pathogens, use and storage of flammable agents and the handling of biohazardous materials. Although we maintain workers' compensation insurance as prescribed by certain jurisdictions in which we operate to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of these materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate, any of these laws or regulations.

Risks Related to Employee Matters and Managing Growth

We may fail to achieve the expected cost savings and related benefits from our 2022 reduction in workforce.

In January 2022, we announced a plan to reduce our workforce to reflect our renewed focus on key priorities and enable us to help achieve a more cost-efficient organization necessary to execute on those priorities. While we completed the reduction in workforce by the end of 2022, the full impact of the reduction in workforce is not yet known.

We may fail to effectively achieve the stated goals of the reduction in workforce. Our plans may also change as we continue to refocus on our key priorities. These actions may take more time than we currently estimate and we may not be able to achieve the cost-efficiencies sought. In addition, while the reduction in workforce was completed in 2022, it may still negatively impact employee morale for those that were not directly impacted, which may increase employee attrition and hinder our ability to achieve our key priorities. Any failure to achieve the expected benefits from the reduction in workforce or from other recent management and personnel related changes could adversely affect our stock price, financial condition and ability to achieve our key priorities.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on key members of our senior management team, including Kenneth Galbraith, the Chair of our board of directors and Chief Executive Officer, Neil Klompas, our President and Chief Operating Officer, Christopher Astle, our Chief Financial Officer, Paul Moore, our Chief Scientific Officer, and other key members of our senior management, scientific and clinical teams. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. The loss of the services of our key senior managers and employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy.

Retention and any future recruitment of qualified scientific, technical, clinical, manufacturing and sales and marketing personnel will also be critical to our success. In addition, we will need to effectively manage our managerial, operational, financial, development and other resources in order to successfully pursue our research, development and commercialization efforts for our existing and future product candidates. Furthermore, replacing key senior managers and employees may be difficult and may take an extended period of time because of the limited talent pool in our industry due to the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. The reduction in workforce announced in January 2022 may also make retention of our current personnel both more important and more challenging. Intense competition for

attracting key skill-sets and the impact of inflationary pressure on wages may limit our ability to attract, retain and motivate key personnel on acceptable terms. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our business strategy will be limited.

As we advance our development and commercialization plans and strategies, we may need to grow or modify our organization, and we may experience difficulty in managing such change, which could disrupt our operations.

As of December 31, 2022, we had 291 full-time employees. As we advance our development and commercialization plans and strategies in the future, we anticipate that we may need to expand or modify our employee base. Additionally, as our product candidates enter and advance through preclinical studies and any clinical trials, we may need to expand our development, manufacturing, regulatory sales and marketing capabilities or contract with other organizations to provide these capabilities for us. Future growth would impose significant added responsibilities on members of management, including the need to identify, recruit, maintain, motivate and integrate additional employees. Also, our management may need to divert a disproportionate amount of their attention away from our day-to-day activities and devote a substantial amount of time to managing any necessary growth activities. We may not be able to effectively manage an expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational errors, loss of business opportunities, loss of employees and reduced productivity amongst remaining employees. Any growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of existing and additional product candidates. If our management is unable to effectively manage any needed growth, our expenses may increase more than expected, our ability to generate or grow revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates and compete effectively with others in our industry will depend on our ability to effectively manage any future growth.

Risks Related to Our Common Stock

Our stock price is likely to be volatile and the market price of our common stock may drop below the price paid by stockholders.

Investors should consider an investment in our common stock as risky and invest only if they can withstand a significant loss and wide fluctuations in the market value of their investment. Investors may be unable to sell their common stock at or above the price they paid for such stock due to fluctuations in the market price of our common stock arising from changes in our operating performance or prospects. Some of the factors that may cause the market price of our common stock to fluctuate or decrease include:

- results and timing of our clinical trials and clinical trials of our competitors' products;
- failure or discontinuation of any of our development programs;
- the success of our partnerships, including our and Jazz's ability and efforts to collaborate to develop and commercialize zanidatamab in the territories covered by the Jazz Collaboration Agreement;
- our ability to achieve milestones and receive associated milestone payments pursuant to the terms of our collaboration agreements;
- issues in manufacturing our product candidates or future approved products;
- regulatory developments or enforcement in the United States and foreign countries with respect to our product candidates or our competitors' products;
- competition from existing products or new products that may emerge;
- developments or disputes concerning patents or other proprietary rights;
- introduction of technological innovations or new commercial products by us or our competitors;

Table of Contents

- announcements by us, our strategic partners or our competitors of significant acquisitions, strategic partnerships, joint ventures, or capital commitments;
- changes in estimates or recommendations by securities analysts that cover our common stock;
- fluctuations in the valuation of companies in the biotechnology industry or otherwise perceived by investors to be comparable to us;
- additional instances of stockholder activism, including unsolicited takeover proposals or proxy contests;
- claims or litigation related to our stockholder rights plan;
- public concern over our product candidates or any future approved products;
- litigation;
- future sales of our common stock;
- stock price and volume fluctuations attributable to inconsistent trading volume levels of our common stock;
- additions or departures of key personnel;
- our ability to execute on our key strategic priorities;
- changes in the structure of health care payment systems in the United States or other countries;
- failure of any of our product candidates, if approved, to achieve commercial success;
- economic and other external factors or other disasters or crises, including pandemics;
- period-to-period fluctuations in our financial condition and results of operations, including the timing of receipt of any milestone or other payments under commercialization or licensing agreements;
- general market conditions and market conditions for biopharmaceutical stocks;
- potential disagreements or disputes with certain of our stockholders;
- overall fluctuations in U.S. equity markets; and
- other factors that may be unanticipated or out of our control.

In addition, the stock market in general, and the stock of biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of the relevant companies, including recently in connection with the COVID-19 pandemic, which has resulted in increased volatility and decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. Broad market and industry factors, including potentially worsening economic conditions and other adverse effects or developments relating to the COVID-19 pandemic, may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this “Risk Factors” section, could have a material adverse effect on the market price of our common stock.

An active trading market for our common stock may not be sustained.

Our common stock was first listed on the NYSE in connection with the completion of the Redomicile Transactions on October 13, 2022. In December 2022, we moved our listing to The Nasdaq Stock Market LLC. There can be no assurance that an active trading market for our common stock will be sustained or continue to be as active or liquid as was the trading market for Zymeworks BC’s common shares prior to the Redomicile Transactions, and the trading price of our common stock may be effectively lower than the trading price of Zymeworks BC’s common shares. If an active market for our common stock does not continue, it may be difficult for our stockholders to sell their stock without depressing the market price for the common stock or sell their common stock at or above the prices at which they acquired their common stock or sell their common stock at the time they would like to sell. Any inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling common stock and may impair our ability to acquire other companies or technologies by using our common stock as consideration.

We may fail to meet the continued listing requirements of The Nasdaq Stock Market LLC. If Nasdaq delists our shares of common stock from trading on its exchange, we could face significant material adverse consequences, including:

Table of Contents

- significant impairment of the liquidity for our common stock, which may substantially decrease the market price of our common stock;
- a limited availability of market quotations for our securities;
- a determination that our common stock qualifies as a “penny stock” which will require brokers trading in our common stock to adhere to more stringent rules and possibly resulting in a reduced level of trading activity in the secondary trading market for our common stock;
- a limited amount of news and analyst coverage for our company; and
- a decreased ability to issue additional securities or obtain additional financing in the future.

Substantial future sales of our common stock, or the perception that these sales could occur, may cause the price of our common stock to drop significantly, even if our business is performing well.

A large volume of sales of our common stock could decrease the prevailing market price of our common stock and could impair our ability to raise additional capital through the sale of equity securities in the future. Even if a substantial number of sales of our common stock does not occur, the mere perception of the possibility of these sales could depress the market price of our common stock and have a negative effect on our ability to raise capital in the future.

Our management team has broad discretion to use the net proceeds from public and private and debt financings as well as funds received pursuant to our strategic collaborations, and its investment of these proceeds may not yield a favorable return. They may invest the proceeds in ways with which our stockholders disagree.

Our management team has broad discretion in the application of the net proceeds we received pursuant to our January 2022 public offering of common shares and pre-funded warrants to purchase common shares, as well as funds we receive from time to time pursuant to our strategic collaborations and that we may receive from future fundraising efforts, including pursuant to any “at-the-market” equity offering programs we may use from time to time, and we could spend or invest the proceeds in ways with which our stockholders disagree. Accordingly, stockholders will need to rely on our management team’s judgment with respect to the use of these proceeds. However, the failure by management to apply these funds effectively could negatively affect our ability to operate and grow our business.

We cannot specify with certainty all of the particular uses for the net proceeds to be received from our fundraising efforts or for the funds received from time to time pursuant to our strategic collaborations. In addition, the amount, allocation and timing of our actual expenditures will depend upon numerous factors, including additional milestone payments received from our strategic partnerships and royalties received on sale of any future approved product. Accordingly, we will have broad discretion in using these proceeds. Until the net proceeds are used, they may be placed in investments that do not produce significant income or that may lose value.

If you purchase shares of our common stock sold in this offering, you will experience immediate and substantial dilution in the net tangible book value of your shares. In addition, we may issue additional equity or convertible debt securities in the future, which may result in additional dilution to investors.

The price per share of our common stock being offered may be higher than the net tangible book value per share of our outstanding common stock prior to this offering. Assuming that an aggregate of 18,867,924 shares of our common stock are sold at a price of \$7.95 per share, the last reported sale price of our common stock on Nasdaq on March 6, 2023, for aggregate gross proceeds of approximately \$150.0 million, and after deducting commissions and estimated offering expenses payable by us, new investors in this offering would incur immediate dilution of \$0.62 per share.

For a more detailed discussion of the foregoing, see the section entitled “Dilution” below. To the extent outstanding stock options or warrants are exercised, there will be further dilution to new investors. In addition, to the extent we need to raise additional capital in the future and we issue additional shares of common stock or securities convertible or exchangeable for our common stock, our then existing stockholders may experience dilution and the new securities may have rights senior to those of our common stock offered in this offering.

We do not anticipate paying cash dividends for the foreseeable future, and accordingly, stockholders must rely on stock appreciation for any return on their investment.

We have never paid any dividends on our common stock. We currently intend to retain our future earnings, if any, to fund the development and growth of our business and do not anticipate that we will declare or pay any cash dividends on our common stock in the foreseeable future. As a result, capital appreciation, if any, of our common stock will be the sole source of gain on investment in our common stock for the foreseeable future. Investors seeking cash dividends should not invest in our common stock.

Any future determination to pay dividends will be at the discretion of our board of directors and will depend upon many factors, including our results of operations, financial position, capital requirements, distributable reserves, credit terms, general economic conditions and other factors as our board of directors may deem relevant from time to time. Consequently, future dividends payable to investors are not guaranteed.

Our principal stockholders, in aggregate, could exert substantial influence over us which could delay or prevent a change in corporate control or result in the entrenchment of management or the board of directors.

Our principal stockholders, being our stockholders that beneficially own 5% or more of our common stock, together with their affiliates and related persons, in aggregate, beneficially own approximately 51.4% of our outstanding common stock as of December 31, 2022. Our directors and executive officers beneficially own, in the aggregate, approximately 1.9% of our outstanding common stock as of December 31, 2022. Our principal stockholders, if acting together (with or without our directors and executive officers), may have the ability to exert substantial influence over the outcome of matters submitted to our stockholders for approval, including the election and removal of directors and any merger or sale of all or substantially all of our assets. In addition, our principal stockholders, if acting together (with or without our directors and executive officers), may have the ability to exert substantial influence over the management and affairs of our company. Accordingly, this concentration of ownership could harm the market price of our common stock by:

- delaying, deferring, or preventing a change in control;
- entrenching our management or the board of directors;
- impeding a merger, takeover, or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

We have recently qualified as a smaller reporting company, and any decision on our part to comply only with certain reduced reporting and disclosure requirements applicable to such companies could make our common stock less attractive to investors.

As a result of our public float (the market value of our common stock held by non-affiliates) as of June 30, 2022, we qualify as a “smaller reporting company,” as defined under the Exchange Act. In addition, we are a “non-accelerated filer” as defined under the Exchange Act. For as long as we continue to be a smaller reporting company or a non-accelerated filer, we may choose to take advantage of exemptions from various reporting requirements applicable to other public companies that are not smaller reporting companies or non-accelerated filers, as applicable, including, but not limited to, an exemption from the requirement that our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting under Section 404. We have opted not to obtain such

attestation from our independent registered public accounting firm in connection with our Annual Report on Form 10-K. This decision may have a detrimental impact on our ability to maintain the adequacy of our internal control over financial reporting, and any failure to maintain adequacy, or inability to produce accurate financial statements or other reports on a timely basis, could increase our operating costs and could materially impair our ability to operate our business.

For so long as we choose to rely on any of these disclosure exemptions, the information we provide stockholders will be different than the information that is available with respect to other public companies. Moreover, if some investors find our common stock less attractive as a result of any choices to reduce our disclosure, there may be a less active trading market for our common stock and the market price of our common stock may be more volatile.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Under the Sarbanes-Oxley Act of 2002, we are required to establish and maintain effective internal control over financial reporting and adequate disclosure controls and procedures. Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Even if our management concludes that our internal control over financial reporting is effective, our independent registered public accounting firm may conclude that there are material weaknesses with respect to our internal controls or the level at which our internal controls are documented, designed, implemented or reviewed. Undetected material weaknesses in our internal controls could lead to financial statement restatements and require us to incur the expense of remediation.

We have transitioned to a new enterprise resource planning system, which we believe will lead to improvements in our internal control over financial reporting. Although we have completed this transition to a new enterprise resource planning system, the full impact of this transition is not yet known. If, during the evaluation and testing process of our internal controls, we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses in our internal controls over financial reporting in the future. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets. Furthermore, if we cannot provide reliable financial reports or prevent fraud, including as a result of remote working by our employees, our business and results of operations would likely be materially and adversely affected.

Delaware law and provisions in our amended and restated certificate of incorporation and amended and restated bylaws might delay, discourage or prevent a change in control of Zymeworks or changes in our management, thereby depressing the market price of our common stock.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may make the acquisition of Zymeworks more difficult or delay or prevent changes in control of its management. Among other things, these provisions:

- authorize our board of directors to issue shares of preferred stock and determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval;
- permit only the board of directors to establish the number of directors and fill vacancies and newly created directorships on the board, provided that the board of directors' ability to increase the size of the board and fill vacancies and newly created directorships will be subject to the restrictions in our amended and restated certificate of incorporation and amended and restated bylaws;

Table of Contents

- establish that members of our board of directors serve in one of three staggered terms of three years each;
- provide that our directors may only be removed by the affirmative vote of at least 66 2/3% of the voting power of the shares cast on such proposal;
- permit stockholders to only take actions at a duly called annual or special meeting and not by written consent;
- require that stockholders give advance notice to nominate directors or submit proposals for consideration at stockholder meetings;
- not provide for cumulative voting rights in the election of directors;
- provide that special meetings of Zymeworks' stockholders may be called only by the board of directors, the chairperson of the board of directors, Zymeworks' chief executive officer, president or the secretary upon request from holders of no less than 20% of our outstanding voting stock, subject to the limitations and requirements set forth in our amended and restated bylaws; and
- require a super-majority vote of stockholders to amend some of the provisions described above.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the DGCL, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any "interested stockholder" for a period of three years following the date on which the stockholder became an "interested stockholder" unless certain conditions are met.

These provisions, alone or together, could delay, discourage or prevent a transaction involving a change in control of Zymeworks. These provisions could also discourage proxy contests and make it more difficult for stockholders to elect directors of their choosing and to cause Zymeworks to take other corporate actions they desire, any of which, under certain circumstances, could limit the opportunity for our stockholders to receive a premium for their shares of common stock, and could also affect the price that some investors are willing to pay for our common stock.

The stockholders' rights plan adopted by our board of directors may discourage a third party from acquiring us in a manner that could result in a premium price to our stockholders.

On October 12, 2022, we entered into a Preferred Stock Rights Agreement, or the "New Rights Plan," pursuant to which our board of directors authorized and declared a dividend distribution of one right, or each, a "Right," for each share of our common stock outstanding on October 13, 2022, or the "Record Date," and for each share of common stock that becomes outstanding between the Record Date and the earlier of the date the Rights become exercisable and the expiration of the Rights. Each Right entitles the registered holder to purchase from us one one-thousandth of a share of our Series B Participating Preferred Stock at an exercise price of \$74.00, subject to adjustment. In general terms, the New Rights Plan works by imposing a significant penalty upon any person or group that acquires 10 percent or more (or 20 percent or more in the case of certain institutional investors who report their holdings on Schedule 13G) of the shares of our common stock without the approval of our board of directors. As a result, the overall effect of the New Rights Plan and the issuance of the Rights may be to render more difficult or discourage a merger, amalgamation, arrangement, take-over bid, tender or exchange offer or other business combination involving us that is not approved by our board of directors. However, neither the New Rights Plan nor the Rights should interfere with any merger, amalgamation, arrangement, take-over bid, tender or exchange offer or other business combination approved by the Board. The terms of the New Rights Plan are substantively similar in all material respects to the terms of the Zymeworks BC Preferred Shares Rights Agreement, which expired in connection with the completion of the Redomicile Transactions.

Our amended and restated bylaws designate a state or federal court located within the State of Delaware as the exclusive forum for substantially all disputes between Zymeworks and its stockholders, and also provide that the federal district courts are the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, each of which could limit our stockholders' ability to choose the judicial forum for disputes with Zymeworks or its directors, officers, stockholders or employees.

Our amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, stockholders, officers or other employees to Zymeworks or our stockholders, (3) any action arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws or (4) any other action asserting a claim that is governed by the internal affairs doctrine shall be the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, another State court in Delaware or the federal district court for the District of Delaware), except for any claim as to which such court determines that there is an indispensable party not subject to the jurisdiction of such court (and the indispensable party does not consent to the personal jurisdiction of such court within ten days following such determination), which is vested in the exclusive jurisdiction of a court or forum other than such court or for which such court does not have subject matter jurisdiction. This provision does not apply to any action brought to enforce a duty or liability created by the Exchange Act and the rules and regulations thereunder.

Section 22 of the Securities Act establishes concurrent jurisdiction for federal and state courts over Securities Act claims. Accordingly, both state and federal courts have jurisdiction to hear such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated bylaws provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States will be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

Any person or entity purchasing or otherwise acquiring or holding or owning (or continuing to hold or own) any interest in any of our securities shall be deemed to have notice of and consented to the foregoing bylaw provisions. Although we believe these exclusive forum provisions benefit us by providing increased consistency in the application of Delaware law and federal securities laws in the types of lawsuits to which each applies, the exclusive forum provisions may limit a stockholder's ability to bring a claim in a judicial forum of its choosing for disputes with us or our current or former directors, officers, stockholders or other employees, which may discourage such lawsuits against us and our current and former directors, officers, stockholders and other employees. Our stockholders will not be deemed to have waived its compliance with the federal securities laws and the rules and regulations thereunder as a result of our exclusive forum provisions.

The enforceability of similar exclusive forum provisions in other companies' organizational documents have been challenged in legal proceedings, and, while certain courts have determined these provisions are enforceable, it is possible that a court of law could rule that these types of provisions are inapplicable or unenforceable if they are challenged in a proceeding or otherwise. If a court were to find either exclusive forum provision contained in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur significant additional costs associated with resolving such action in other jurisdictions, which could harm our financial condition and results of operations.

General Risk Factors

We are at risk of securities class action litigation.

Securities class action litigation has often been brought against companies following a decline in the market price of their securities. This risk is especially relevant for us because biotechnology companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could materially harm our business.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. We cannot assure that analysts will cover us or provide accurate or favorable coverage. If one or more of the analysts who cover us downgrade our stock or change their opinion of our common stock negatively, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our stock price or trading volume to decline. Moreover, the research and reports that analysts publish may suggest a price for our common stock that does not fully or accurately reflect the true value of our company. Furthermore, even if such analyst publications are favorable, these reports could have negative consequences for us.

USE OF PROCEEDS

The amount of net proceeds from this offering will depend upon the number of shares of our common stock sold and the market prices at which they are sold. There can be no assurance that we will be able to sell any shares of our common stock under or fully utilize the Sales Agreement as a source of financing.

We intend to use the net proceeds from the sale of shares of our common stock pursuant to this offering, if any, together with our existing cash and cash equivalents, (i) to continue research and development relating to zanidatamab zovodotin and our other preclinical and discovery-stage programs and (ii) for general corporate purposes. We have negative operating cash flow and it is expected that the proceeds from the offering will be used to fund operating cash flow. We expect our current cash, cash equivalents and short-term investments, combined with certain anticipated milestone payments from our existing collaboration agreements, including our agreement with Jazz, and the anticipated net proceeds from this offering, to fund our planned operations through 2026, and potentially beyond. These estimates include certain future milestone payments which are dependent upon the successful completion of specified research and development activities by Zymeworks and our collaborators and therefore are uncertain at this time.

The key business objectives we intend to meet with the net proceeds are to continue research and development relating to zanidatamab zovodotin and our other preclinical and discovery-stage programs. These objectives will require additional capital exceeding our cash on hand resources even after giving effect to the offering. In addition, actual costs and development time may exceed management's current expectations. It is unlikely that we will generate sufficient operating cash flow to meet the total capital obligations in the proposed development time frame. Accordingly, we will need to raise additional capital in the future over and above the current offering.

Our management will have broad discretion in the application of the net proceeds, if any, from this offering, and the amounts and timing of our actual expenditures will depend on numerous factors, including those listed under the section titled "Risk Factors" in this prospectus supplement and the accompanying base shelf prospectus and the documents incorporated by reference herein and therein. We therefore cannot estimate with certainty the amount of net proceeds to be used for the purposes described above. While we intend to spend the net proceeds of the offering as stated above, there may be circumstances where, for sound business reasons, a re-allocation of funds may be necessary or advisable.

DILUTION

If you invest in shares of our common stock, your interest will be diluted to the extent of the difference between the price per share you pay in this offering and the net tangible book value per share of our common stock immediately after you purchase shares in this offering. As of December 31, 2022, our net tangible book value was approximately \$454.5 million, or approximately \$7.21 per share, based on 63,059,501 shares of common stock outstanding as of December 31, 2022. Our net tangible book value per share represents the amount of our total tangible assets reduced by the amount of our total liabilities, divided by the total number of shares of common stock outstanding as of December 31, 2022.

After giving effect to the sale of our common stock in the aggregate amount of \$150,000,000 at an assumed offering price of \$7.95 per common stock, which is the last reported sale price of our common stock on Nasdaq on March 6, 2023, and after deducting estimated offering expenses and commissions payable by us, our net tangible book value as of December 31, 2022 would have been \$600.4 million, or \$7.33 per share. This represents an immediate increase in net tangible book value of \$0.12 per share to our existing stockholders and an immediate dilution in net tangible book value of \$0.62 per share to new investors in this offering.

The following table illustrates this calculation on a per share of common stock basis:

Assumed public offering price per share	\$7.95
Net tangible book value per share at December 31, 2022	\$7.21
Increase in net tangible book value per share attributable to the offering	\$0.12
As adjusted net tangible book value per share after giving effect to the offering	<u>\$7.33</u>
Dilution in net tangible book value per share to new investors in this offering	<u>\$0.62</u>

The number of shares of common stock shown as outstanding in the table above is based on 63,059,501 shares of common stock outstanding as of December 31, 2022 and excludes:

- 1,374,601 shares of common stock issuable upon the exercise of fully-vested outstanding options to purchase shares of common stock, at a weighted average exercise price of C\$20.23 per share, and 2,553,862 shares of common stock issuable upon the exercise of fully-vested outstanding options to purchase shares of common stock, at a weighted average exercise price of \$20.86 per share, in each case as of December 31, 2022;
- 772,540 shares of common stock issuable upon the exercise of unvested outstanding options to purchase shares of common stock, at a weighted average exercise price of C\$16.86 per share, and 2,311,283 shares of common stock issuable upon the exercise of unvested outstanding options to purchase shares of common stock, at a weighted average exercise price of \$14.38 per share, in each case as of December 31, 2022;
- 700,000 shares of common stock issuable upon the exercise of unvested outstanding options to purchase shares of common stock, as of December 31, 2022, at a weighted average exercise price of \$12.36 per share;
- 227,223 shares of common stock issuable upon vesting of outstanding restricted stock units outstanding as of December 31, 2022;
- 3,205,132 shares of common stock reserved for future issuance under our stock option plan and 1,722,239 shares of common stock reserved for future issuance under our employee stock purchase plan, in each case as of December 31, 2022;

[Table of Contents](#)

- 50,000 shares of common stock reserved for future issuance under our Inducement Stock Option and Equity Compensation Plan as of December 31, 2022;
- 1,424,533 shares of common stock issuable upon the exchange of the Exchangeable Shares as of December 31, 2022; and
- 2,079,224 shares of common stock issuable upon the exercise of pre-funded warrants as of December 31, 2022.

To the extent that outstanding options are exercised or other shares are issued, investors purchasing shares of our common stock in this offering may experience further dilution. In addition, we may choose to issue additional shares of our common stock, or securities convertible into or exchangeable for shares of our common stock, in the future. The issuance of these securities could result in further dilution for investors purchasing shares of our common stock in this offering.

PLAN OF DISTRIBUTION

We have previously entered into a sales agreement, or the Sales Agreement, with Cantor Fitzgerald & Co., or Cantor. Pursuant to this prospectus supplement, we may offer and sell shares of our common stock having an aggregate gross sales price of up to \$150,000,000 from time to time through Cantor acting as sales agent. A copy of the Sales Agreement was filed as an exhibit to a Current Report on Form 8-K and is incorporated by reference into this prospectus supplement.

Upon delivery of a placement notice and subject to the terms and conditions of the Sales Agreement, Cantor may sell shares of our common stock by any method permitted by law deemed to be an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act. We may instruct the Cantor not to sell common stock if the sales cannot be effected at or above the price designated by us from time to time. We or Cantor may suspend the offering of common stock upon notice and subject to other conditions.

We will pay Cantor commissions, in cash, for its service in acting as agent in the sale of our common stock. Cantor will be entitled to compensation at a commission rate of up to 3.0% of the sales price per share sold under the Sales Agreement. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We have also agreed to reimburse Cantor for certain specified expenses, including the fees and disbursements of their legal counsel in an amount not to exceed \$75,000 and certain ongoing expenses. We estimate that the total expenses for the offering, excluding compensation and reimbursements payable to Cantor under the terms of the Sales Agreement, will be approximately \$250,000.

Settlement for sales of shares of our common stock will occur on the second business day following the date on which any sales are made, or on some other date that is agreed upon by us and Cantor in connection with a particular transaction, in return for payment of the net proceeds to us. Sales of our common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Cantor may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Cantor will use its commercially reasonable efforts, consistent with its sales and trading practices, to solicit offers to purchase the common stock under the terms and subject to the conditions set forth in the Sales Agreement. In connection with the sale of the common stock on our behalf, Cantor will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Cantor will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to Cantor against certain civil liabilities, including liabilities under the Securities Act.

The offering of shares of our common stock pursuant to the Sales Agreement will terminate upon the termination of the Sales Agreement as permitted therein. We and Cantor may each terminate the Sales Agreement at any time upon ten days’ prior notice.

Cantor and its affiliates may in the future provide various investment banking, commercial banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M, Cantor will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus supplement.

This prospectus supplement and the accompanying prospectus may be made available in electronic format on a website maintained by Cantor and Cantor may distribute this prospectus supplement and the accompanying prospectus electronically.

LEGAL MATTERS

Certain legal matters in connection with the securities offered hereby will be passed upon on behalf of the Company by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Cantor Fitzgerald & Co. is being represented in connection with this offering by Cooley LLP, New York, New York.

EXPERTS

The consolidated financial statements of Zymeworks as of December 31, 2021 and 2020, and for each of the years in the three-year period ended December 31, 2021, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2021, have been incorporated by reference herein in reliance upon the reports of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and accompanying base shelf prospectus are part of the registration statement on Form S-3 (File No. 333-259970) that Zymeworks BC filed with the SEC under the Securities Act. In connection with the Redomicile Transactions completed on October 13, 2022, we assumed the registration statement on Form S-3 as the successor registrant to Zymeworks BC pursuant to Rule 414.

This prospectus supplement and accompanying base shelf prospectus do not contain all of the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or accompanying base shelf prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus supplement and the accompanying base shelf prospectus for a copy of such contract, agreement or other document.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to you, free of charge, on the SEC's website at www.sec.gov. You may also obtain additional information by visiting our website at www.zymeworks.com. The references to www.zymeworks.com in this prospectus supplement, the accompanying base shelf prospectus and the documents incorporated by reference herein or therein are inactive textual references only, and the information found on our internet website is not incorporated by reference into, and should not be considered part of, this prospectus supplement, the accompanying base shelf prospectus or the documents incorporated by reference herein or therein. Investors should not rely on any such information in deciding whether to invest in our common stock.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to “incorporate by reference” information into this prospectus supplement which has been previously filed with the SEC, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement, except for any information superseded by information included or subsequently incorporated by reference in this prospectus supplement. Either we or Zymeworks BC have filed the documents listed below with the SEC under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and these documents are incorporated herein by reference (other than those documents or the portions of those documents furnished pursuant to Items 2.02 or 7.01 of any Current Report on Form 8-K and, except as may be noted in any such Form 8-K, exhibits filed on such form that are related to such information):

- Zymeworks BC’s [Annual Report on Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on February 24, 2022;
- Zymeworks BC’s [Amendment No. 1 to Annual Report on Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on May 2, 2022;
- Zymeworks BC’s Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2022 and June 30, 2022, filed with the SEC on [May 4, 2022](#) and [August 4, 2022](#), respectively;
- our Quarterly Report on [Form 10-Q](#) for the quarterly period ended September 30, 2022, filed with the SEC on November 8, 2022;
- Zymeworks BC’s Current Reports on Form 8-K filed with the SEC on [January 5, 2022](#); [January 19, 2022](#); [January 27, 2022](#); [January 31, 2022](#); [February 25, 2022](#); [March 9, 2022](#); [May 2, 2022](#) (Amendment No. 1 to Form 8-K originally filed with the SEC on January 19, 2022); [May 26, 2022](#); [June 10, 2022](#); [July 15, 2022](#); [August 5, 2022](#); [August 12, 2022](#); [August 19, 2022](#); [August 26, 2022](#); [September 2, 2022](#); [September 8, 2022](#); [September 22, 2022](#); [October 11, 2022](#); [October 12, 2022](#); [October 18, 2022](#); [October 19, 2022](#) and [October 21, 2022](#);
- our Current Reports on Form 8-K filed with the SEC on [October 13, 2022](#); [October 19, 2022](#); [October 21, 2022](#); [October 28, 2022](#); [November 9, 2022](#); [November 18, 2022](#); [November 29, 2022](#); [December 5, 2022](#); [December 9, 2022](#); [December 19, 2022](#); [December 19, 2022](#); [December 21, 2022](#); [December 30, 2022](#); [January 4, 2023](#); and [January 19, 2023](#);
- our Form 8-K12B, filed with the SEC on [October 13, 2022](#);
- the description of our common stock and the preferred stock purchase rights associated with our common stock contained in the Registration Statement on [Form 8-A](#) relating thereto, filed with the SEC on December 15, 2022, including any amendment or report filed for the purpose of updating such description; and
- all other documents filed by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after December 31, 2022 but before the date of this prospectus supplement.

All documents that we file (but not those that we furnish) with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus supplement and prior to the termination of the offering of common stock hereby will be deemed to be incorporated by reference into this prospectus supplement and will automatically update and supersede the information in this prospectus supplement and any previously filed document.

[Table of Contents](#)

We will provide to each person, including any beneficial owner, to whom a copy of this prospectus supplement is delivered, a copy of any or all of the information that has been incorporated by reference in this prospectus supplement but not delivered with this prospectus supplement (other than the exhibits to such documents which are not specifically incorporated by reference herein). We will provide this information at no cost to the requester upon written or oral request to:

Zymeworks Inc.
108 Patriot Drive, Suite A
Middletown, Delaware 19709
Attn: Corporate Secretary
Phone: (302) 274-8744

S-78



zymeworks

Up to \$150,000,000

Common Stock

PROSPECTUS SUPPLEMENT

CANTOR

March 7, 2023

PROSPECTUS



Up to 2,737,836 Shares

Common Stock

We are registering the issuance, from time to time, of up to 2,737,836 shares of our common stock consisting of:

- up to 658,612 shares of common stock issuable upon the exchange of exchangeable shares, or the Exchangeable Shares, in the capital of Zymeworks ExchangeCo Ltd., or ExchangeCo, a company existing under the laws of British Columbia and our indirect subsidiary, which issued the Exchangeable Shares to certain shareholders of Zymeworks BC Inc., or Zymeworks BC, in connection with a series of transactions, including a redomicile that closed on October 13, 2022, or the Redomicile Transactions; and
- up to 2,079,224 shares of common stock issuable upon the exercise of pre-funded warrants that were originally issued by Zymeworks BC and assumed by us in connection with the Redomicile Transactions.

We will not receive any proceeds from the issuance of shares of our common stock in exchange for Exchangeable Shares. We expect to receive nominal proceeds, if any, from the issuance of shares of our common stock upon the exercise of pre-funded warrants.

Our common stock is listed on the Nasdaq Stock Market LLC, or Nasdaq, under the symbol "ZYME." On March 6, 2023, the last reported sale price of our common stock on Nasdaq was \$7.95 per share.

Investing in our securities involves risks. Please carefully read the information under the headings "[Risk Factors](#)" beginning on page 6 of this prospectus and "Item 1A – Risk Factors" of our most recent report on Form 10-K or 10-Q that is incorporated by reference in this prospectus before you invest in our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is March 7, 2023.

TABLE OF CONTENTS

	<u>Page</u>
ABOUT THIS PROSPECTUS	1
PROSPECTUS SUMMARY	3
RISK FACTORS	6
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS	63
USE OF PROCEEDS	68
DESCRIPTION OF CAPITAL STOCK	69
PLAN OF DISTRIBUTION	70
CERTAIN MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS	71
CERTAIN CANADIAN INCOME TAX CONSIDERATIONS	77
LEGAL MATTERS	82
EXPERTS	82
WHERE YOU CAN FIND MORE INFORMATION	83
INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE	83

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the SEC using a “shelf” registration process pursuant to which we may, from time to time, issue up to 2,737,836 shares of our common stock consisting of (i) up to 658,612 shares of common stock issuable upon the exchange of the Exchangeable Shares and (ii) up to 2,079,224 shares of common stock issuable upon the exercise of pre-funded warrants.

This prospectus provides you with a general description of our common stock that may be issued. Before you invest in our securities, you should read both this prospectus and any applicable prospectus supplement together with the additional information described in the sections titled “Where You Can Find More Information” and “Incorporation by Reference.”

We have not authorized anyone to provide you with information that is different from that contained, or incorporated by reference, in this prospectus, any applicable prospectus supplement or in any related free writing prospectus. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus and any applicable prospectus supplement or any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the applicable prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Market data and certain industry forecasts used in this prospectus and the documents incorporated by reference herein or therein were obtained from market research, publicly available information and industry publications. We believe that these sources are generally reliable, but the accuracy and completeness of this information is not guaranteed. We have not independently verified such information, and we do not make any representation as to the accuracy of such information.

Unless otherwise indicated in this prospectus, all dollar amounts and references to “\$” or “US\$” are to U.S. dollars and references to “C\$” are to Canadian dollars. This prospectus and the documents incorporated by reference herein and therein contain translations of some Canadian dollar amounts into U.S. dollars solely for your convenience.

In this prospectus, unless the context otherwise requires or otherwise expressly states, all references to “we,” “us,” “our” or similar terms, as well as references to “Zymeworks” or the “Company,” (i) for periods until the completion of the Redomicile Transactions (as defined below), refer to Zymeworks BC Inc. (formerly known as “Zymeworks Inc.”), or Zymeworks BC, either alone or together with its wholly owned subsidiaries, Zymeworks Biopharmaceuticals Inc., Zymeworks Pharmaceuticals Limited, Zymeworks Inc. (formerly known as Zymeworks Delaware Inc.), Zymeworks CallCo ULC, or CallCo, Zymeworks ExchangeCo Ltd., or ExchangeCo, and Zymeworks Management Inc. and (ii) for periods after the completion of the Redomicile Transactions, refer to Zymeworks Inc., either alone or together with its subsidiaries, including, as applicable, Zymeworks BC, Zymeworks Biopharmaceuticals Inc., Zymeworks Pharmaceuticals Limited, CallCo, ExchangeCo, Zymeworks Management Inc., Zymeworks Zanidatamab Inc., and Zymeworks Lifesciences Pte. Ltd.

Furthermore, except as otherwise indicated, references to “Merck,” “BMS,” “GSK,” “Daiichi Sankyo,” “Janssen,” “LEO,” “BeiGene,” “Iconic,” “Pfizer,” “Atreca” and “Jazz” refer to Merck Sharp & Dohme Research GmbH, Celgene Corporation and Celgene Alpine Investment Co. LLC (now a Bristol-Myers Squibb company), GlaxoSmithKline Intellectual Property Development Limited, Daiichi Sankyo Co., Ltd., Janssen Biotech, Inc., LEO Pharma A/S, BeiGene Ltd., Iconic Therapeutics, Inc., Pfizer Inc., Atreca, Inc. and Jazz Pharmaceuticals Ireland Limited, respectively.

[Table of Contents](#)

We own or have rights to trademarks, service marks or trade names that we use in connection with the operation of our business. In addition, our names, logos and website names and addresses are our service marks or trademarks. Our registered trademarks include Azymetric, Zymeworks, ZymeCAD, EFECT, ZymeLink and the phrase “Building Better Biologics”. The other trademarks, trade names and service marks appearing in this prospectus and documents incorporated by reference herein and therein are the property of their respective owners. Solely for convenience, the trademarks, service marks, tradenames and copyrights referred to in this prospectus are listed without the ©, ® and TM symbols, but we will assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensors to these trademarks, service marks and tradenames.

PROSPECTUS SUMMARY

This summary highlights selected information that is presented in greater detail elsewhere, or incorporated by reference, in this prospectus. It does not contain all of the information that may be important to you and your investment decision. Before investing in our securities, you should carefully read this entire prospectus, including the matters set forth in the section titled “Risk Factors” and the financial statements and related notes and other information that we incorporate by reference herein, including our Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q. Unless the context indicates otherwise, references in this prospectus to “Zymeworks,” “we,” “our” and “us” refer, collectively, to Zymeworks Inc., a Delaware corporation, and its subsidiaries taken as a whole.

Company Overview

Zymeworks is a biotechnology company committed to the discovery, development, and commercialization of novel, multifunctional biotherapeutics. Zymeworks’ mission is to make a meaningful difference for people impacted by difficult-to-treat cancers and other serious diseases. Zymeworks’ complementary therapeutic platforms and fully integrated drug development engine provide the flexibility and compatibility to precisely engineer and develop highly differentiated antibody-based therapeutic candidates.

Corporate Information

Effective October 13, 2022, we became a Delaware corporation, following receipt of necessary shareholder, stock exchange, and court approvals (which we refer to as the Redomicile Transactions). Zymeworks Inc. was incorporated under the laws of the State of Delaware in June 2022. Our principal executive offices are located at 108 Patriot Drive, Suite A, Middletown, Delaware 19709, and our telephone number is (302) 274-8744. Our predecessor, now named Zymeworks BC Inc., was originally incorporated on September 8, 2003 under the Canada Business Corporations Act under the name “Zymeworks Inc.” On October 22, 2003, our predecessor was registered as an extra-provincial company under the Company Act (British Columbia), the predecessor to the Business Corporations Act (British Columbia), or the BCBCA. Our predecessor continued to British Columbia under the BCBCA on May 2, 2017. Our corporate website address is www.zymeworks.com.

Risk Factors Summary

Our business is subject to numerous risks and uncertainties, including those highlighted in the section of this prospectus titled “Risk Factors.” The following is a summary of the principal risks we face:

- We have a limited number of product candidates, all which are still in preclinical or clinical development. If we do not obtain regulatory approval of one or more of our product candidates, or experience significant delays in doing so, our business will be materially adversely affected.
- Clinical trials are expensive, time consuming, difficult to design and implement, and involve uncertain outcomes. Furthermore, the results of previous preclinical studies and clinical trials may not be predictive of future results, and the results of our current and planned clinical trials may not satisfy the requirements of the FDA or comparable regulatory authorities outside the United States.
- Our long-term prospects depend in part upon discovering, developing and commercializing additional product candidates, which may fail in development or suffer delays that adversely affect their commercial viability.
- Our product candidates may have undesirable side effects that may delay or prevent marketing approval or, if approval is received, require them to be taken off the market, require them to include safety warnings or otherwise limit their sales; no regulatory agency has made any determination that any of our product candidates are safe or effective for use by the general public for any indication.

- We face significant competition, and if our competitors develop and market products that are more effective, safer or less expensive than our product candidates, our commercial opportunities will be negatively impacted.
- If any of our product candidates receive regulatory approval, the approved products may not achieve broad market acceptance among physicians, patients, the medical community and third-party payors, in which case revenue generated from their sales would be limited.
- We may not be successful in our efforts to use our therapeutic platforms to build a pipeline of product candidates.
- If any product liability lawsuits are successfully brought against us or any of our strategic partners, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.
- Security breaches and incidents, loss of data and other disruptions could compromise sensitive information related to our business or protected health information or prevent us from accessing critical information and expose us to liability, which could adversely affect our business and our reputation.
- Current and future legislation may increase the difficulty and cost for us to commercialize any products that we or our strategic partners develop and affect the prices we may obtain.
- We have incurred significant losses since inception and anticipate that we will continue to incur losses for the foreseeable future. We have no products approved for commercial sale, and to date we have not generated any revenue or profit from product sales. We may never achieve or sustain profitability.
- We will require substantial additional funding, which may not be available to us on acceptable terms, or at all, and, if not available, may require us to delay, scale back, or cease our product development programs or operations.
- We will depend on our collaborative relationship with Jazz to further develop and commercialize zanidatamab, and if our relationship is not successful or is terminated, we may be delayed in or unable to effectively develop and/or commercialize zanidatamab, which could have a material adverse effect on our business.
- Our existing strategic partnerships are important to our business, and future strategic partnerships will likely also be important to us. If we are unable to maintain our strategic partnerships, or if these strategic partnerships are not successful, our business could be adversely affected.
- We rely on third-party manufacturers to produce our product candidates and on other third parties to provide supplies and store, monitor and transport bulk drug substance and drug product. We and our third-party partners may encounter difficulties with respect to these activities that could delay or impair our ability to initiate or complete our clinical trials or commercialize approved products.
- We rely on third parties to monitor, support, conduct and oversee clinical trials of the product candidates that we are developing and, in some cases, to maintain regulatory files for those product candidates. We may not be able to obtain regulatory approval for our product candidates or commercialize any products that may result from our development efforts if we are not able to maintain or secure agreements with such third parties on acceptable terms, if these third parties do not perform their services as required, or if these third parties fail to timely transfer any regulatory information held by them to us.
- If we are unable to obtain, maintain and enforce patent and trade secret protection for our product candidates and related technology, our business could be materially harmed.

- If we are unable to protect the confidentiality of our proprietary information, the value of our technology and products could be adversely affected.
- Our effective tax rate may change in the future.
- Our stock price is likely to be volatile and the market price of our common stock may drop below the price paid by stockholders.
- Delaware law and provisions in our amended and restated certificate of incorporation and amended and restated bylaws might delay, discourage or prevent a change in control of Zymeworks or changes in our management, thereby depressing the market price of our common stock.

The Shares of Common Stock That May Be Offered

We are registering the issuance, from time to time, of up to 2,737,836 shares of our common stock consisting of:

- up to 658,612 shares of our common stock issuable upon the exchange of Exchangeable Shares; and
- up to 2,079,224 shares of our common stock issuable upon the exercise of pre-funded warrants.

ExchangeCo issued the Exchangeable Shares to certain shareholders of Zymeworks BC in connection with the Redomicile Transactions, pursuant to Section 3(a)(10) of the Securities Act of 1933, as amended, or the Securities Act, and in accordance with the final order of the British Columbia Supreme Court. Zymeworks BC issued the pre-funded warrants in public offerings that closed on June 24, 2019, January 27, 2020 and January 31, 2022, and we subsequently assumed the pre-funded warrants in connection with the Redomicile Transactions.

As of March 3, 2023, 765,921 Exchangeable Shares have been exchanged on a one-to-one basis for 765,921 shares of our common stock and 658,612 Exchangeable Shares are held by former Zymeworks BC shareholders and exchangeable on a one-to-one basis, subject to adjustment, for up to 658,612 shares of our common stock.

In addition, as of March 3, 2023, we had 2,079,224 shares of common stock issuable pursuant to 2,079,224 pre-funded warrants after 1,375,000 shares of common stock were issued upon the exercise of 1,375,000 of such pre-funded warrants on October 25, 2022 and 1,340,000 shares of common stock were issued upon the exercise of a further 1,340,000 of such pre-funded warrants on October 27, 2022.

RISK FACTORS

Investing in our common stock is speculative and involves a high degree of risk. The following risk factors, as well as risks currently unknown to us, could materially adversely affect our future business, operations and financial condition and could cause them to differ materially from the estimates described in forward-looking information relating to us, or our business, property or financial results, each of which could cause purchasers of our common stock to lose part or all of their investment. In addition to the other information contained in this prospectus and the documents incorporated by reference herein and therein, prospective investors should carefully consider the factors described in the section titled “Risk Factors” in our Quarterly Report on Form 10-Q for the three months ended September 30, 2022 and the factors set out below in evaluating Zymeworks and its business before making an investment in our common stock. Our Risk Factors are not guarantees that no such conditions exist as of the date of this report and should not be interpreted as an affirmative statement that such risks or conditions have not materialized, in whole or in part.

Risks Related to Our Business and the Development and Commercialization of Our Product Candidates

We have a limited number of product candidates, all which are still in preclinical or clinical development. If we do not obtain regulatory approval of one or more of our product candidates, or experience significant delays in doing so, our business will be materially adversely affected.

We currently have no products approved for sale or marketing in any country, and may never be able to obtain regulatory approval for any of our product candidates. As a result, we are not currently permitted to market any of our product candidates in the United States or in any other country until we obtain regulatory approval from the FDA or comparable regulatory authorities outside the United States. Our product candidates are in preclinical or clinical development and we have not submitted an application, or received marketing approval, for any of our product candidates. Obtaining regulatory approval of our product candidates will depend on many factors, including:

- completing clinical trials that demonstrate the efficacy and safety of our product candidates;
- preparation and submission to the appropriate regulatory authorities of an application for marketing approval that includes substantial evidence of safety, purity and potency from results of nonclinical testing and clinical trials;
- establishing and maintaining adequate commercial manufacturing arrangements or establishing our own commercial manufacturing capabilities or reliable arrangements with third-party contract manufacturers;
- potential pre-approval audits of nonclinical sites, clinical trial sites, and third-party manufacturing sites that generated the data and product in support of the marketing application; and
- launching commercial sales, marketing and distribution operations.

Many of these factors are wholly or partially beyond our control, including clinical advancement, the regulatory submission process and changes in the competitive landscape. If we do not achieve one or more of these factors in a timely manner, we could experience significant delays or an inability to develop our product candidates at all.

Clinical trials are expensive, time consuming, difficult to design and implement, and involve uncertain outcomes. Furthermore, the results of previous preclinical studies and clinical trials may not be predictive of future results, and the results of our current and planned clinical trials may not satisfy the requirements of the FDA or comparable regulatory authorities outside the United States.

We have not previously submitted a Biologics License Application, or BLA, to the FDA or similar marketing applications to foreign health authorities. A BLA must include extensive preclinical and clinical data and supporting information to establish the product candidate’s safety, purity and efficacy for each desired indication. The BLA must also include significant information regarding the manufacturing controls for the product. The novel nature of our product candidates may introduce uncertain, complex, expensive and lengthy challenges that could impact regulatory approval. Even if we eventually complete clinical testing and receive approval of any regulatory filing for our product candidates, the FDA or foreign health authorities may approve our product candidates for a more limited indication or a narrower patient population than we originally requested.

There is typically an extremely high rate of attrition from the failure of product candidates proceeding through preclinical studies and clinical trials. Positive or timely results from preclinical or early-stage trials do not ensure positive or timely results in late-stage clinical trials or product approval by the FDA or comparable regulatory authorities outside the United States. We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective for use in a diverse population before we can seek regulatory approvals for their commercial sale. Our clinical trials may produce negative or inconclusive results, and we or any of our current and future strategic partners may decide, or regulators may require us, to conduct additional clinical or preclinical testing. In some instances, there can be significant variability in safety or efficacy results between different preclinical studies and clinical trials of the same product candidate due to numerous factors, including changes in clinical trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. Moreover, success in preclinical studies or early-stage clinical trials does not mean that future clinical trials or registrational clinical trials will be successful because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and comparable regulatory authorities outside the United States, despite having progressed through preclinical studies and initial clinical trials. Product candidates that have shown promising results in early clinical trials may suffer significant setbacks in subsequent clinical trials or registrational clinical trials. For example, a number of companies in the pharmaceutical industry have suffered significant setbacks in late-stage clinical trials, even after obtaining promising results in earlier-stage clinical trials. Similarly, interim results of a clinical trial do not necessarily predict final results.

There is a high failure rate for biopharmaceutical products proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development. For example, the FDA's Oncology Center of Excellence initiated Project Optimus to reform the dose optimization and dose selection paradigm in oncology drug development and Project FrontRunner to help develop and implement strategies to support approvals in the early clinical setting, among other goals. How the FDA plans to implement those goals and their impact on specific clinical programs and the industry are unclear.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the FDA or foreign health authorities may disagree with the design, implementation or data analyses of our clinical trials;
- the FDA or foreign health authorities may determine that our product candidate(s) do not have adequate risk-benefit ratio or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- the FDA or foreign health authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a BLA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or foreign health authorities may fail to approve the manufacturing processes, test procedures and specifications or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and

- the approval policies or regulations of the FDA or foreign health authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Additionally, we have conducted, and may in the future conduct, clinical trials outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA and its determination that the trials also complied with all applicable U.S. laws and regulations. If the FDA does not accept the data from any clinical trials we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or halt our development of any future product candidates.

If clinical trials for our product candidates are prolonged, delayed or stopped, we may be unable to obtain regulatory approval and commercialize our product candidates on a timely basis, or at all, which would require us to incur additional costs and delay our receipt of any product revenue.

We are currently evaluating zanidatamab in Phase 1, Phase 2, and Phase 3 clinical trials, including certain ongoing pivotal clinical trials, and zanidatamab zovodotin in a Phase 1 clinical trial in patients with recurrent or metastatic HER2-expressing solid tumors. We may experience delays in our ongoing or future preclinical studies or clinical trials, and we do not know whether future preclinical studies or clinical trials will begin on time, need to be redesigned, enroll an adequate number of patients on time or be completed on schedule, if at all. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during clinical development, and, because our product candidates are in an early stage of development, there is a high risk of failure and we may never succeed in developing marketable products. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials, particularly because early trials have smaller numbers of subjects tested. In addition, it is not uncommon for product candidates to exhibit unforeseen safety or efficacy issues, such as immunogenicity, when tested in humans despite promising results in preclinical animal models.

Any clinical trials that we may conduct may not demonstrate the safety and efficacy profiles necessary to obtain regulatory approval to market our product candidates. As we continue developing our product candidates, serious adverse events, undesirable side effects, or unexpected characteristics may emerge, causing us to abandon these product candidates or limit their development to more narrow uses or subpopulations in which the risk-benefit ratio is more acceptable.

Patients treated with our product candidates may experience side effects or adverse events that are unrelated to our product candidates but may still impact the success of our clinical trials. The inclusion of patients with significant co-morbidities in our clinical trials may result in deaths or other adverse medical events due to an underlying condition or other therapies or medications that such patients may be using. Any of these events could prevent us from obtaining regulatory approval or achieving or maintaining market acceptance and impair our ability to commercialize our product candidates. In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to a variety of factors, including, but not limited to, changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants.

The commencement or completion of these planned clinical trials could be substantially delayed or prevented by many factors, including:

- further discussions with the FDA or other regulatory agencies regarding the scope or design of our clinical trials;
- the limited number of, and competition for, suitable sites to conduct our clinical trials, many of which may already be engaged in other clinical trial programs, including some that may be for the same indication as our product candidates;
- any delay or failure to obtain approval or agreement to commence a clinical trial in any of the countries where enrollment is planned;

[Table of Contents](#)

- inability to obtain sufficient funds required for a clinical trial;
- clinical holds on, or other regulatory objections to, a new or ongoing clinical trial;
- delay or failure to manufacture sufficient supplies of the product candidate for our clinical trials;
- delay or failure to reach agreement on acceptable clinical trial agreement terms or clinical trial protocols with prospective sites or contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different sites or CROs;
- delay or failure to obtain an institutional review board, or IRB, approval to conduct a clinical trial at a prospective site;
- slower than expected rates of patient recruitment and enrollment;
- failure of patients to complete the clinical trial;
- the inability to enroll a sufficient number of patients in studies to ensure adequate statistical power to detect statistically significant treatment effects;
- unforeseen safety issues, including severe or unexpected drug-related adverse effects experienced by patients, including possible deaths;
- lack of efficacy during clinical trials;
- termination of our clinical trials by one or more clinical trial sites;
- inability or unwillingness of patients or clinical investigators to follow our clinical trial protocols;
- inability to monitor patients adequately during or after treatment by us or our CROs;
- our CROs or clinical study sites failing to comply with the trial protocol or regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, deviating from the protocol or dropping out of a study;
- the inability to address any noncompliance with regulatory requirements or safety concerns that arise during the course of a clinical trial;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or foreign health authorities for violations of applicable regulatory requirements;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical trial sites, including due to a facility manufacturing any of our product candidates or any of their components being ordered by the FDA or foreign health authorities to temporarily or permanently shut down due to violations of current good manufacturing processes, or cGMP, regulations or other applicable requirements, or cross-contaminations of product candidates in the manufacturing process;
- the need to repeat or terminate clinical trials as a result of inconclusive or negative results or unforeseen complications in testing;
- our clinical trials may be suspended or terminated upon a breach or pursuant to the terms of any agreement with, or for any other reason by, current or future strategic partners that have responsibility for the clinical development of any of our product candidates; and
- receiving untimely or unfavorable feedback from applicable regulatory authorities regarding the trial or requests from regulatory authorities to modify the design of a trial.

We could also experience delays in physicians enrolling patients in clinical trials of our product candidates in lieu of prescribing existing treatments or other clinical trials. Furthermore, a clinical trial may be suspended or terminated by us, the IRBs for the institutions in which such trials are being conducted, the Data Monitoring Committee for such trial, or by the FDA or foreign health authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or foreign health authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical

trial. If we experience termination of, or delays in the completion of, any clinical trial of our product candidates, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenue will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenue.

Securing regulatory approval also requires the submission of information about the manufacturing processes and inspection of manufacturing facilities by the relevant regulatory authority. The FDA or foreign health authorities may fail to approve our manufacturing processes or facilities, whether run by us or our contract manufacturing organizations. In addition, if we make manufacturing changes to our product candidates in the future, we may need to conduct additional preclinical and/or clinical studies to bridge our modified product candidates to earlier versions.

Changes in regulatory requirements, policies and guidelines may also occur and we may need to significantly amend clinical trial protocols to reflect these changes with appropriate regulatory authorities. These changes may require us to renegotiate terms with CROs or resubmit clinical trial protocols to IRBs for re-examination, which may impact the costs, timing or successful completion of a clinical trial. Our clinical trials may be suspended or terminated at any time by the FDA, other regulatory authorities, the IRB overseeing the clinical trial at issue, any of our clinical trial sites with respect to that site, or us.

Any failure or significant delay in commencing or completing clinical trials for our product candidates would adversely affect our ability to obtain regulatory approval, and our commercial prospects and ability to generate product revenue will be diminished.

In addition, even if the trials are successfully completed, clinical data are often susceptible to varying interpretations and analyses, and we cannot guarantee that the FDA or foreign health authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. We cannot guarantee that the FDA or foreign health authorities will view any of our product candidates as having adequate safety and efficacy profiles even if favorable results are observed in these clinical trials, and we may receive unexpected or unfavorable feedback from the FDA or foreign health authorities regarding satisfaction of safety, purity and potency (including clinical efficacy), amongst other factors. To the extent that the results of the trials are not satisfactory to the FDA or foreign health authorities for support of a marketing application, approval of our product candidates may be significantly delayed, or we may be required to expend significant additional resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates.

Our long-term prospects depend in part upon discovering, developing and commercializing additional product candidates, which may fail in development or suffer delays that adversely affect their commercial viability.

Our future operating results are dependent in part on our ability to successfully discover, develop, obtain regulatory approval for and commercialize product candidates beyond those we currently have in clinical development. A product candidate can unexpectedly fail at any stage of preclinical and clinical development. Our investments in our early-stage research and development efforts may not yield any promising product candidates. Even if our research and development efforts yield product candidates that advance into clinical studies, the historical failure rate for product candidates is high due to risks relating to safety, efficacy, clinical execution, changing standards of medical care and other unpredictable variables. The results from preclinical testing or early clinical trials of a product candidate may not be predictive of the results that will be obtained in later stage clinical trials of the product candidate.

The success of other product candidates we may develop will depend on many factors, including the following:

- generating sufficient data to support the initiation or continuation of clinical trials;
- obtaining regulatory permission to initiate clinical trials;
- contracting with the necessary parties to conduct clinical trials;
- successful enrollment of patients in, and the completion of, clinical trials on a timely basis;
- the timely manufacture of sufficient quantities of the product candidate for use in clinical trials; and

- adverse events in the clinical trials.

Even if we successfully advance any other product candidates into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in this “Risk Factors” section. Accordingly, we cannot assure you that we will ever be able to discover, develop, obtain regulatory approval of, commercialize or generate significant revenue from our other product candidates.

If we, or any of our partners, are unable to enroll patients in clinical trials, we will be unable to complete these trials on a timely basis or at all.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of subjects to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, ability to obtain and maintain patient consents, risk that enrolled subjects will drop out before completion, competing clinical trials and clinicians’ and patients’ perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. In particular, we are developing certain of our product candidates for the treatment of rare diseases, which have limited pools of patients from which to draw for clinical testing. If we, or any of our strategic partners that perform clinical tests for our product candidates, are unable to enroll a sufficient number of patients to complete clinical testing, we will be unable to gain marketing approval for such product candidates and our business will be harmed.

In addition, the U.S. federal Right to Try Act, among other things, provides a federal framework for patients to access certain investigational new drug products that have completed a Phase 1 clinical trial. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA approval under the FDA expanded access program. While there is no obligation to make product candidates available to eligible patients as a result of the Right to Try Act, new and emerging legislation regarding expanded access to unapproved drugs could negatively impact enrollment in our clinical trials and our business in the future.

The design or our execution of clinical trials may not support regulatory approval.

The design or execution of a clinical trial can determine whether its results will support regulatory approval, and flaws in the design or execution of a clinical trial may not become apparent until the clinical trial is well advanced. In some instances, there can be significant variability in safety or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We do not know whether any Phase 2, Phase 3 or other clinical trials we or any of our strategic partners may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates.

Further, the FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and in determining when or whether regulatory approval will be obtained for any of our product candidates. Our product candidates may not be approved even if they achieve their primary endpoints in any Phase 3 clinical trials or registration trials. The FDA or other non-U.S. regulatory authorities may disagree with our trial design and our interpretation of data from preclinical studies and clinical trials. In addition, any of these regulatory authorities may change requirements for the approval of a product candidate even after reviewing and providing comments or advice on a protocol for a pivotal Phase 3 clinical trial that has the potential to result in FDA or other agencies’ approval. In addition, any of these regulatory authorities may also approve a product candidate for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-marketing clinical trials. The FDA or other non-U.S. regulatory authorities may not approve the labeling claims that we believe would be necessary or desirable for the successful commercialization of our product candidates.

Interim, preliminary or top-line data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim, preliminary or top-line data from clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary or top-line data previously published. As a result, interim, preliminary and top-line data should be viewed with caution until the final data are available. Adverse differences between interim, preliminary or top-line data and final data could significantly harm our reputation and business prospects. Moreover, preliminary, interim and top-line data are subject to the risk that one or more of the clinical outcomes may materially change as more patient data become available when patients mature on study, patient enrollment continues or as other ongoing or future clinical trials with a product candidate further develop. Past results of clinical trials may not be predictive of future results.

In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically more extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. Similarly, even if we are able to complete our planned and ongoing preclinical studies and clinical trials of our product candidates according to our current development timeline, the positive results from such preclinical studies and clinical trials of our product candidates may not be replicated in subsequent preclinical studies or clinical trial results.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical and other nonclinical findings made while clinical trials were underway or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical, nonclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or other regulatory approval.

The Fast Track and Breakthrough Therapy designations we have received for zanidatamab may not result in faster development, regulatory review or approval process.

The FDA has granted Fast Track designations to zanidatamab for the first-line treatment of patients with HER2-overexpressing GEA in combination with standard of care chemotherapy and for previously treated or recurrent gene-amplified biliary tract cancers, or BTC. These Fast Track designations do not ensure that we will experience a faster development, regulatory review or approval process compared to conventional FDA procedures or that we will ultimately obtain regulatory approval. Additionally, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. The FDA also granted Breakthrough Therapy designation for zanidatamab for treatment of patients with previously treated HER2 gene-amplified locally advanced/unresectable or metastatic BTC. While we anticipate meeting with the FDA in 2023 to discuss the data readout from the HERIZON-BTC-01 study in support of submitting a BLA for zanidatamab in patients with previously treated HER2 gene-amplified BTC, the receipt of a Breakthrough Therapy designation for a product candidate may not ultimately result in a faster development process or review, and it does not in any way assure approval of a product candidate by the FDA. In addition, designation as a Breakthrough Therapy is within the discretion of the FDA and the FDA may decide to rescind a Breakthrough Therapy designation if it believes that a designated product candidate no longer meets the conditions for qualification of this program. If our clinical development program is suspended, terminated, or put on clinical hold due to unexpected adverse events or other issues, including clinical supply issues, we may not realize all the benefits associated with the Fast Track designation. Furthermore, Fast Track designation does not change the standards for approval, and the designation alone does not guarantee qualification for the FDA's priority review procedures.

Zanidatamab has also been granted Breakthrough Therapy designation from the Center for Drug Evaluation in China for treating patients with BTC who have failed prior systemic therapies.

Development of product candidates in combination with other therapies could expose us to additional risks.

Even if any of our product candidates were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA, the European Medicines Agency, or EMA, or other comparable foreign regulatory authorities could revoke approval of the therapy used in combination with any of our product candidates, or safety, efficacy, manufacturing or supply issues could arise with these existing therapies. In addition, it is possible that existing therapies with which our product candidates are approved for use could themselves fall out of favor or be relegated to later lines of treatment. This could result in the need to identify other combination therapies for our product candidates or our own products being removed from the market or being less successful commercially. We may also evaluate our product candidates in combination with one or more other cancer therapies that have not yet been approved for marketing by the FDA, EMA or comparable foreign regulatory authorities. We will not be able to market and sell any product candidate in combination with any such unapproved cancer therapies that do not ultimately obtain marketing approval. If the FDA, EMA or other comparable foreign regulatory authorities do not approve or revoke their approval of these other therapies, or if safety, efficacy, commercial adoption, manufacturing or supply issues arise with the therapies we choose to evaluate in combination with any other product candidate, we may be unable to obtain approval of or successfully market any one or all of the product candidates we develop.

Additionally, if the third-party providers of therapies or therapies in development used in combination with our product candidates are unable to produce sufficient quantities for clinical trials or for commercialization of our product candidates, or if the cost of combination therapies are prohibitive, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified product candidates from being developed, or approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA to review and clear or approve new product candidates can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, including delays or disruptions due to the COVID-19 pandemic, travel restrictions, staffing shortages, government shutdowns and furloughs, may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In response to the COVID-19 pandemic and travel restrictions, the FDA has issued industry guidance regarding plans to employ remote interactive evaluations and risk management methods, among other considerations, to meet user fee commitments and goal dates as well as plans toward resuming standard operational levels. Recently, President Biden announced that the administration intends to end the COVID-19 national and public health emergencies on May 11, 2023. The full impact of this termination of the public health emergencies on the FDA and other regulatory policies and operations are unclear. However, if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, or if the FDA and other agencies experience other delays, backlogs or disruptions, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Successful development of our current and future product candidates is uncertain and we may discontinue or reprioritize the development of any of our product candidates at any time, at our discretion.

Before obtaining regulatory approval for the commercial distribution of our product candidates, we must conduct, at our own expense, extensive preclinical tests and clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Preclinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. Additionally, the results from nonclinical testing or early clinical trials of a product candidate may not predict the results that will be obtained in subsequent human clinical trials of that product candidate. There is a high failure rate for drugs proceeding through clinical studies. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in any future clinical development could have a material adverse effect on our business and operating results. Alternatively, management may elect to discontinue development of certain product candidates to accommodate a shift in corporate strategy, despite positive clinical results. Based on our operating results and business strategy, among other factors, we may discontinue the development of any of our product candidates under development or reprioritize our focus on other product candidates at any time and at our discretion.

Additionally, because we have limited financial and managerial resources, we focus on research programs, therapeutic platforms and product candidates that we identify for specific indications. As a result, we may forgo or delay pursuit of opportunities with other therapeutic platforms or product candidates or for other indications that later prove to have greater commercial potential. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights.

Our product candidates may have undesirable side effects that may delay or prevent marketing approval or, if approval is received, require them to be taken off the market, require them to include safety warnings or otherwise limit their sales; no regulatory agency has made any determination that any of our product candidates are safe or effective for use by the general public for any indication.

All of our product candidates are still in preclinical or clinical development. Consequently, all of our product candidates are required to undergo ongoing safety testing in humans as part of clinical trials. Unforeseen side effects from any of our product candidates could arise either during clinical development or, if approved by regulatory authorities, after the approved product has been marketed. Zanidatamab and zanidatamab zovodotin continue to be evaluated in clinical trials, and the results of these and future clinical trials may show that zanidatamab, zanidatamab zovodotin or our other product candidates cause undesirable or unacceptable side effects, which could interrupt, delay or halt clinical trials, and result in delay of, or failure to obtain, marketing approval from the FDA and other regulatory authorities, or result in marketing approval from the FDA and other regulatory authorities with restrictive label warnings, limited patient populations or potential product liability claims. Even if we believe that our clinical trials and preclinical studies demonstrate the safety and efficacy of our product candidates, only the FDA and other comparable regulatory agencies may ultimately make such determination. No regulatory agency has made any such determination that any of our product candidates are safe or effective for use by the general public for any indication.

If any of our product candidates receive marketing approval and we or others later identify undesirable or unacceptable side effects caused by such products:

- regulatory authorities may require us to take our approved product off the market;
- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies, or impose a risk evaluation and mitigation strategy that includes restrictions and conditions on product distribution, prescribing and/or dispensing;
- we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product;
- we may be subject to limitations on how we may promote the product;
- sales of the product may decrease significantly;
- we may be subject to litigation or product liability claims; and

- our reputation may suffer.

Any of these events could prevent us or our current or future strategic partners from achieving or maintaining market acceptance of the affected product or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating revenue from the sale of any future products.

We face significant competition, and if our competitors develop and market products that are more effective, safer or less expensive than our product candidates, our commercial opportunities will be negatively impacted.

The life sciences industry is highly competitive and subject to rapid and significant technological change. We are currently developing biotherapeutics that will compete with other drugs and therapies that currently exist or are being developed. Products we may develop in the future are also likely to face competition from other drugs and therapies, some of which we may not currently be aware. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, universities and other research institutions. Many of our competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and in manufacturing pharmaceutical products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development and collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we develop obsolete. As a result of all of these factors, our competitors may succeed in obtaining patent protection or FDA approval or discovering, developing and commercializing products in our field before we do.

Specifically, there are a large number of companies developing or marketing treatments for cancer and autoimmune disorders, including many major pharmaceutical and biotechnology companies. These treatments consist both of small-molecule drug products, as well as biologics that work by using various antibody therapeutic platforms to address specific cancer targets. For additional information relating to the competitive environment we operate in, see Item 1. “Business – Competition.”

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, more convenient or less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for our product candidates, which could result in our competitors establishing a strong market position before we are able to enter the market.

Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. In addition, the biopharmaceutical industry is characterized by rapid technological change. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical.

In addition, we expect to compete with biosimilar versions of already approved products like trastuzumab or pertuzumab, and even if our product candidates achieve marketing approval, they may be challenged to achieve a price premium over competitive biosimilar products and will compete for market share with them.

The Biologics Price Competition and Innovation Act of 2009, which is included in the Patient Protection and Affordable Care Act, or PPACA, authorized the FDA to approve similar versions of innovative biologics, commonly known as biosimilars. Under the PPACA, a manufacturer may submit an application for licensure of a biologic product that is “biosimilar to” or “interchangeable with” a previously approved biologic product or “reference product.” Manufacturers may not submit an application for a biosimilar to the FDA until four years following

approval of the reference product, and the FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if our product candidates, if approved, are deemed to be reference products eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. Additionally, from time to time, there are proposals to repeal or modify the PPACA, including proposals that could significantly shorten the exclusivity period for biologics.

If any of our product candidates receive regulatory approval, the approved products may not achieve broad market acceptance among physicians, patients, the medical community and third-party payors, in which case revenue generated from their sales would be limited.

The commercial success of our product candidates will depend upon their acceptance among physicians, patients and the medical community. The degree of market acceptance of our product candidates will depend on a number of factors, including:

- limitations or warnings contained in the approved labeling for a product candidate;
- changes in the standard of care for the targeted indications for any of our product candidates;
- limitations in the approved clinical indications for our product candidates;
- demonstrated clinical safety and efficacy compared to other products;
- sales, marketing and distribution support;
- availability of coverage and extent of reimbursement from managed care plans and other third-party payors;
- timing of market introduction and perceived effectiveness of competitive products;
- availability of alternative therapies at similar or lower cost, including generic, biosimilar and over-the-counter products;
- the extent to which the product candidate is approved for inclusion on formularies of hospitals and managed care organizations;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy for particular diseases;
- whether the product can be used effectively with other therapies to achieve higher response rates;
- adverse publicity about our product candidates or favorable publicity about competitive products;
- convenience and ease of administration of our products; and
- potential product liability claims.

If any of our product candidates are approved, but do not achieve an adequate level of acceptance by physicians, patients and the medical community, we may not generate sufficient revenue from these products, and we may not become or remain profitable. In addition, efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful.

We may be unable to obtain orphan drug exclusivity in specific indications for zanidatamab or in future product candidates that we may develop. If our competitors are able to obtain orphan product exclusivity for their products in specific indications, we may not be able to have competing products approved in those indications by the applicable regulatory authority for a significant period of time.

The FDA has granted Orphan Drug Designation to zanidatamab for the treatment of BTC and gastric cancer, including cancer of the gastroesophageal junction, the EMA has granted Orphan Drug Designation to zanidatamab for the treatment of gastric cancer and BTC, and we may seek Orphan Drug Designation for additional indications in the future. Orphan Drug Designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

Generally, if a product candidate with an Orphan Drug Designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same drug for the same indication for that time period. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for Orphan Drug Designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. The loss of Orphan Drug Designation could have a negative effect on our ability to successfully commercialize our product candidates, earn revenues and achieve profitability.

Even if orphan drug exclusivity for zanidatamab is obtained, or is obtained for any other product candidates that receive an Orphan Drug Designation in the future, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Further, in the United States, even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition submitted by a competitor if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. If we are unable to manufacture sufficient supply of our product to meet the needs of patients, the FDA can withdraw our orphan exclusive marketing rights or approve another marketing application for the same drug product before the expiration of the exclusivity period.

Further, in *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299 (11th Cir. 2021), the court disagreed with the FDA's longstanding position that the orphan drug exclusivity only applies to the approved use or indication within an eligible disease, and not to all uses or indications within the entire disease or condition. In particular, the circuit court held that the orphan drug exclusivity for Catalyst's drug blocked the FDA's approval of another drug for all uses or indications within the same orphan-designated disease, Lambert-Eaton myasthenic syndrome, or LEMS, even though Catalyst's drug was approved at that time only for use in the treatment of LEMS in adults. Accordingly, the court ordered the FDA to set aside the approval of a drug indicated for LEMS in children. This decision created uncertainty in the application of the orphan drug exclusivity. On January 24, 2023, the FDA published a notice in the Federal Register to clarify that while the agency complies with the court's order in Catalyst, the FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the Catalyst order – that is, the agency will continue tying the scope of orphan drug exclusivity to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan designated disease or condition that have not yet been approved. It is unclear how future litigation, legislation, agency decisions, and administrative actions will impact the scope of the orphan drug exclusivity.

Even if we obtain FDA approval of any of our product candidates, we may never obtain approval or commercialize such products outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials, which would be costly and time consuming. Regulatory requirements can vary widely from country to country and region to region and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any product

[Table of Contents](#)

candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our target market will be reduced and our ability to realize the full market potential of our products will be harmed.

Our ability to eventually generate significant revenues from product sales will depend on a number of factors, including:

- successful completion of preclinical studies;
- submission of INDs or other regulatory applications for our planned clinical trials or future clinical trials and authorizations from regulators to initiate clinical studies;
- successful enrollment in, and completion of, clinical trials;
- achieving favorable results from clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing and maintaining sufficient manufacturing capabilities, whether internally or with third parties, for clinical and commercial supply;
- obtaining pricing, reimbursement, and hospital formulary access;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in combination with other products;
- sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials and commercialization activities;
- effectively competing with other therapies;
- developing and implementing successful marketing and reimbursement strategies;
- obtaining and maintaining patent, trade secret and other intellectual property protection and regulatory exclusivity for our product candidates; and
- maintaining a continued acceptable safety profile of any product following approval, if any.

If we do not achieve one or more of these requirements in a timely manner, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

We cannot be certain that our clinical trials will be initiated and completed on time, if at all, or whether our planned clinical strategy will be acceptable to the FDA or foreign health authorities. To become and remain profitable, we must develop, obtain approval for and eventually commercialize products, if approved, that generate significant revenue. In addition, it is not uncommon for product candidates to exhibit unforeseen safety issues or inadequate efficacy when tested in humans despite promising results in preclinical animal models or earlier trials, and we may ultimately be unable to demonstrate adequate safety and efficacy of our product candidates to obtain marketing approval. Even if we obtain approval and begin commercializing one or more of our product candidates, we may never generate revenue that is significant or large enough to achieve profitability.

Even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development, manufacturing and other expenditures to develop and market additional product candidates. Our failure to become or remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations.

Reimbursement decisions by third-party payors may have an adverse effect on pricing and market acceptance. If there is not sufficient reimbursement for our products, it is less likely that our products will be widely used.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. Many countries require approval of the sale price of a drug before it can be marketed. The pricing review period begins after marketing or product licensing approval is granted in most cases. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product and negatively impact the revenues we are able to generate from the sale of the product in that country.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other third-party payors. In many jurisdictions, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our products. If we are not currently capturing the scientific and clinical data that will be required for reimbursement approval, we may be required to conduct additional trials, which may delay or suspend reimbursement approval. Additionally, in the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of a product candidate that receives regulatory approval to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

Even if our product candidates are approved for sale by the appropriate regulatory authorities, market acceptance and sales of these products will depend on reimbursement policies and may be affected by future healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will reimburse and establish payment levels. We cannot be certain that reimbursement will be available for any products that we develop. If reimbursement is not available or is available on a limited basis, we may not be able to successfully commercialize any of our approved products.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, also called the Medicare Modernization Act, or MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation established Medicare Part D, which expanded Medicare coverage for outpatient prescription drug purchases by the elderly but provided authority for limiting the number of drugs that will be covered in any therapeutic class. The MMA also introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. We expect to experience pricing pressures in connection with the sale of any products that we develop, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals. In August 2022, Congress passed the Inflation Reduction Act of 2022, which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single-source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. The impact of these legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is unclear. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA, EMA or other regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses.

Interim reimbursement levels for new drugs, if applicable, may also be insufficient to cover our and any collaborator's costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that currently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our or any collaborator's inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products that we or our strategic partners develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize product candidates and our overall financial condition.

If the market opportunities for any product that we or our strategic partners develop are smaller than we believe they are, our revenue may be adversely affected and our business may suffer.

We intend to initially focus our independent product candidate development on treatments for oncology. Our projections of addressable patient populations that have the potential to benefit from treatment with our product candidates are based on estimates. If our projections are inaccurate, the market opportunities for any of our product candidates could be significantly diminished and have an adverse material impact on our business.

We may not be successful in our efforts to use our therapeutic platforms to build a pipeline of product candidates.

We intend to use our therapeutic platforms to build a pipeline of product candidates and progress these product candidates through clinical development for the treatment of a variety of diseases. Although our research and development efforts to date have resulted in a pipeline of product candidates directed at various cancers, we may not be able to develop product candidates that are safe and effective. In addition, although we expect that our therapeutic platforms will allow us to develop further product candidates, they may not prove to be successful at doing so. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. If we do not continue to successfully develop and begin to commercialize product candidates, we will face difficulty in obtaining product revenue in future periods, which could result in significant harm to our financial position and adversely affect our stock price.

Even if we receive regulatory approval to commercialize any of the product candidates that we develop, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or subject to certain conditions of approval, and may contain requirements for potentially costly post-approval trials, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the marketed product.

For any approved product, we will be subject to ongoing regulatory obligations and extensive oversight by regulatory authorities, including with respect to manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product. These requirements include submissions of safety and other post-approval information and reports, as well as continued compliance with cGMP and good clinical practice, or GCP, for any clinical trials that we or our strategic partners conduct after approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product;
- withdrawal of the product from the market or voluntary or mandatory product recalls;

- fines, warning letters or holds on clinical trials;
- refusal by the FDA, EMA or another applicable regulatory authority to approve pending applications or supplements to approved applications filed by us or our strategic partners, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

Occurrence of any of the foregoing could have a material and adverse effect on our business and results of operations. Further, the FDA's or other ex-U.S. regulators' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

The FDA strictly regulates manufacturers' promotional claims of drug products. In particular, a drug product may not be promoted by manufacturers for uses that are not approved by the FDA, as reflected in the FDA-approved labeling, although healthcare professionals are permitted to use drug products for off-label uses. The FDA, the Department of Justice, the Inspector General of the Department of Health and Human Services, among other government agencies, actively enforce the laws and regulations prohibiting manufacturers' promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including large civil and criminal fines, penalties, and enforcement actions. The FDA has also imposed consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed for companies that engaged in such prohibited activities. If we cannot successfully manage the promotion of our approved product candidates, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

If any product liability lawsuits are successfully brought against us or any of our strategic partners, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability lawsuits related to the testing of our product candidates in seriously ill patients, and will face an even greater risk if product candidates are approved by regulatory authorities and introduced commercially. Product liability claims may be brought against us or our strategic partners by participants enrolled in our clinical trials, patients, health care providers or others using, administering or selling any of our future approved products. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities. Regardless of their merit or eventual outcome, liability claims may result in:

- decreased demand for any future approved products;
- injury to our reputation;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- increased regulatory scrutiny;
- significant litigation costs;
- substantial monetary awards to, or costly settlement with, patients or other claimants;
- product recalls or a change in the indications for which they may be used;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize our product candidates.

We may need to have in place increased product liability coverage when we begin the commercialization of our product candidates. Insurance coverage is becoming increasingly expensive. As a result, we may be unable to maintain or obtain sufficient insurance at a reasonable cost to protect us against losses that could have a material adverse effect on our business. A successful product liability claim or series of claims brought against us, particularly if judgments exceed any insurance coverage we may have, could decrease our cash resources and adversely affect our business, financial condition and results of operation.

Patients with cancer and other diseases targeted by our product candidates are often already in severe and advanced stages of disease and have both known and unknown significant pre-existing and potentially life-threatening health risks. During the course of treatment, patients may suffer adverse events, including death, for reasons that may be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our product candidates, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which we do not believe that an adverse event is related to our product candidates, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may interrupt our sales efforts, delay our regulatory approval process in other countries, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations.

If we or any of our third-party manufacturers encounter manufacturing difficulties, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or prevented.

The manufacture of biological drug products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques, process and quality controls. Manufacturers of biologic products often encounter difficulties in production and sourcing, particularly in scaling up or out, validating the production process and assuring high reliability of the manufacturing processes (including the absence of contamination), in light of variations and supply constraints of key components. These problems include logistics and shipping, difficulties with production costs and yields, quality control, including consistency, stability, purity and efficacy of the product, product testing, operator error and availability of qualified personnel, as well as compliance with applicable federal, state and foreign regulations. If contaminants are discovered in our supply of our product candidates or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure you that any stability, purity, and efficacy failures, deficiencies, or other issues relating to the manufacture of our product candidates will not occur in the future. Our research and development activities also involve the controlled use of potentially hazardous substances, including chemical and biological materials, by our third-party manufacturers. While we currently outsource all manufacturing to third parties, we and our manufacturers are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury, and any related liability, resulting from medical or hazardous materials.

Material modifications in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates are developed through preclinical to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability, or our strategic partners' ability, to commence product sales and generate revenue.

Strategic transactions could disrupt our business, cause dilution to our stockholders and otherwise harm our business.

We actively evaluate various strategic transactions on an ongoing basis. For example, we may acquire other businesses, products or technologies as well as pursue strategic alliances, joint ventures, investments in complementary businesses, out-licensing agreements, divestitures or other transactions. Any of these transactions could be material to our financial condition and operating results and expose us to many risks, including:

- disruption in our relationships with existing strategic partners or suppliers as a result of such a transaction;
- unanticipated liabilities related to acquired companies;
- difficulties integrating acquired personnel, technologies and operations into our existing business;
- retention of key employees;
- diversion of management time and focus from operating our business to management of strategic alliances or joint ventures or acquisition integration challenges;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and marketing approvals;
- increases in our expenses and reductions in our cash available for operations and other uses; and
- possible write-offs or impairment charges relating to acquired businesses.

Also, the anticipated benefit of any strategic transaction may not materialize or such strategic transaction may be prohibited. Additionally, future acquisitions or dispositions could result in potentially dilutive issuances of our equity securities, the incurrence of debt, contingent liabilities or amortization expenses or write-offs of goodwill, any of which could harm our financial condition. We cannot predict the number, timing or size of any future strategic alliances, joint ventures, investments, acquisitions, divestitures or other strategic transactions, or the effect that any such transactions might have on our operating results.

Many governments impose strict price controls, which may adversely affect our future profitability.

In many countries, particularly in those in the EU, prescription drug pricing and reimbursement is subject to governmental control. In those countries that impose price controls, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our strategic partners may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies.

Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we or our strategic partners might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay commercial launch of the product candidate, possibly for lengthy time periods, and negatively impact the revenue that is generated from the sale of the product in that country. If reimbursement of such product candidates is unavailable or limited in scope or amount, if pricing is set at unsatisfactory levels, or if there is competition from lower priced cross-border sales, our profitability will be negatively affected.

Security breaches and incidents, loss of data and other disruptions could compromise sensitive information related to our business or protected health information or prevent us from accessing critical information and expose us to liability, which could adversely affect our business and our reputation.

In the ordinary course of our business, we and our CROs and other service providers collect, store and otherwise process petabytes of sensitive data, including legally protected health information, personal information, intellectual property and proprietary business information owned or controlled by ourselves or our strategic partners. We manage and maintain our applications and data by utilizing a combination of on-site systems, managed data center systems and cloud-based data center systems. These applications and data encompass a wide variety of business-critical information, including research and development information, commercial information and business and financial information. We face four primary risks relative to protecting this critical information: loss of access risk, inappropriate disclosure risk, inappropriate modification risk and the risk of being unable to adequately monitor our controls over the first three risks.

Although we take measures designed to protect sensitive information from unauthorized access or disclosure, our information technology and infrastructure and those of our CROs and our other third-party service providers may utilize may be vulnerable to attacks by hackers or viruses or breached, interrupted or compromised due to inadvertent or intentional actions by our employees, contractors, business partners, and/or other third parties, or from cyber-attacks by malicious third parties (including supply chain cyber-attacks or the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information). Any such breach, incident, or interruption could compromise systems and networks used in our business and lead to the loss, destruction, alteration, prevention of access to, disclosure, or dissemination of, or damage or unauthorized access to, our data (including trade secrets or other confidential information, intellectual property, proprietary business information, and personal information) or data that is processed or maintained on our behalf, or other assets, which could result in financial, legal, business and reputational harm to us. Any such event could result in legal claims, demands and litigation or governmental investigations or other proceedings, liability under laws that protect the privacy of personal information, such as the Health Insurance Portability and Accountability Act of 1996, or “HIPAA”, and regulatory penalties and other liabilities. Although we have implemented security measures and a formal enterprise security program designed to prevent unauthorized access to sensitive data, there is no guarantee that we or our third-party service providers can protect our systems or networks or other systems or networks used in our business from security breaches, incidents, or compromises. Any loss, destruction, alteration, prevention of access to, disclosure, or dissemination of, or damage or unauthorized access to, our data or other data that is processed or maintained on our behalf could also disrupt our operations (including our ability to conduct our analyses, pay providers, conduct research and development activities, collect, process and prepare company financial information, provide information about any future products, and manage the administrative aspects of our business) and damage our reputation, any of which could adversely affect our business.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, impose certain requirements relating to the privacy, security, transmission and breach reporting of individually identifiable health information upon entities subject to the law, such as health plans, healthcare clearinghouses and healthcare providers and their respective business associates and subcontractors that perform services for them that involve individually identifiable health information. Mandatory penalties for HIPAA violations can be significant, and criminal and monetary penalties, as well as injunctive relief, may be imposed for HIPAA violations. Although most drug manufacturers are not directly subject to HIPAA, prosecutors are increasingly using HIPAA-related theories of liability against drug manufacturers and their agents and we also could be subject to criminal penalties if we knowingly obtain individually identifiable health information from a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

Furthermore, in the event of a breach as defined by HIPAA, HIPAA regulations impose specific reporting requirements to regulators, individuals impacted by the breach and, in some cases, the media. Issuing such notifications can be costly, time and resource intensive, and can generate significant negative publicity. Breaches of HIPAA may also constitute contractual violations that could lead to contractual damages or terminations. In addition to HIPAA, other applicable data privacy and security obligations, including U.S. state data breach notification laws, may require us to notify relevant stakeholders of any security breaches or incidents that result in the unauthorized disclosure, or dissemination of, personal information. Such disclosures are costly, and the disclosures or the failure to comply with such requirements, could lead to adverse impacts.

Furthermore, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on other third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business.

In addition, we may face increased cybersecurity risks due to our reliance on internet technology given that we have employees at three office locations (Vancouver, Seattle, and Dublin) and a significant number of employees who work remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities.

We are subject to stringent and changing obligations related to privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation, fines and penalties, disruptions of our business operations, reputational harm and other adverse business consequences.

U.S. states have enacted and are considering enacting laws relating to the protection of personal information (including health and other data of patients, research subjects, and other individuals), which may be more rigorous than, or impose additional requirements beyond those required by, HIPAA. For example, the California Consumer Privacy Act, or CCPA, which became effective on January 1, 2020, gives California consumers expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used. The CCPA allows for statutory fines for noncompliance (up to \$7,500 per violation) as well as a limited private right of action for data breaches, which may increase the volume of data breach litigation. In addition, the California Privacy Rights Act of 2020, or CPRA, which went into effect on January 1, 2023, expands the CCPA by, among other things, giving California residents the ability to limit use of certain sensitive personal information, establishing restrictions on personal information retention, expanding the types of data breaches subject to the CCPA's private right of action, and establishing a new California Privacy Protection Agency to implement and enforce the new law. While limited CCPA exemptions may apply to portions of our business, the recency of the CCPA's implementing regulations and the California Attorney General's enforcement activity means obligations under the CCPA, as modified by the CPRA, could evolve in the future, which may increase our compliance costs and potential liability. Many similar privacy and security laws have been proposed at the federal level and in other states, certain of which have been enacted, including such laws in Colorado, Connecticut, Utah and Virginia. These or other proposed or enacted laws relating to privacy and security could similarly increase our compliance obligations and costs in the future.

We may also become subject to laws and regulations in non-U.S. countries covering privacy and security and the protection of health-related and other personal information. In particular, the European Economic Area, or EEA has adopted privacy and security protection laws and regulations that impose significant compliance obligations. Laws and regulations in these jurisdictions apply broadly to the collection, use, storage, disclosure, processing and security of information that identifies or may be used to identify an individual, such as names, contact information, and sensitive personal information such as health data. These laws and regulations are subject to frequent revisions and differing interpretations, and have generally become more stringent over time.

The General Data Protection Regulation 2016/679, or GDPR, applies to the processing of personal information and imposes many requirements for controllers and processors of personal information, including, for example, higher standards for obtaining consent from individuals to process their personal information, more robust disclosures to individuals and a strengthened individual data rights regime, shortened timelines for data breach notifications, limitations on retention and secondary use of information, increased requirements pertaining to health data and pseudonymized (i.e., key-coded) data and additional obligations when contracting third-party processors in connection with the processing of the personal information. The GDPR allows EEA countries to make additional laws and regulations further limiting the processing of genetic, biometric or health data. Failure to comply with the requirements of the GDPR and the applicable national privacy and security laws of EEA countries may result in fines of up to €20,000,000 or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, and other administrative penalties; we may also be liable should any individual who has suffered financial or non-financial damage arising from our infringement of the GDPR exercise their right to receive compensation against us. Furthermore, adverse publicity relating to our failure to comply with the GDPR could cause a loss of goodwill, which could have an adverse effect on our reputation, brand, business and financial condition. Additionally, the United Kingdom, or UK, has implemented legislation similar to the GDPR, referred to as the UK GDPR, which provides for fines of up to the greater of £17.5 million or 4% of global turnover.

Certain jurisdictions, including the EEA, have enacted data localization laws and cross-border personal information transfer laws. For example, absent appropriate safeguards or other circumstances, the GDPR generally restricts the transfer of personal information to countries outside the EEA, such as the United States, which the European Commission does not consider to provide an adequate level of personal information protection. On July 16, 2020, the Court of Justice of the European Union, or CJEU, invalidated the European Union-U.S. Privacy Shield, or Privacy Shield, as a data transfer mechanism for transferring personal information from the EEA to the United States. While the European Union, or EU, standard contractual clauses, or EU SCCs, remain a valid mechanism to transfer personal information to third countries outside the EEA, the CJEU's ruling has also imposed enhanced due diligence obligations on data exporters and importers to ensure that the laws of the country to which the personal information is transferred offer a level of data protection that is essentially equivalent to the EEA. Also, the EU has issued updated EU SCCs, and the UK has issued its own standard contractual clauses, or UK SCCs, that are required to be implemented over time. Although we do not transfer personal data from the EEA to the United States via the Privacy Shield, the CJEU's decision means that the status of transfers of personal information from the EEA and other regions, including the UK, to the United States is subject to significant regulatory uncertainty. To the extent we transfer personal information from other jurisdictions to the United States, we may not be able to implement or maintain an appropriate data transfer mechanism to continue such international transfers of data. Additionally, the CJEU's invalidation of the Privacy Shield, the revised EU SCCs and new UK SCCs, regulatory guidance and opinions, and other developments relating to cross-border data transfer may require us to implement additional contractual and technical safeguards for any personal information transferred out of the EEA, UK, or other regions, which may increase compliance costs, lead to increased regulatory scrutiny or liability, and may require additional contractual negotiations, which may adversely impact our business, financial condition, and operating results.

Separate from, and in addition to, requirements under the GDPR and UK GDPR, certification requirements for the hosting of health data will vary by jurisdiction. To the extent we operate in various EEA countries or the UK, there might be other national healthcare regulations or regulatory requirements with which we will be required to comply. For example, France requires hosts of health data to obtain a prior certification with the competent certification body.

The interpretation and application of consumer, health-related and privacy and security laws in the United States, the EEA, and elsewhere are often uncertain, contradictory and in flux. Any failure or perceived failure to comply with federal, state or foreign laws or regulations, contractual or other legal obligations related to privacy or security may result in claims, warnings, communications, requests or investigations from individuals, supervisory authorities or other legal or regulatory authorities in relation to our processing of personal information, and regulatory investigations or other proceedings. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. If so, this could result in government-imposed fines or orders requiring that we change our practices, which could adversely affect our business. In addition, these privacy regulations vary between states, may differ from country to country, and may vary based on whether testing is performed in the United States or in the local country. Complying with these various laws could cause us to incur substantial costs or require us to change our business practices and compliance procedures in a manner adverse to our business.

Current and future legislation may increase the difficulty and cost for us to commercialize any products that we or our strategic partners develop and affect the prices we may obtain.

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change healthcare systems in ways that could affect our ability to sell any of our product candidates profitably, if such product candidates are approved for sale. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

In March 2010, the PPACA became law in the United States. The PPACA may affect the operational results of companies in the pharmaceutical industry, including us, by imposing on them additional costs. For example, effective January 1, 2010, PPACA increased the minimum Medicaid drug rebates for pharmaceutical companies and imposed an annual fee on certain branded prescription drugs and biologics. Since the enactment of PPACA, there have been executive, judicial and Congressional challenges to certain aspects of the PPACA, including judicial challenges in the Fifth Circuit Court and the United States Supreme Court. In June 2021, the United States Supreme

Court held that Texas and other challengers had no legal standing to challenge the PPACA, dismissing the case without specifically ruling on the constitutionality of the PPACA. Accordingly, the PPACA remains in effect in its current form. It is unclear how future litigation or healthcare measures promulgated by the Biden administration will impact our business, financial condition and results of operations. Complying with any new legislation or changes in healthcare regulation could be time-intensive and expensive, resulting in a material adverse effect on our business.

Other legislative changes have been proposed and adopted since the PPACA was enacted. For example, the Bipartisan Budget Act of 2018, among other things, amended the PPACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans. The Budget Control Act of 2011, which calls for aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, began in 2013 and, due to subsequent legislative amendments, will remain in effect through 2031, with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on potential customers for our product candidates, if approved, and, accordingly, our future financial operations. We are unable to predict the future course of federal or state health care legislation or foreign regulations relating to the marketing, pricing and reimbursement of pharmaceutical products.

There have been U.S. Congressional inquiries, presidential executive orders, and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. Additionally, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. As discussed above, Congress passed the Inflation Reduction Act of 2022, which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single-source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. The implementation of cost containment measures, including the prescription drug provisions under the Inflation Reduction Act, as well as other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved. Complying with any new legislation and regulatory changes could be time-intensive and expensive, resulting in a material adverse effect on our business.

Further, many states have proposed or enacted legislation that seeks to indirectly or directly regulate pharmaceutical drug pricing, such as by requiring biopharmaceutical manufacturers to publicly report proprietary pricing information or to place a maximum price ceiling on pharmaceutical products purchased by state agencies. For example, a number of states are considering or have enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our products candidates. We cannot be sure to what extent these and future legislative and regulatory efforts, whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform

measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate, if approved, is prescribed or used.

In the EU similar political, economic and regulatory developments may affect our ability to profitably commercialize any future products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. Our future products, if any, might not be considered medically reasonable and necessary for a specific indication or cost-effective by third-party payors, an adequate level of reimbursement might not be available for such products, and third-party payors' reimbursement policies might adversely affect our or our strategic partners' ability to sell any future products profitably.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-approval testing and other requirements.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or elsewhere. If we or our strategic partners are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our strategic partners are not able to maintain regulatory compliance, our product candidates may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

Unstable or unfavorable global market and economic conditions may have adverse consequences on our business, financial condition and stock price.

Global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, increases in the rate of inflation and uncertainty about economic stability. We cannot assure you that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our business, financial condition, and stock price may be adversely affected by any such economic downturn, volatile business environment, or large-scale unpredictable or unstable market conditions, including a prolonged government shutdown, geopolitical events such as the conflict between Russia and Ukraine, or a global pandemic such as the COVID-19 pandemic.

If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

Our business may become subject to economic, political, regulatory and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. We have physical operations and personnel in Canada, the United States, and Ireland, and maintain offices in these three countries. We have recently established a subsidiary in Singapore, and intend to hire personnel and establish an office there. In addition, some of our suppliers and collaborative and clinical trial relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic instability or weakness, including inflation, reduced growth, diminished credit availability, weakened consumer confidence or increased unemployment;
- instability in the international geopolitical environment, including as a result of the Russian invasion of Ukraine;
- sociopolitical instability in particular foreign economies and markets;
- differing regulatory requirements for drug approvals in foreign countries;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers, including any changes that China may impose as a result of political tensions between Canada and China or the United States and China;
- regulatory changes and economic conditions following the UK's withdrawal from the EU and uncertainty related to the terms of the withdrawal;
- changes in non-U.S. currency exchange rates and currency controls;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- differing reimbursement regimes, including price controls;
- negative consequences from changes in tax laws;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities outside the United States;
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires; and
- supply and other disruptions resulting from the impact of public health epidemics, including the COVID-19 pandemic, on our strategic partners, third-party manufacturers, suppliers and other third parties upon which we rely.

Our business has been and may continue to be adversely affected by the COVID-19 pandemic.

The COVID-19 pandemic has had a broad adverse impact on the global economy across many industries and has resulted in significant governmental measures being implemented to control the spread of the virus, including quarantines, travel restrictions and business shutdowns, as well as significant volatility in global financial markets. Recently, President Biden announced that the administration intends to end the COVID-19 national and public health emergencies on May 11, 2023. The full impact of this termination of the public health emergencies on the FDA and other regulatory policies and operations are unclear.

Certain clinical trial activities, including patient enrollment and site activations, may be delayed or otherwise impacted by COVID-19 or another pandemic or epidemic, or emergence of other infectious diseases. Although we do not currently anticipate any further material impacts to our business from COVID-19 or another pandemic or epidemic, these and similar, and perhaps more severe, disruptions in our operations could negatively impact our business and financial condition in the future, but the extent of such impact will depend on future developments, which are highly uncertain and cannot be predicted, such as the location, duration and severity of outbreaks (including future potential waves or cycles), travel restrictions and social distancing, business closures or disruptions, and the effectiveness of actions taken to contain and treat the disease and to address its impact, including on financial markets.

If a resurgence of COVID-19, the emergence of another pandemic or epidemic, or the emergence of other infectious diseases were to occur, a lack of coordinated response on risk mitigation and global vaccination deployment could result in significant increases to the duration and severity of such event and could have a corresponding negative impact on our business. For example, insufficient vaccine availability, reduced effectiveness of vaccines over time or against new variants, or resistance to vaccination by certain persons may result in increasing infection and hospitalization rates, which have been and could be further complicated by the emergence of more virulent or infectious variants of the virus or other diseases.

If the COVID-19 pandemic, another pandemic or epidemic, or other infectious diseases surge, worsen or continue for a prolonged period of time, particularly in regions where we or our strategic partners and suppliers do business, we could experience disruptions that could significantly impact our current and planned clinical trials, preclinical research and other business activities, including:

- disruption to and delays in preclinical research activities due to extended closure or reduced capacity of lab facilities;
- further delays or difficulties in enrolling patients in our ongoing and planned clinical trials;
- patients discontinuing their treatment or follow-up visits;
- further delays or difficulties in clinical site initiation, including limitations on access to sites, limitations to site initiation activities that can be carried out remotely, and limitations on the number of clinical site staff on site from time to time;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- shortages, disruptions in supply, logistics or other activities related to the procurement of materials and other supplies, which could have a negative impact on our ability to conduct preclinical research, initiate or complete our clinical trials or commercialize our product candidates;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of clinical trials;
- interruption of key business activities due to illness and/or quarantine of key individuals and delays associated with recruiting, hiring and training new temporary or permanent replacements for such key individuals, both internally and at our third-party service providers and strategic partners;
- limitations in resources that would otherwise be focused on the conduct of our business or our current or planned clinical trials or preclinical research, including because of sickness, the desire to avoid contact with large groups of people, restrictions on travel, or prolonged stay-at-home or similar working arrangements;
- delays in receiving approvals from regulatory authorities to initiate our planned clinical trials;
- changes in regulations as part of a response to the COVID-19 pandemic, another pandemic or epidemic, or other infectious diseases, which may require us to change the ways in which our clinical trials are conducted and incur unexpected costs, or require us to discontinue clinical trials altogether;
- delays in necessary interactions with regulators (including the FDA), ethics committees and other important agencies and contractors due to limitations in employee resources or furlough of government or contractor personnel;
- disruptions to our strategic partners' operations, which could delay the development of our product candidates in certain geographical regions and thereby affect the timing of development and commercial milestone payments and royalties on potential future product sales we may receive; and
- limitations on our ability to recruit any necessary preclinical research, clinical, regulatory and other professional staff on the timeframe required to support our research and development programs.

In addition, COVID-19, another pandemic or epidemic, or other infectious diseases could disrupt the global financial markets, reducing our ability to access capital, which could negatively affect our liquidity. If a resurgence of COVID-19, the emergence of another pandemic or epidemic, or the emergence of other infectious diseases were to occur, the volatility of the financial market may be heightened, which could adversely impact the value of our common stock.

Our business and current and future relationships with customers and third-party payors in the United States and elsewhere will be subject, directly or indirectly, to applicable federal and state anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens, and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors in the United States and elsewhere play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval.

Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers, and third-party payors and other entities may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, including the federal Anti-Kickback Statute and the federal False Claims Act, that may constrain the business or financial arrangements and relationships through which we conduct clinical research on product candidates and market, sell and distribute any products for which we obtain marketing approval. In addition, we may be subject to transparency laws and patient privacy regulation by the federal government and by the U.S. states and foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, impose criminal or civil penalties, as applicable, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government (including the Medicare and Medicaid programs) or other third-party payor claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- HIPAA established the federal offense of health care fraud, which among other things, imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g. public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services relating to healthcare matters;
- HIPAA, as amended by HITECH, and its implementing regulations, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without the appropriate authorization by entities subject to the law, such as health plans, healthcare clearinghouses and healthcare providers and their respective business associates and their covered subcontractors;
- the federal Open Payments program under the Physician Payments Sunshine Act, created under Section 6002 of the PPACA and its implementing regulations, requires applicable group purchasing organizations and manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to HHS information related to "payments or other transfers of value" made in the previous year to covered recipients, including physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors, other health care professionals (such as nurse practitioners and physician assistants) and teaching hospitals, and information regarding ownership and investment interests held by physicians (as defined above) or their immediate family members; and

- analogous and similar state and foreign laws and regulations, including: state anti-kickback and false claims laws that may apply to our business practices (including research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by state governmental and non-governmental third-party payors, including private insurers); state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government; state laws that require drug manufacturers to track gifts and other remuneration and items of value provided to healthcare professionals and entities and file reports relating to pricing and marketing information; and state and foreign laws that govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of any available statutory exceptions and safe harbors, it is possible that some of our current and future business activities could be subject to challenge under one or more of such laws.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. Any failure or perceived failure by us to comply with such laws, regulations, or case law may result in governmental investigations or enforcement actions, litigation, claims and other proceedings, harm our reputation, and could result in significant liability. Additionally, if our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including damages, fines, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws and the curtailment or restructuring of our operations, which could have a material adverse effect on our business. If any of the physicians or other providers or entities with whom we expect to do business, including our strategic partners, is found not to be in compliance with applicable laws, it may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which could also materially affect our business.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations that can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, the United Kingdom Bribery Act 2010, the Proceeds of Crime Act 2002, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other partners from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We currently engage third parties for clinical trials outside of the United States and we may in the future engage third parties to sell our products outside of the United States once we enter a commercialization phase, or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violation of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

Third-party manufacturers may not be able to comply with U.S. export control regulations, cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in a necessity to replace current third parties, resulting in the possibility of supply delays, clinical holds on our trials, sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business, financial condition, results of operations and growth prospects.

We have received an unsolicited, non-binding proposal from an existing investor to purchase our Company.

In April 2022, All Blue Falcons FZE, or All Blue Falcons, an existing stockholder, submitted an unsolicited, non-binding proposal to purchase our Company for \$10.50 per share in cash. Our board of directors carefully reviewed the proposal and, in May 2022, unanimously determined that the unsolicited, non-binding proposal substantially undervalued our Company and was not in the best interest of the Company and its stockholders. While All Blue Falcons has not submitted a follow-up proposal and we have not had subsequent engagement with All Blue Falcons following our rejection of the non-binding proposal, reviewing this matter has in the past and may in the future divert management's and our board of directors' attention and has and may require us to incur significant costs related to our engagement of advisors. Any further actions by All Blue Falcons or others may disrupt our business and operations by causing uncertainty among and potentially loss of current and prospective employees, partners, suppliers and other constituencies important to our success or delay certain initiatives, transactions or the like that we are pursuing. Any of the foregoing could materially and negatively impact our business and financial results. The price of our common stock could be subject to price fluctuations due to the uncertainty associated with any such matter.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since inception and anticipate that we will continue to incur losses for the foreseeable future. We have no products approved for commercial sale, and to date we have not generated any revenue or profit from product sales. We may never achieve or sustain profitability.

We are a clinical-stage biopharmaceutical company. We have incurred significant losses since our inception. Our net income for the year ended December 31, 2022 was \$124.3 million, while our net loss for the years ended December 31, 2021 and 2020 was \$211.8 million and \$180.6 million, respectively. As of December 31, 2022, our accumulated deficit was \$558.8 million. We expect to continue to incur losses for the foreseeable future as we continue our research and development of, and seek regulatory approvals for, our product candidates, prepare for and begin to commercialize any approved product candidates and add infrastructure, which may include personnel, to support our product development efforts. In addition, inflationary pressure could adversely impact our financial results. The net losses and negative cash flows incurred to date, together with expected future losses, have had, and likely will continue to have, an adverse effect on our stockholders' deficit and working capital. The amount of future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability.

To become and remain profitable, we must succeed in developing and commercializing product candidates with significant market potential. This will require us to be successful in a range of challenging activities for which we are only in the preliminary stages, including developing product candidates, obtaining regulatory approval for such product candidates, and manufacturing, marketing and selling those product candidates for which we may obtain regulatory approval. We may never succeed in these activities and may never generate revenue from product sales that is significant enough to achieve profitability. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to become or remain profitable would depress our market value and could impair our ability to raise capital, expand our business, develop other product candidates, or continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of uncertainty. We have never generated any revenue from product sales and may never be profitable.

We have devoted substantially all of our financial resources and efforts to developing our proprietary therapeutic platforms, identifying potential product candidates and conducting preclinical studies and clinical trials. We and our partners are still developing our product candidates, and we have not completed development of any products. Our revenue to date has been primarily revenue from the license of our proprietary therapeutic platforms for the development of product candidates by others or revenue from our strategic partners. Our ability to generate revenue and achieve profitability depends in large part on our ability, alone or with our strategic partners, to achieve milestones and to successfully complete the development of, obtain the necessary regulatory approvals for, and commercialize, product candidates. We do not anticipate generating revenue from sales of products in the near term.

We will require substantial additional funding, which may not be available to us on acceptable terms, or at all, and, if not available, may require us to delay, scale back, or cease our product development programs or operations.

We are currently advancing two of our product candidates through clinical development as well as other potential product candidates through discovery and preclinical development. Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. In order to obtain regulatory approval, we will be required to conduct clinical trials for each indication for each of our product candidates. Although our collaboration agreements with Jazz and BeiGene provide for the future funding requirements for our lead asset, zanidatamab, we will continue to require additional funding to complete the development and commercialization of zanidatamab zovodotin, and to continue to advance the development of our other product candidates, and such funding may not be available on acceptable terms or at all. If sufficient funds on acceptable terms are not available when needed, or at all, we could be forced to significantly reduce operating expenses and delay, scale back or eliminate one or more of our development programs or our business operations. For example, in January 2022, we began implementing a Company-wide reduction in workforce to help achieve a more cost-efficient organization, which we believe will enhance our ability to execute on our key priorities. While we completed the reduction in workforce by the end of 2022, the full impact of the reduction in workforce is not yet known.

Our future funding requirements will depend on many factors, including:

- the number and characteristics of other product candidates that we pursue;
- the scope, progress, timing, cost and results of research, preclinical development, and clinical trials;
- the costs, timing and outcome of seeking and obtaining FDA and non-U.S. regulatory approvals;
- the costs associated with manufacturing our product candidates and establishing sales, marketing and distribution capabilities;
- our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make in connection with the licensing, filing, defense and enforcement of any patents or other intellectual property rights;
- our ability to achieve the anticipated cost reductions from the reduction in workforce implemented in 2022;
- our ability to hire when needed additional management, scientific and medical personnel;
- the effect of competing products that may limit market penetration of our product candidates;
- our need to implement additional internal systems and infrastructure, including financial and reporting systems; and
- the economic and other terms, timing of and success of our existing strategic partnerships, and any collaboration, asset monetization, licensing, or other arrangements into which we may enter in the future, including the timing of receipt of any milestone or royalty payments under these agreements.

Until we can generate a sufficient amount of product revenue to finance our cash requirements, which we may never do, we expect to finance future cash needs primarily through a combination of public and private equity offerings, debt financings, asset monetization, strategic partnerships and grant funding.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish substantial rights.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these new securities may include liquidation or other preferences that adversely affect our stockholders' rights as common stockholders. Debt financing, if available at all, may involve agreements that include covenants limiting or restricting our ability to take specific actions such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise additional funds through partnerships, collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, product candidates, or future revenue streams, or grant licenses on terms that are not favorable to us. We cannot assure that we will be able to obtain additional funding if and when necessary. If we are unable to obtain adequate financing on a timely basis, we could be required to delay, scale back or eliminate one or more of our development programs or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to Our Dependence on Third Parties

We will depend on our collaborative relationship with Jazz to further develop and commercialize zanidatamab, and if our relationship is not successful or is terminated, we may be delayed in or unable to effectively develop and/or commercialize zanidatamab, which could have a material adverse effect on our business.

In October 2022, Zymeworks BC entered into the Jazz Collaboration Agreement with Jazz. Pursuant to the terms of the agreement, we received a \$50 million upfront payment following receipt of HSR Clearance and delivery of licenses and technology transfer to Jazz and a further payment of \$325 million following Jazz's decision to continue the collaboration after readout of the top-line clinical data from HERIZON-BTC-01. We are also eligible to receive additional milestone payments upon achievement of certain regulatory and commercial milestones, as well as tiered royalties on Jazz's net sales of licensed products. We will depend on Jazz to collaborate with us to develop and commercialize zanidatamab in the territories covered by the Jazz Collaboration Agreement and, as a result, the eventual success or commercial viability of zanidatamab is largely beyond our control. Following receipt of the initial payments totaling \$375 million, any future financial returns to us depend in large part on achievement of regulatory and commercialization milestones, plus a share of any revenue from sales. Therefore, our success, and any associated financial returns to us and our investors, will depend in significant part on Jazz's performance under the Jazz Collaboration Agreement.

We are subject to a number of additional specific risks associated with our dependence on our collaborative relationship with Jazz, including:

- adverse decisions by Jazz regarding the development and commercialization of zanidatamab;
- possible disagreements as to the timing, nature and extent of development plans, including clinical trials or regulatory approval strategy;
- loss of significant rights if we fail to meet our obligations under the agreement;
- changes in key management personnel at Jazz; and
- possible disagreements with Jazz regarding the agreement, for example, with regard to ownership of intellectual property rights.

If either we or Jazz fail to perform our respective obligations, any clinical trial, regulatory approval or development progress could be significantly delayed or halted, could result in costly or time-consuming litigation or arbitration and could have a material adverse effect on our business.

Decisions by Jazz to emphasize other drug candidates currently in its portfolio ahead of zanidatamab, or to add competitive agents to its portfolio could result in a decision to terminate the agreement, in which event, among other things, we may be responsible for paying any remaining costs of ongoing or future clinical trials. If Jazz decides to terminate the Jazz Collaboration Agreement, we may be delayed in or unable to effectively develop and/or commercialize zanidatamab, which could have a material adverse effect on our business.

Any of the above discussed scenarios could adversely affect the timing and extent of the development and commercialization activities related to zanidatamab, which could materially and adversely impact our business.

Our existing strategic partnerships are important to our business, and future strategic partnerships will likely also be important to us. If we are unable to maintain our strategic partnerships, or if these strategic partnerships are not successful, our business could be adversely affected.

We have limited capabilities for drug development and commercialization of our product candidates, if approved. Accordingly, we have entered into strategic partnerships with other companies that we believe can provide such capabilities, including our collaboration and license agreements with Jazz, BeiGene, BMS, GSK, Daiichi Sankyo, Janssen, LEO, Iconic, Merck and Atreca. These relationships also have provided us with non-dilutive funding for our wholly owned pipeline and therapeutic platforms and we expect to receive additional funding under these strategic partnerships in the future. Our existing strategic partnerships, and any future strategic partnerships we enter into, may pose a number of risks, including the following:

- strategic partners have significant discretion in determining the efforts and resources that they will apply to these partnerships;
- strategic partners may not perform their obligations as expected;
- strategic partners may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the partners' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- strategic partners may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- strategic partners could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the strategic partners believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than our product candidates;
- product candidates discovered in collaboration with us may be viewed by our strategic partners as competitive with their own product candidates or products, which may cause strategic partners to cease to devote resources to the commercialization of our product candidates;
- a strategic partner with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product candidates;
- disagreements with strategic partners, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- strategic partners may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- strategic partners may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;

- strategic partnerships may be terminated for the convenience of the partner and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates. For example, each of our collaboration and license agreements with Jazz, BeiGene, BMS, GSK, Daiichi Sankyo, Janssen, LEO, Iconic, Merck and Atreca may be terminated for convenience upon the completion of a specified notice period;
- we may elect to enter into additional licensing or collaboration agreements to partner our product candidates in territories we currently retain, and in the event we grant exclusive rights to such partners, we would be precluded from potential commercialization of our product candidates within the territories in which we have a partner; and
- strategic partners may not have the ability or the development capabilities to perform their obligations as expected, including as a result of the impact of the COVID-19 pandemic or the emergence of another pandemic or epidemic on our strategic partners' operations or business.

If our strategic partnerships do not result in the successful development and commercialization of product candidates or if one of our partners terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under our strategic partnership agreements, our development of our therapeutic platforms and product candidates could be delayed and we may need additional resources to develop product candidates and our therapeutic platforms.

We face significant competition in seeking new strategic partners.

For some of our product candidates, we may in the future determine to collaborate with additional pharmaceutical and biotechnology companies for development and potential commercialization of therapeutic products. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the strategic partner's resources and expertise, the terms and conditions of the proposed collaboration and the proposed strategic partner's evaluation of a number of factors. These factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The strategic partner may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate.

Strategic partnerships are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future strategic partners. If we are unable to reach agreements with suitable strategic partners on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay one or more of our other development programs, delay potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into strategic partnerships and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our therapeutic platforms and our business may be materially and adversely affected.

We rely on third-party manufacturers to produce our product candidates and on other third parties to provide supplies and store, monitor and transport bulk drug substance and drug product. We and our third-party partners may encounter difficulties with respect to these activities that could delay or impair our ability to initiate or complete our clinical trials or commercialize approved products.

We do not currently own or operate any manufacturing facilities. We rely on our strategic partners to manufacture product candidates licensed to them or work with multiple third-party contract manufacturers to produce sufficient quantities of materials required for the manufacture of our product candidates for preclinical testing and clinical trials, in compliance with applicable regulatory and quality standards, and intend to do so for the commercial manufacture of our products. If we are unable to arrange for such third-party manufacturing sources, or fail to do so on commercially reasonable terms, we may not be able to successfully produce sufficient supply of product candidate or we may be delayed in doing so. Such failure or substantial delay could materially harm our business.

The manufacture of biopharmaceutical products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. The process of manufacturing our product candidates is susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our product candidates or in the third-party manufacturing facilities in which our product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. All of our engineered antibodies are manufactured by utilizing cells that are stored in a cell bank. We have one master cell bank and one working cell bank utilized for each antibody manufactured in accordance with cGMP. While we believe we would have adequate back up at a secondary storage location, should any cell bank be lost in a catastrophic event, it is possible that we could lose part of a cell bank and have our manufacturing potentially impacted by the need to replace the cell bank. Any adverse developments affecting manufacturing operations for our product candidates, if any are approved, may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our products. We may also have to take inventory write-offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives.

Furthermore, reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates ourselves, including reliance on the third party for regulatory compliance and quality control and assurance, volume production, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control (including a failure to manufacture our product candidates in accordance with our product specifications) and the possibility of termination or nonrenewal of the agreement by the third party at a time that is costly or damaging to us. In addition, the FDA, EMA and other regulatory authorities require that our product candidates be manufactured according to cGMP and similar foreign standards. Pharmaceutical manufacturers and their subcontractors are required to register their facilities or products manufactured at the time of submission of the marketing application and then annually thereafter with the FDA and certain state and foreign agencies. They are also subject to periodic unannounced inspections by the FDA, state and other foreign authorities. Any subsequent discovery of problems with a product, or a manufacturing or laboratory facility used by us or our strategic partners, may result in restrictions on the product or on the manufacturing or laboratory facility, including marketed product recall, suspension of manufacturing, product seizure, or a voluntary withdrawal of the drug from the market. We may have little to no control regarding the occurrence of third-party manufacturer incidents. Any failure by our third-party manufacturers to comply with cGMP or failure to scale up manufacturing processes, including any failure to deliver sufficient quantities of product candidates in a timely manner, could lead to a delay in, or failure to obtain, regulatory approval of any of our product candidates.

In addition to third-party manufacturers, we rely on other third parties to store, monitor and transport bulk drug substance and drug product. If we are unable to arrange for such third-party sources, or fail to do so on commercially reasonable terms, we may not be able to successfully supply sufficient product candidate or we may be delayed in doing so. Such failure or substantial delay could materially harm our business.

In addition, disruptions to ports and other shipping infrastructure, as were experienced during the COVID-19 pandemic, may result in shortages or delays impacting the availability of materials and other supplies, which could negatively impact our manufacturers, suppliers and other third parties on whom we rely. While we have not yet suffered any direct, material negative impacts from these ongoing supply chain disruptions, we cannot be certain that we will not be impacted, which could increase our costs or negatively impact our development timelines.

We rely on third parties to monitor, support, conduct and oversee clinical trials of the product candidates that we are developing and, in some cases, to maintain regulatory files for those product candidates. We may not be able to obtain regulatory approval for our product candidates or commercialize any products that may result from our development efforts if we are not able to maintain or secure agreements with such third parties on acceptable terms, if these third parties do not perform their services as required, or if these third parties fail to timely transfer any regulatory information held by them to us.

We rely on entities outside of our control, which may include academic institutions, CROs, hospitals, clinics and other third-party strategic partners, to monitor, support, conduct and oversee preclinical studies and clinical trials of our current and future product candidates. We also rely on third parties to perform clinical trials on our current and future product candidates when they reach that stage. As a result, we have less control over the timing and cost of these studies and the ability to recruit trial subjects than if we conducted these trials with our own personnel.

If we are unable to maintain or enter into agreements with these third parties on acceptable terms, or if any such engagement is terminated prematurely, we may be unable to enroll patients on a timely basis or otherwise conduct our trials in the manner we anticipate. In addition, there is no guarantee that these third parties will devote adequate time and resources to our studies or perform as required by our contract or in accordance with regulatory requirements, including maintenance of clinical trial information regarding our product candidates. These third parties, in turn, may face their own constraints in obtaining the resources and personnel needed to perform the work for which we engage them. If these third parties fail to meet expected deadlines, fail to transfer to us any regulatory information in a timely manner, fail to adhere to protocols or fail to act in accordance with regulatory requirements or our agreements with them, or if they otherwise perform in a substandard manner or in a way that compromises the quality or accuracy of their activities or the data they obtain, then clinical trials of our product candidates may be extended or delayed with additional costs incurred, or our data may be rejected by the FDA, EMA or other regulatory agencies.

Ultimately, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities.

We and our CROs are required to comply with GCP regulations and guidelines enforced by the FDA, the competent authorities of the member states of the EU and comparable foreign regulatory authorities for products in clinical development. Regulatory authorities enforce these GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and clinical trial sites. If we or any of our CROs fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and our submission of marketing applications may be delayed or the FDA may require us to perform additional clinical trials before approving our marketing applications. Upon inspection, the FDA could determine that any of our clinical trials fail or have failed to comply with applicable GCP regulations. In addition, our clinical trials must be conducted with product produced under the cGMP regulations enforced by the FDA, and our clinical trials may require a large number of test subjects. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and increase our costs. Moreover, our business may be implicated if any of our CROs violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

If any of our clinical trial sites terminate for any reason, we may experience the loss of follow-up information on patients enrolled in our ongoing clinical trials unless we are able to transfer the care of those patients to another qualified clinical trial site. Further, if our relationship with any of our CROs is terminated, we may be unable to enter into arrangements with alternative CROs on commercially reasonable terms, or at all.

Switching or adding CROs or other suppliers can involve substantial cost and require extensive management time and focus. In addition, there is a natural transition period when a new CRO or supplier commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. If we are required to seek alternative supply arrangements, the resulting delays and potential inability to find a suitable replacement could materially and adversely impact our business.

We rely on third parties for various operational and administrative aspects of our business, including for certain cloud-based software platforms, which impact our financial, operational and research activities. If any of these third parties fail to provide timely, accurate and ongoing service or if the cloud-based platforms suffer outages that we are unable to mitigate, our business may be adversely affected.

We currently rely upon third-party consultants and contractors to provide certain operational and administrative services, including external financial, legal, clinical and research consultation. The failure of any of these third parties to provide accurate and timely service may adversely impact our business operations. In addition, if such third-party service providers were to cease operations, temporarily or permanently, face financial distress or other business disruption, or increase their fees, or if our relationships with these providers deteriorate, we could suffer increased costs until an equivalent provider could be found, if at all, or we could develop internal capabilities, if ever.

In addition, if we are unsuccessful in choosing or finding high-quality partners, if we fail to negotiate cost-effective relationships with them, or if we ineffectively manage these relationships, it could have an adverse impact on our business and financial performance.

Further, our operations depend on the continuing and efficient operation of our information technology and communications systems and infrastructure, and specifically on “cloud-based” platforms. These platforms are vulnerable to damage or interruption from earthquakes, vandalism, sabotage, terrorist attacks, floods, fires, power outages, telecommunications failures, and computer viruses or other deliberate attempts to harm the systems. The occurrence of a natural or intentional disaster, any decision to close a facility we are using without adequate notice, or particularly an unanticipated problem at our cloud-based virtual server facility, could result in harmful interruptions in our service, resulting in adverse effects to our business.

Risks Related to Our Intellectual Property

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our future approved products or impair our competitive position. For example, certain patents and patent applications held by third parties cover Fab and Fc region engineering methods for bispecific antibodies, and antibodies having mutations in Fab heavy and light chain regions and Fc regions to generate correctly paired bispecific antibodies. If our products or our strategic partners’ products incorporate any Fab or Fc region mutations covered by any claims of these patents or patents that may issue from these applications, and if licenses for them are not available on commercially reasonable terms or at all, and we are unable to invalidate or render unenforceable those patents, our business could be materially harmed.

We are also aware of third-party patents and patent applications containing claims directed to compositions and methods for treating various forms of cancer with antibodies targeting HER2, alone or in combination with other anti-cancer agents, which patents and applications could potentially be construed to cover our product candidates and the use thereof to treat cancer. If our products or our strategic partners’ products were found to infringe any such patents, and if licenses for them are not available on commercially reasonable terms, or at all, and we were unable to invalidate or render unenforceable those patents, our business could be materially harmed. These patents may not expire before we receive marketing authorization for our product candidates, and could delay the commercial launch of one or more future products. There is also no assurance that there are not third-party patents or patent applications of which we are aware, but which we do not believe are relevant to our business, which may, nonetheless, ultimately be found to limit our ability to make, use, sell, offer for sale or import our future approved products or impair our competitive position.

Patents that we may ultimately be found to infringe could be issued to third parties. Third parties may have or obtain valid and enforceable patents or proprietary rights that could block us from developing product candidates using our technology. Our failure to obtain a license to any patent covering any technology that we require may materially harm our business, financial condition and results of operations. Moreover, our failure to maintain a license to any patent covering any technology that we require may also materially harm our business, financial condition and results of operations. Furthermore, we would be exposed to a threat of litigation.

In the pharmaceutical industry, significant litigation and other proceedings regarding patents, patent applications, trademarks and other intellectual property rights are commonplace. Any such lawsuits and proceedings could be costly and could affect our results of operations and divert the attention of our management and scientific personnel. Some of our competitors may be able to sustain the cost of such litigation and proceedings more effectively than we can because of their substantially greater resources. There is a risk that a court would decide that we or our strategic partners are infringing a third party's patents and would order us or our strategic partners to stop the activities or stop the manufacture, use, or sale of any product covered by the patents. In that event, we or our strategic partners may not have a viable alternative to the technology protected by the patent and may need to halt work on the affected product candidate or cease commercialization of an approved product. In addition, there is a risk that a court would order us or our strategic partners to pay third-party damages or some other monetary award, depending upon the jurisdiction. An adverse outcome in any litigation or other proceeding could subject us to significant liabilities to third parties, potentially including treble damages and attorneys' fees if we are found to have willfully infringed, and we may be required to cease using the technology that is at issue or to license the technology from third parties. We may not be able to obtain any required licenses on commercially acceptable terms or at all. Any of these outcomes could have a material adverse effect on our business.

If we are unable to obtain, maintain and enforce patent and trade secret protection for our product candidates and related technology, our business could be materially harmed.

Our strategy depends on our ability to identify and seek patent protection for our discoveries. This process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we have licensed from third parties. Therefore, our owned or in-licensed patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Our patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our current and future product candidates in the United States or in other countries.

Moreover, the patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has been the subject of much litigation. The issuance of a patent does not ensure that it is valid or enforceable. Third parties may challenge the validity, enforceability or scope of our issued patents, and such patents may be narrowed, invalidated, circumvented, or deemed unenforceable. In addition, changes in law may introduce uncertainty in the enforceability or scope of patents owned by biotechnology companies. If our patents are narrowed, invalidated or held unenforceable, third parties may be able to commercialize our technology or products and compete directly with us without payment to us. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, and such prior art could potentially invalidate one or more of our patents or prevent a patent from issuing from one or more of our pending patent applications. There is also no assurance that there is not prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our patents and patent applications, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim.

Furthermore, even if our patents are unchallenged, they may not adequately protect our intellectual property, provide exclusivity for our product candidates, prevent others from designing around our claims or provide us with a competitive advantage. The legal systems of certain countries do not favor the aggressive enforcement of patents, and the laws of other countries may not allow us to protect our inventions with patents to the same extent as the laws of the United States. Because patent applications in the United States and many other jurisdictions are typically not

published until 18 months after filing, or in some cases not at all, and because publications of discoveries in scientific literature lag behind actual discoveries, we cannot be certain that we were the first to make the inventions claimed in our issued patents or pending patent applications, or that we were the first to file for protection of the inventions set forth in our patents or patent applications. As a result, we may not be able to obtain or maintain protection for certain inventions. Therefore, the issuance, validity, enforceability, scope and commercial value of our patents in the United States and in other countries cannot be predicted with certainty and, as a result, any patents that we own or license may not provide sufficient protection against competitors. We may not be able to obtain or maintain patent protection from our pending patent applications, from those we may file in the future, or from those we may license from third parties. Moreover, even if we are able to obtain patent protection, such patent protection may be of insufficient scope to achieve our business objectives. In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our own patented product and practicing our own patented technology.

Our patents covering one or more of our products or product candidates could be found invalid or unenforceable if challenged.

Any of our intellectual property rights could be challenged or invalidated despite measures we take to obtain patent and other intellectual property protection with respect to our product candidates and proprietary technology. For example, if we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the United States and in some other jurisdictions, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld material information from the U.S. Patent and Trademark Office, or USPTO, or the applicable foreign counterpart, or made a misleading statement, during prosecution. A litigant or the USPTO itself could challenge our patents on this basis even if we believe that we have conducted our patent prosecution in accordance with the duty of candor and in good faith. The outcome following such a challenge is unpredictable.

With respect to challenges to the validity of our patents, for example, there might be invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on a product candidate. Even if a defendant does not prevail on a legal assertion of invalidity and/or unenforceability, our patent claims may be construed in a manner that would limit our ability to enforce such claims against the defendant and others. The cost of defending such a challenge, and any resulting loss of patent protection, could have a material adverse impact on one or more of our product candidates and our business.

Enforcing our intellectual property rights against third parties may also cause such third parties to file other counterclaims against us, which could be costly to defend and could require us to pay substantial damages, cease the use, manufacture, or sale of certain products or enter into a license agreement and pay royalties (which may not be possible on commercially reasonable terms or at all). Any efforts to enforce our intellectual property rights are also likely to be costly and may divert the efforts of our scientific and management personnel.

Our intellectual property rights will not necessarily provide us with competitive advantages.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we or our strategic partners own or have exclusively licensed;
- others may independently develop similar or alternative technologies without infringing our intellectual property rights;

- issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- we may obtain patents for certain compounds many years before we obtain marketing approval for products containing such compounds, and because patents have a limited life, which may begin to run prior to the commercial sale of the related product, the commercial value of our patents may be limited;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may fail to develop additional proprietary technologies that are patentable;
- the laws of certain countries may not protect our intellectual property rights to the same extent as the laws of the United States, or we may fail to apply for or obtain adequate intellectual property protection in all the jurisdictions in which we operate; and
- the patents of others may have an adverse effect on our business, for example by preventing us from marketing one or more of our product candidates for one or more indications.

Any of the aforementioned threats to our competitive advantage could have a material adverse effect on our business.

We may become involved in lawsuits to protect or enforce our patents and trade secrets, which could be expensive, time consuming and unsuccessful.

Third parties may seek to market biosimilar versions of any approved products. Alternatively, third parties may seek approval to market their own products similar to or otherwise competitive with our product candidates. In these circumstances, we may need to defend or assert our patents, including by filing lawsuits alleging patent infringement. The outcome following legal assertions of invalidity and unenforceability is unpredictable. In any of these types of proceedings, a court or agency with jurisdiction may find our patents invalid or unenforceable. Even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

Even after they have issued, our patents and any patents that we license may be challenged, narrowed, invalidated or circumvented. If our patents are invalidated or otherwise limited or will expire prior to the commercialization of our product candidates, other companies may be better able to develop products that compete with ours, which could adversely affect our competitive business position, business prospects and financial condition. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

The following are examples of litigation and other adversarial proceedings or disputes that we could become a party to involving our patents or patents licensed to us:

- we or our strategic partners may initiate litigation or other proceedings against third parties to enforce our patent or trade secret rights;
- third parties may initiate litigation or other proceedings seeking to invalidate patents owned by or licensed to us or to obtain a declaratory judgment that their product or technology does not infringe our patents or patents licensed to us;
- third parties may initiate opposition or reexamination proceedings challenging the validity or scope of our patent rights, requiring us or our strategic partners and/or licensors to participate in such proceedings to defend the validity and scope of our patents;
- there may be a challenge or dispute regarding inventorship or ownership of patents or trade secrets currently identified as being solely or co-owned by us or by a licensor who has granted a license to us;

- the USPTO may initiate an interference between patents or patent applications owned by or licensed to us and those of our competitors, requiring us or our strategic partners and/or licensors to participate in an interference proceeding to determine the priority of invention, which could jeopardize our patent rights; or
- third parties may seek approval to market biosimilar versions of our future approved products prior to expiration of relevant patents owned by or licensed to us, requiring us to defend our patents, including by filing lawsuits alleging patent infringement.

These lawsuits and proceedings would be costly and could affect our results of operations and divert the attention of our managerial and scientific personnel. Adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our licensors can. There is a risk that a court or administrative body would decide that our patents are invalid, unenforceable or not infringed or trade secrets not misappropriated by a third party's activities, or that the scope of certain issued claims must be further limited. An adverse outcome in a litigation or proceeding involving our own patents or trade secrets could limit our ability to assert our patents or trade secrets against these or other competitors, affect our ability to receive royalties or other licensing consideration from our licensees, and may curtail or preclude our ability to exclude third parties from making, using and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition.

We may not be able to prevent, alone or with our licensors or licensees, infringement or misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have an adverse effect on the price of our common stock.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to develop a platform that is similar to, or better than, ours in a way that is not covered by the claims of our patents;
- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of our patents;
- we might not have been the first to make the inventions covered by patents or pending patent applications;
- we might not have been the first to file patent applications for these inventions;
- any patents that we obtain may not provide us with any competitive advantages or may ultimately be found invalid or unenforceable; or
- we may not develop additional proprietary technologies that are patentable or that afford meaningful trade secret protection.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain protection under the Hatch-Waxman Amendments and similar legislation in other countries for extending the term of patents covering each of our product candidates, our business may be materially harmed.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced, possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

If we are unable to protect the confidentiality of our proprietary information, the value of our technology and products could be adversely affected.

In addition to patent protection, we also rely on other proprietary rights, including protection of trade secrets, and other proprietary information. For example, we treat our confidential and proprietary computational technologies, including unpatented know-how and other proprietary information, as trade secrets. We enter into confidentiality agreements with our employees, consultants, strategic partners and others upon the commencement of their relationships with us. These agreements provide that all confidential information developed by the individual or made known to the individual by us during the course of the individual's relationship with us be kept confidential and not disclosed to third parties. Our agreements with employees and our personnel policies also provide that any inventions conceived by the individual in the course of rendering services to us shall be our exclusive property. However, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. We cannot guarantee that we have entered into such agreements with each party that has or may have had access to, or houses or hosts, our trade secrets or proprietary information or that has been involved in the development of intellectual property. Further, despite such agreements, such inventions or confidential information may become disclosed or assigned to third parties. Monitoring unauthorized uses and disclosures is difficult and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. To the extent that our employees, consultants or contractors use technology or know-how owned by third parties in their work for us, disputes may arise between us and those third parties as to the rights in such technology or know-how or in related inventions. To the extent that an individual who is not obligated to assign rights in intellectual property to us is rightfully an inventor of intellectual property, we may need to obtain an assignment or a license to that intellectual property from that individual, or a third party or from that individual's assignee. Such assignment or license may not be available on commercially reasonable terms or at all.

We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems and cloud storage sources, but such security measures may be breached, including through cyber-hacking or cyberattacks, and we may not have adequate remedies for any breach.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. The disclosure of our trade secrets would impair our competitive position and may materially harm our business, financial condition and results of operations. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to maintain trade secret protection could adversely affect our competitive business position. In addition, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, or if we otherwise lose protection for our trade secrets or proprietary know-how, the value of this information may be greatly reduced and our business and competitive position could be harmed. Adequate remedies may not exist in the event of unauthorized use or disclosure of our proprietary information.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously or concurrently employed at research institutions and/or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, or we, have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers, or that patents and applications we have filed to protect inventions of these employees, even those related to one or more of our product candidates, are rightfully owned by their former or concurrent employer. Litigation may be necessary to defend against these claims. Such trade secrets or other proprietary information could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by regulations and governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents or applications will be due to the USPTO and various foreign patent offices at various points over the lifetime of our patents or applications. We have systems in place to remind us to pay these fees, and we rely on our outside patent annuity service to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

Although we are not currently experiencing any claims challenging the inventorship or ownership of our patents, we may in the future be subject to claims that former employees, strategic partners or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. While it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. For example, the assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, or we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Patent protection and patent prosecution for some of our product candidates may be dependent on, and the ability to assert patents and defend them against claims of invalidity may be maintained by, third parties.

There may be times in the future when certain patents that relate to our product candidates or any approved products are controlled by our licensees or licensors. Although we may, under such arrangements, have rights to consult with our strategic partners on actions taken as well as back-up rights of prosecution and enforcement, we have in the past and may in the future relinquish rights to prosecute and maintain patents and patent applications within our portfolio as well as the ability to assert such patents against infringers.

If any current or future licensee or licensor with rights to prosecute, assert or defend patents related to our product candidates fails to appropriately prosecute and maintain patent protection for patents covering any of our product candidates, or if patents covering any of our product candidates are asserted against infringers or defended against claims of invalidity or unenforceability in a manner that adversely affects such coverage, our ability to develop and commercialize any such product candidate may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products.

Changes in patent laws or patent jurisprudence could diminish the value of patents in general, thereby impairing our ability to protect our products.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. We cannot predict the breadth of claims that may be allowed or found to be enforceable in our patents, in our strategic partners' patents or in third-party patents. Recent U.S. Supreme Court rulings have either narrowed the scope of patent protection available in certain circumstances or weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this has created uncertainty with respect to the validity, scope and value of patents, once obtained.

For our U.S. patent applications containing a priority claim after March 16, 2013, there is a greater level of uncertainty in the patent law. In September 2011, the Leahy-Smith America Invents Act, also known as the America Invents Act, or AIA, was signed into law. The AIA includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation.

The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have an adverse effect on our business. An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties disclosing or claiming the same invention. A third party that has filed, or files a patent application in the USPTO after March 16, 2013, but before us, could be awarded a patent covering a given invention, even if we had made the invention before it was made by the third party. This requires us to be cognizant of the time from invention to filing of a patent application.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal court necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action.

Depending on decisions by the U.S. Congress, the U.S. federal courts, the USPTO or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that may weaken our and our licensors' ability to obtain new patents or to enforce existing patents we and our licensors or partners may obtain in the future.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some countries do not protect intellectual property rights to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our current or future products, if any, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Recent U.S. Supreme Court cases have narrowed the scope of what is considered patentable subject matter, for example, in the areas of software and diagnostic methods involving the association between treatment outcome and biomarkers. This could impact our ability to patent certain aspects of our technology in the United States.

Many companies have encountered significant problems in protecting and defending intellectual property rights in jurisdictions other than the United States. The legal systems of certain countries do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Additionally, the requirements for patentability may differ in certain countries. For example, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In India, unlike the United States, there is no link between regulatory approval of a drug and its patent status. In addition to India, certain countries in Europe and developing countries, including China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

Geo-political actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors or licensees and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors or licensees. For example, the United States, Canadian, and foreign government actions related to Russia's invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees that have citizenship or nationality in, are registered in, or have a predominately primary place of business or profit-making activities in the United States and other countries that Russia has deemed unfriendly without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

As another example, the complexity and uncertainty of European patent laws have increased in recent years. In Europe, a new unitary patent system will likely be introduced by the end of 2023, which would significantly impact European patents, including those granted before the introduction of such a system. Under the unitary patent system, European applications will soon have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court, or UPC. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. Patents granted before the implementation of the UPC will have the option of opting out of the jurisdiction of the UPC and remaining as national patents in the UPC countries. Patents that remain under the jurisdiction of the UPC will be potentially vulnerable to a single UPC-based revocation challenge that, if successful, could invalidate the patent in all countries who are signatories to the UPC. We cannot predict with certainty the long-term effects of any potential changes.

We use open source software in connection with our internal research and development programs, which could negatively affect our ability to develop products and subject us to litigation or other actions.

We use open source software in connection with our internal research and development programs. The terms of many open source licenses have not been interpreted by U.S. courts or courts outside of the U.S., and there is a risk that these licenses could be construed in a way that could impose unanticipated conditions or restrictions on our ability to use this software. As a result, we could be subject to lawsuits by parties claiming ownership of what we believe to be open source software, or claiming that software we developed using such open source software is a derivative work of open source software and demanding the release of portions of our source code, or otherwise seeking to enforce the terms of the applicable open source license. Litigation could be costly for us to defend, have a negative effect on our financial condition and results of operations or require us to devote additional research and development resources to change our platform and offerings.

If we were to combine our proprietary software with open source software in a certain manner, we could, under certain open source licenses, be required to release the source code of our proprietary software to the public. While we monitor our use of open source software and try to ensure that none is used in a manner that would require us to disclose our proprietary source code or that would otherwise breach the terms of an open source agreement, such use could inadvertently occur, or could be claimed to have occurred, in part because open source license terms are often ambiguous. If we inappropriately use open source software, or if the license terms for open source software that we use change, we may be required to re-engineer our platform, incur additional costs, discontinue the use of some or all of our platform or take other remedial actions.

In addition to risks related to license requirements, usage of open source software can lead to greater risks than use of third-party commercial software, because open source licensors generally do not provide warranties or assurance of title or controls on origin of the software. In addition, many of the risks associated with usage of open source software, such as the lack of warranties or assurances of title, cannot be eliminated, and could, if not properly addressed, negatively affect our business. We have established processes to help alleviate these risks, including a review process for the use of open source software, but we cannot be sure that all of our use of open source software is in a manner that is consistent with our current policies and procedures, or will not subject us to liability. Any of these risks could be difficult to eliminate or manage and, if not addressed, could have an adverse effect on our business, financial condition and results of operations.

We will need to obtain FDA approval for any proposed product candidate names, and any failure or delay associated with such approval may adversely affect our business.

Any proprietary name or trademark we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the USPTO. The FDA typically conducts a review of proposed product candidate names, including an evaluation of the potential for confusion with other product names. The FDA may also object to a product name if it believes the name inappropriately implies certain medical claims or contributes to an overstatement of efficacy. If the FDA objects to any product candidate names we propose, we may be required to adopt an alternative name for our product candidates. If we adopt an alternative name, we would lose the benefit of any existing trademark applications for such product candidate and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product candidates.

Risks Related to the Redomicile Transactions

We may fail to realize certain benefits of the Redomicile Transactions, including as a result of the shares of our common stock not being included in a U.S. stock market index.

We believe that the Redomicile Transactions will enhance stockholder value over the long-term and raise the profile and marketability of our capital stock in the United States through, among other things, the ability to attract deeper and growing pools of passive investment capital in the United States, particularly if shares of our common stock are included in certain U.S. stock market indices and other investment vehicles that only include securities of U.S.-incorporated companies. However, if shares of our common stock are not included in such U.S. stock market indices, this could result in increased selling pressure and/or decreased demand for our common stock that would increase stock price volatility or cause the market price of the shares of our common stock to fall. Initial inclusion and continued inclusion in a stock market index or fund is not guaranteed and is subject to numerous factors which can be applied subjectively by the entity managing the index or fund. There are no assurances that we will be included in any U.S. stock market indices or funds in a timely manner, or at all. Even if we are included in a U.S. stock market index or fund, the entities managing such indices or funds may change their inclusion criteria, resulting in the future exclusion from such index or fund.

In addition, we incurred a number of non-recurring costs associated with the Redomicile Transactions, including legal fees, accountants' fees, proxy solicitor fees, filing fees, mailing expenses and financial printing expenses. The completion of the Redomicile Transactions and the associated reorganization of our corporate structure may result in additional and unforeseen expenses in the future. While it is expected that benefits of the Redomicile Transactions will offset these transaction costs over time, this net benefit may not be achieved in the short-term or at all. These combined factors could adversely affect our business and overall financial condition. The success of the Redomicile Transactions will depend, in part, on our ability to realize the anticipated benefits associated with the Redomicile Transactions and associated reorganization of our corporate structure, and we may not be able to realize such benefits on a timely basis or at all.

The Redomicile Transactions may result in sales of shares of our common stock by certain retail and institutional stockholders or investment funds that are not permitted to hold shares of our common stock under their internal guidelines.

The Redomicile Transactions may result in sales of shares of our common stock by certain retail and institutional stockholders or investment funds (including Canadian-focused funds) that are not permitted to hold shares of our common stock under their internal guidelines, or are limited in the size of any such investments. Such sales could result in increased selling pressure and/or decreased demand for shares of our common stock, which could increase stock price volatility or cause the market price of the shares of our common stock to fall. As a result of the foregoing, certain of these investors may be required under their internal guidelines to sell their shares at times when, or at prices for which, they would otherwise not have sold. If an investor sells its shares at a time when the market price is lower than their cost basis in the shares, the investor will suffer a loss that could be significant to such investor.

Our business may be impacted by the uncertainty associated with the Redomicile Transactions.

Following completion of the Redomicile Transactions, our principal executive offices are located in Middletown, Delaware. We have physical operations and personnel in Canada, the United States, and Ireland, and maintain offices in these three countries. Our executive officers and directors are located in several jurisdictions, including the United States, Canada and the United Kingdom.

Certain relationships, including with employees, suppliers, CROs, partners, collaborators, governments and other stakeholders, may be subject to disruption due to uncertainty associated with the Redomicile Transactions. Specifically, certain stakeholders may be reluctant to engage in business with us following the completion of the Redomicile Transactions or may impose additional conditions on or apply less favorable terms to transactions involving us. This could have an adverse effect on our business and operations.

In connection with the completion of the Redomicile Transactions we may need to enter into certain new arrangements which may not be on terms as favorable as arrangements entered into by Zymeworks BC.

In connection with completion of the Redomicile Transactions we may need to enter into new arrangements as the ultimate parent company to Zymeworks BC and its subsidiaries. While we anticipate such terms will be materially consistent with existing arrangements, there is no assurance that such arrangement will not impose additional operating or financial restrictions on us, or that such arrangements will be on commercially reasonable terms or terms that are acceptable to us.

In addition, the completion of the Redomicile Transactions may have triggered certain technical change in control, right of first offer, notice, consent, assignment or other provisions in agreements to which Zymeworks BC or our other subsidiaries are a party. If we are unable to assert that such provisions should not apply, or we are unable to comply with or negotiate waivers of those provisions, the counterparties may exercise their rights and remedies under the agreements, including potentially terminating such agreements or seeking monetary damages. Even if we are able to negotiate waivers, the counterparties may require a fee for such waivers or seek to renegotiate the agreements on terms less favorable to us.

Negative publicity resulting from the Redomicile Transactions could adversely affect our business and the market price of our common stock.

Transactions similar to the Redomicile Transactions that have been undertaken by other companies have in some cases generated significant news coverage, some of which has been negative. Negative publicity generated by the Redomicile Transactions could cause certain persons with whom we have a business relationship to be more reluctant to do business with us. In addition, negative publicity could cause certain of our employees, particularly those in Canada, to perceive uncertainty regarding future opportunities available to them. Either of these events could have a significant adverse impact on our business. Negative publicity could also cause some of our stockholders to sell their shares or decrease the demand for new investors to purchase such shares, which could have an adverse impact on the price of our common stock.

Our current organizational structure may result in certain tax and operational inefficiencies that may adversely affect our business, financial condition and results of operations.

On October 13, 2022, the Redomicile Transactions were completed, which were governed by a transaction agreement dated July 14, 2022, as restated and amended on August 18, 2022, or the “Restated and Amended Transaction Agreement,” by and among Zymeworks BC, us, CallCo and ExchangeCo. Pursuant to the terms of the Restated and Amended Transaction Agreement, we, Zymeworks BC, CallCo and ExchangeCo agreed, among other things, to use reasonable efforts to take certain corporate steps and actions, as may be necessary or desirable, to effect and implement certain post-arrangement transactions following the implementation of the arrangement under the BCBCA, or the “Post-Arrangement Transactions,” including the movement of certain subsidiaries of Zymeworks BC so that they become our directly, wholly-owned subsidiaries. Following Zymeworks BC’s entry into the Jazz Collaboration Agreement, we reevaluated the potential impacts of completing the Post-Arrangement Transactions and have determined that completing the Post-Arrangement Transactions as contemplated in the Restated and Amended Transaction Agreement would result in negative tax consequences. As a result, we are evaluating alternatives to the previously contemplated Post-Arrangement Transactions with our advisors. We cannot be certain that we will be able to identify and implement an alternative set of post-arrangement transactions. Even if we do identify an alternative set of post-arrangement transactions, we cannot be certain that such alternative will result in a more tax-efficient or operationally-efficient organizational structure. While we are evaluating alternative approaches, our current organizational structure may result in certain tax and operational inefficiencies that may adversely affect our business, financial condition and results of operations.

Our effective tax rate may change in the future.

We are subject to U.S. federal income taxes on our earnings and the earnings of our non-U.S. subsidiaries in a manner that may adversely impact our effective tax rate. For example, we may have to include additional amounts in income under the so-called “global intangible low-taxed income” regime or as a result of the application of “controlled foreign corporation” rules. In addition, the United States has enacted the Inflation Reduction Act, which, among other changes, imposes a 1% excise tax on certain stock buybacks and an alternative minimum tax on adjusted financial statement income. In addition, our Canadian tax attributes (including net operating loss and tax credit carryforwards and deductible Scientific Research and Experimental Development Expenditure carryforwards) will generally not be available to offset U.S. income and may be subject to limitation.

Further, our future operations and business structure may result in increased tax burden. For example, changes in our clinical development plans and business or commercialization strategies may result in an increased effective tax rate. Taxation of international business operations and intercompany transactions, including transactions between us and non-U.S. subsidiaries, is complicated. Any changes in the U.S. or non-U.S. taxation of such activities may increase our worldwide effective tax rate and harm our business, financial condition, and results of operations.

Enforcement of rights against us in Canada may be limited.

Following the Redomicile Transactions, our principal executive offices are located in Middletown, Delaware and the majority of our directors, officers and experts reside outside of Canada. Accordingly, it may not be possible for our stockholders to effect service of process within Canada upon us or the majority of our directors, officers or experts, or to enforce judgments obtained in Canadian courts against us or the majority of our directors, officers or experts.

Risks Related to the Exchangeable Shares

The Exchangeable Shares will not be listed on any stock exchange.

Pursuant to the Redomicile Transactions, holders of Zymeworks BC common shares exchanged their Zymeworks BC common shares for shares of our common stock or, at their election with respect to all or a portion of their Zymeworks BC common shares and subject to applicable eligibility criteria and an overall cap, exchangeable shares (the “Exchangeable Shares”) in the capital of ExchangeCo. The Exchangeable Shares will not be listed on any stock exchange. Although Exchangeable Shares are exchangeable at the option of the holder for shares of our common stock, there is no market through which the Exchangeable Shares may be sold, and holders may not be able to sell their Exchangeable Shares.

Holders of Exchangeable Shares may experience a delay in receiving shares of our common stock from the date they request an exchange, which may affect the value of the shares the holder receives in such exchange.

Holders of Exchangeable Shares who request an exchange may not receive shares of our common stock until a period of time after the applicable request is received. During this period, the market price of our common stock may increase or decrease. Any such increase or decrease would affect the value of the consideration to be received by such a holder of Exchangeable Shares upon a subsequent sale of shares of our common stock received in the exchange.

There may be a taxable event for a holder of Exchangeable Shares beyond such holder’s control.

A holder of Exchangeable Shares will be considered to have disposed of Exchangeable Shares (i) on a redemption (including pursuant to a retraction request) of such Exchangeable Shares by holders of Exchangeable Shares or ExchangeCo, and (ii) on an acquisition of such Exchangeable Shares by us or CallCo. Although each is a taxable event, the Canadian federal income tax consequences of the disposition will be different depending on whether the event giving rise to the disposition is a redemption or an acquisition.

Prior to the sunset date of the Exchangeable Shares, ExchangeCo may redeem Exchangeable Shares in limited circumstances, and ExchangeCo shall redeem the Exchangeable Shares on the sunset date. Accordingly, an Eligible Holder may have a taxable event in a transaction beyond their control.

The tax treatment of Exchangeable Shares for non-Canadian tax purposes is uncertain.

The tax treatment of Exchangeable Shares for non-Canadian tax purposes, including U.S. federal income tax purposes, is uncertain. Holders of Exchangeable Shares who are subject to taxation in jurisdictions other than Canada should consult with their tax advisors regarding the tax treatment of Exchangeable Shares under non-Canadian tax laws and regulations.

Risks Related to Additional Legal and Compliance Matters

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, insider trading, and noncompliance with our policies and procedures.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with federal and state health care fraud and abuse laws and regulations, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Conduct and Business Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions. In addition, employees may become subject of allegations of gender discrimination and other misconduct that are not in compliance with our policies and procedures, which, regardless of the ultimate outcome, may result in adverse publicity that could materially harm our brand, reputation and business.

If we or our contractors or agents market products in a manner that violates healthcare fraud and abuse laws, or if we violate government price reporting laws and transparency laws, we may be subject to civil or criminal penalties.

In addition to FDA restrictions on the marketing of pharmaceutical products, federal and state healthcare laws restrict certain business practices in the biopharmaceutical industry. Although we currently do not have any products on the market, we may be subject, and if our product candidates are approved and we begin commercialization will be subject, to additional healthcare laws and regulations enforced by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. These state and federal healthcare laws, commonly referred to as “fraud and abuse” laws, have been applied to restrict certain marketing practices in the pharmaceutical industry, and include anti-kickback, false claims, data privacy and security and transparency statutes and regulations.

Federal false claims laws prohibit, among other things, any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, or causing to be made, a false statement to get a false claim paid. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. Most states also have statutes or regulations similar to the federal anti-kickback law and federal false claims laws, which may apply to items such as pharmaceutical products and services reimbursed by private insurers. Administrative, civil and criminal sanctions may be imposed under these federal and state laws.

[Table of Contents](#)

The federal civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

HIPAA created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, including private third-party payors, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of, or payment for, healthcare benefits, items or services.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by HITECH, and its implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates-independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, and newly empowered state attorneys general with the authority to enforce HIPAA. In January 2013, the Office for Civil Rights of the U.S. Department of Health and Human Services issued the Final Omnibus Rule under HIPAA pursuant to HITECH that makes significant changes to the privacy, security and breach notification requirements and penalties. The Final Omnibus Rule generally took effect in September 2013 and enhances certain privacy and security protections, and strengthens the government's ability to enforce HIPAA. The Final Omnibus Rule also enhanced requirements for both covered entities and business associates regarding notification of breaches of unsecured protected health information. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways. These state laws may not have the same effect and often are not preempted by HIPAA, thus complicating compliance efforts.

Additionally, the PPACA also included the federal Physician Payments Sunshine Act, which requires applicable group purchasing organizations and manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually information related to certain payments or other transfers of value made in the previous year to covered recipients, including physicians, as defined by law, and teaching hospitals and, effective for data reported in 2022, expanded to include nurse practitioners, physician assistants, clinical nurse specialists, certified registered nurse anesthetists and anesthesiologist assistants, and certified nurse-midwives, including certain ownership and investment interests held by physicians or their immediate family members. Failure to comply with the required reporting requirements could subject applicable reporting entities such as manufacturers to substantial civil monetary penalties.

Also, many states have similar healthcare statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Certain states require pharmaceutical companies to implement a comprehensive compliance program that includes a limit or outright ban on expenditures for, or payments to, individual medical or health professionals and/or require pharmaceutical companies to track and report gifts and other payments made to physicians and other healthcare providers.

If our operations are found to be in violation of any of the healthcare laws or regulations described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion of products from reimbursement under government programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings or the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products will be sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

If we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.

Our research and development involves, and may in the future involve, the use of potentially hazardous materials and chemicals. Our operations may produce hazardous waste products. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards mandated by local, state and federal laws and regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations and fire and building codes, including those governing laboratory procedures, exposure to blood-borne pathogens, use and storage of flammable agents and the handling of biohazardous materials. Although we maintain workers' compensation insurance as prescribed by certain jurisdictions in which we operate to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of these materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate, any of these laws or regulations.

Risks Related to Employee Matters and Managing Growth

We may fail to achieve the expected cost savings and related benefits from our 2022 reduction in workforce.

In January 2022, we announced a plan to reduce our workforce to reflect our renewed focus on key priorities and enable us to help achieve a more cost-efficient organization necessary to execute on those priorities. While we completed the reduction in workforce by the end of 2022, the full impact of the reduction in workforce is not yet known.

We may fail to effectively achieve the stated goals of the reduction in workforce. Our plans may also change as we continue to refocus on our key priorities. These actions may take more time than we currently estimate and we may not be able to achieve the cost-efficiencies sought. In addition, while the reduction in workforce was completed in 2022, it may still negatively impact employee morale for those that were not directly impacted, which may increase employee attrition and hinder our ability to achieve our key priorities. Any failure to achieve the expected benefits from the reduction in workforce or from other recent management and personnel related changes could adversely affect our stock price, financial condition and ability to achieve our key priorities.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on key members of our senior management team, including Kenneth Galbraith, the Chair of our board of directors and Chief Executive Officer, Neil Klompas, our President and Chief Operating Officer, Christopher Astle, our Chief Financial Officer, Paul Moore, our Chief Scientific Officer, and other key members of our senior management, scientific and clinical teams. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. The loss of the services of our key senior managers and employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy.

Retention and any future recruitment of qualified scientific, technical, clinical, manufacturing and sales and marketing personnel will also be critical to our success. In addition, we will need to effectively manage our managerial, operational, financial, development and other resources in order to successfully pursue our research, development and commercialization efforts for our existing and future product candidates. Furthermore, replacing key senior managers and employees may be difficult and may take an extended period of time because of the limited talent pool in our industry due to the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. The reduction in workforce announced in January 2022 may also make retention of our current personnel both more important and more challenging. Intense competition for

attracting key skill-sets and the impact of inflationary pressure on wages may limit our ability to attract, retain and motivate key personnel on acceptable terms. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our business strategy will be limited.

As we advance our development and commercialization plans and strategies, we may need to grow or modify our organization, and we may experience difficulty in managing such change, which could disrupt our operations.

As of December 31, 2022, we had 291 full-time employees. As we advance our development and commercialization plans and strategies in the future, we anticipate that we may need to expand or modify our employee base. Additionally, as our product candidates enter and advance through preclinical studies and any clinical trials, we may need to expand our development, manufacturing, regulatory sales and marketing capabilities or contract with other organizations to provide these capabilities for us. Future growth would impose significant added responsibilities on members of management, including the need to identify, recruit, maintain, motivate and integrate additional employees. Also, our management may need to divert a disproportionate amount of their attention away from our day-to-day activities and devote a substantial amount of time to managing any necessary growth activities. We may not be able to effectively manage an expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational errors, loss of business opportunities, loss of employees and reduced productivity amongst remaining employees. Any growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of existing and additional product candidates. If our management is unable to effectively manage any needed growth, our expenses may increase more than expected, our ability to generate or grow revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates and compete effectively with others in our industry will depend on our ability to effectively manage any future growth.

Risks Related to Our Common Stock

Our stock price is likely to be volatile and the market price of our common stock may drop below the price paid by stockholders.

Investors should consider an investment in our common stock as risky and invest only if they can withstand a significant loss and wide fluctuations in the market value of their investment. Investors may be unable to sell their common stock at or above the price they paid for such stock due to fluctuations in the market price of our common stock arising from changes in our operating performance or prospects. Some of the factors that may cause the market price of our common stock to fluctuate or decrease include:

- results and timing of our clinical trials and clinical trials of our competitors' products;
- failure or discontinuation of any of our development programs;
- the success of our partnerships, including our and Jazz's ability and efforts to collaborate to develop and commercialize zanidatamab in the territories covered by the Jazz Collaboration Agreement;
- our ability to achieve milestones and receive associated milestone payments pursuant to the terms of our collaboration agreements;
- issues in manufacturing our product candidates or future approved products;
- regulatory developments or enforcement in the United States and foreign countries with respect to our product candidates or our competitors' products;
- competition from existing products or new products that may emerge;
- developments or disputes concerning patents or other proprietary rights;
- introduction of technological innovations or new commercial products by us or our competitors;

[Table of Contents](#)

- announcements by us, our strategic partners or our competitors of significant acquisitions, strategic partnerships, joint ventures, or capital commitments;
- changes in estimates or recommendations by securities analysts that cover our common stock;
- fluctuations in the valuation of companies in the biotechnology industry or otherwise perceived by investors to be comparable to us;
- additional instances of stockholder activism, including unsolicited takeover proposals or proxy contests;
- claims or litigation related to our stockholder rights plan;
- public concern over our product candidates or any future approved products;
- litigation;
- future sales of our common stock;
- stock price and volume fluctuations attributable to inconsistent trading volume levels of our common stock;
- additions or departures of key personnel;
- our ability to execute on our key strategic priorities;
- changes in the structure of health care payment systems in the United States or other countries;
- failure of any of our product candidates, if approved, to achieve commercial success;
- economic and other external factors or other disasters or crises, including pandemics;
- period-to-period fluctuations in our financial condition and results of operations, including the timing of receipt of any milestone or other payments under commercialization or licensing agreements;
- general market conditions and market conditions for biopharmaceutical stocks;
- potential disagreements or disputes with certain of our stockholders;
- overall fluctuations in U.S. equity markets; and
- other factors that may be unanticipated or out of our control.

In addition, the stock market in general, and the stock of biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of the relevant companies, including recently in connection with the COVID-19 pandemic, which has resulted in increased volatility and decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. Broad market and industry factors, including potentially worsening economic conditions and other adverse effects or developments relating to the COVID-19 pandemic, may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this “Risk Factors” section, could have a material adverse effect on the market price of our common stock.

An active trading market for our common stock may not be sustained.

Our common stock was first listed on the NYSE in connection with the completion of the Redomicile Transactions on October 13, 2022. In December 2022, we moved our listing to The Nasdaq Stock Market LLC. There can be no assurance that an active trading market for our common stock will be sustained or continue to be as active or liquid as was the trading market for Zymeworks BC’s common shares prior to the Redomicile Transactions, and the trading price of our common stock may be effectively lower than the trading price of Zymeworks BC’s common shares. If an active market for our common stock does not continue, it may be difficult for our stockholders to sell their stock without depressing the market price for the common stock or sell their common stock at or above the prices at which they acquired their common stock or sell their common stock at the time they would like to sell. Any inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling common stock and may impair our ability to acquire other companies or technologies by using our common stock as consideration.

We may fail to meet the continued listing requirements of The Nasdaq Stock Market LLC. If Nasdaq delists our shares of common stock from trading on its exchange, we could face significant material adverse consequences, including:

- significant impairment of the liquidity for our common stock, which may substantially decrease the market price of our common stock;
- a limited availability of market quotations for our securities;
- a determination that our common stock qualifies as a “penny stock” which will require brokers trading in our common stock to adhere to more stringent rules and possibly resulting in a reduced level of trading activity in the secondary trading market for our common stock;
- a limited amount of news and analyst coverage for our company; and
- a decreased ability to issue additional securities or obtain additional financing in the future.

Substantial future sales of our common stock, or the perception that these sales could occur, may cause the price of our common stock to drop significantly, even if our business is performing well.

A large volume of sales of our common stock could decrease the prevailing market price of our common stock and could impair our ability to raise additional capital through the sale of equity securities in the future. Even if a substantial number of sales of our common stock does not occur, the mere perception of the possibility of these sales could depress the market price of our common stock and have a negative effect on our ability to raise capital in the future.

Our management team has broad discretion to use the net proceeds from public and private and debt financings as well as funds received pursuant to our strategic collaborations, and its investment of these proceeds may not yield a favorable return. They may invest the proceeds in ways with which our stockholders disagree.

Our management team has broad discretion in the application of the net proceeds we received pursuant to our January 2022 public offering of common shares and pre-funded warrants to purchase common shares, as well as funds we receive from time to time pursuant to our strategic collaborations and that we may receive from future fundraising efforts, including pursuant to any “at-the-market” equity offering programs we may use from time to time, and we could spend or invest the proceeds in ways with which our stockholders disagree. Accordingly, stockholders will need to rely on our management team’s judgment with respect to the use of these proceeds. However, the failure by management to apply these funds effectively could negatively affect our ability to operate and grow our business.

We cannot specify with certainty all of the particular uses for the net proceeds to be received from our fundraising efforts or for the funds received from time to time pursuant to our strategic collaborations. In addition, the amount, allocation and timing of our actual expenditures will depend upon numerous factors, including additional milestone payments received from our strategic partnerships and royalties received on sale of any future approved product. Accordingly, we will have broad discretion in using these proceeds. Until the net proceeds are used, they may be placed in investments that do not produce significant income or that may lose value.

We do not anticipate paying cash dividends for the foreseeable future, and accordingly, stockholders must rely on stock appreciation for any return on their investment.

We have never paid any dividends on our common stock. We currently intend to retain our future earnings, if any, to fund the development and growth of our business and do not anticipate that we will declare or pay any cash dividends on our common stock in the foreseeable future. As a result, capital appreciation, if any, of our common stock will be the sole source of gain on investment in our common stock for the foreseeable future. Investors seeking cash dividends should not invest in our common stock.

Any future determination to pay dividends will be at the discretion of our board of directors and will depend upon many factors, including our results of operations, financial position, capital requirements, distributable reserves, credit terms, general economic conditions and other factors as our board of directors may deem relevant from time to time. Consequently, future dividends payable to investors are not guaranteed.

Our principal stockholders, in aggregate, could exert substantial influence over us which could delay or prevent a change in corporate control or result in the entrenchment of management or the board of directors.

Our principal stockholders, being our stockholders that beneficially own 5% or more of our common stock, together with their affiliates and related persons, in aggregate, beneficially own approximately 51.4% of our outstanding common stock as of December 31, 2022. Our directors and executive officers beneficially own, in the aggregate, approximately 1.9% of our outstanding common stock as of December 31, 2022. Our principal stockholders, if acting together (with or without our directors and executive officers), may have the ability to exert substantial influence over the outcome of matters submitted to our stockholders for approval, including the election and removal of directors and any merger or sale of all or substantially all of our assets. In addition, our principal stockholders, if acting together (with or without our directors and executive officers), may have the ability to exert substantial influence over the management and affairs of our company. Accordingly, this concentration of ownership could harm the market price of our common stock by:

- delaying, deferring, or preventing a change in control;
- entrenching our management or the board of directors;
- impeding a merger, takeover, or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

We have recently qualified as a smaller reporting company, and any decision on our part to comply only with certain reduced reporting and disclosure requirements applicable to such companies could make our common stock less attractive to investors.

As a result of our public float (the market value of our common stock held by non-affiliates) as of June 30, 2022, we qualify as a “smaller reporting company,” as defined under the Exchange Act. In addition, beginning with our Annual Report on Form 10-K for the year ending December 31, 2022, we will be a “non-accelerated filer” as defined under the Exchange Act. For as long as we continue to be a smaller reporting company or a non-accelerated filer, we may choose to take advantage of exemptions from various reporting requirements applicable to other public companies that are not smaller reporting companies or non-accelerated filers, as applicable, including, but not limited to, an exemption from the requirement that our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting under Section 404. We have opted not to obtain such attestation from our independent registered public accounting firm in connection with this Annual Report on Form 10-K. This decision may have a detrimental impact on our ability to maintain the adequacy of our internal control over financial reporting, and any failure to maintain adequacy, or inability to produce accurate financial statements or other reports on a timely basis, could increase our operating costs and could materially impair our ability to operate our business.

For so long as we choose to rely on any of these disclosure exemptions, the information we provide stockholders will be different than the information that is available with respect to other public companies. Moreover, if some investors find our common stock less attractive as a result of any choices to reduce our disclosure, there may be a less active trading market for our common stock and the market price of our common stock may be more volatile.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Under the Sarbanes-Oxley Act of 2002, we are required to establish and maintain effective internal control over financial reporting and adequate disclosure controls and procedures. Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Even if our management concludes that our internal control over financial reporting is effective, our independent registered public accounting firm may conclude that there are material weaknesses with respect to our internal controls or the level at which our internal controls are documented, designed, implemented or reviewed. Undetected material weaknesses in our internal controls could lead to financial statement restatements and require us to incur the expense of remediation.

We have transitioned to a new enterprise resource planning system, which we believe will lead to improvements in our internal control over financial reporting. Although we have completed this transition to a new enterprise resource planning system, the full impact of this transition is not yet known. If, during the evaluation and testing process of our internal controls, we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses in our internal controls over financial reporting in the future. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets. Furthermore, if we cannot provide reliable financial reports or prevent fraud, including as a result of remote working by our employees, our business and results of operations would likely be materially and adversely affected.

Delaware law and provisions in our amended and restated certificate of incorporation and amended and restated bylaws might delay, discourage or prevent a change in control of Zymeworks or changes in our management, thereby depressing the market price of our common stock.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may make the acquisition of Zymeworks more difficult or delay or prevent changes in control of its management. Among other things, these provisions:

- authorize our board of directors to issue shares of preferred stock and determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval;
- permit only the board of directors to establish the number of directors and fill vacancies and newly created directorships on the board, provided that the board of directors' ability to increase the size of the board and fill vacancies and newly created directorships will be subject to the restrictions in our amended and restated certificate of incorporation and amended and restated bylaws;
- establish that members of our board of directors serve in one of three staggered terms of three years each;
- provide that our directors may only be removed by the affirmative vote of at least 66 2/3% of the voting power of the shares cast on such proposal;
- permit stockholders to only take actions at a duly called annual or special meeting and not by written consent;
- require that stockholders give advance notice to nominate directors or submit proposals for consideration at stockholder meetings;
- not provide for cumulative voting rights in the election of directors;

- provide that special meetings of Zymeworks' stockholders may be called only by the board of directors, the chairperson of the board of directors, Zymeworks' chief executive officer, president or the secretary upon request from holders of no less than 20% of our outstanding voting stock, subject to the limitations and requirements set forth in our amended and restated bylaws; and
- require a super-majority vote of stockholders to amend some of the provisions described above.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the DGCL, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any "interested stockholder" for a period of three years following the date on which the stockholder became an "interested stockholder" unless certain conditions are met.

These provisions, alone or together, could delay, discourage or prevent a transaction involving a change in control of Zymeworks. These provisions could also discourage proxy contests and make it more difficult for stockholders to elect directors of their choosing and to cause Zymeworks to take other corporate actions they desire, any of which, under certain circumstances, could limit the opportunity for our stockholders to receive a premium for their shares of common stock, and could also affect the price that some investors are willing to pay for our common stock.

The stockholders' rights plan adopted by our board of directors may discourage a third party from acquiring us in a manner that could result in a premium price to our stockholders.

On October 12, 2022, we entered into a Preferred Stock Rights Agreement, or the "New Rights Plan," pursuant to which our board of directors authorized and declared a dividend distribution of one right, or each, a "Right," for each share of our common stock outstanding on October 13, 2022, or the "Record Date," and for each share of common stock that becomes outstanding between the Record Date and the earlier of the date the Rights become exercisable and the expiration of the Rights. Each Right entitles the registered holder to purchase from us one one-thousandth of a share of our Series B Participating Preferred Stock at an exercise price of \$74.00, subject to adjustment. In general terms, the New Rights Plan works by imposing a significant penalty upon any person or group that acquires 10 percent or more (or 20 percent or more in the case of certain institutional investors who report their holdings on Schedule 13G) of the shares of our common stock without the approval of our board of directors. As a result, the overall effect of the New Rights Plan and the issuance of the Rights may be to render more difficult or discourage a merger, amalgamation, arrangement, take-over bid, tender or exchange offer or other business combination involving us that is not approved by our board of directors. However, neither the New Rights Plan nor the Rights should interfere with any merger, amalgamation, arrangement, take-over bid, tender or exchange offer or other business combination approved by the Board. The terms of the New Rights Plan are substantively similar in all material respects to the terms of the Zymeworks BC Preferred Shares Rights Agreement, which expired in connection with the completion of the Redomicile Transactions.

Our amended and restated bylaws designate a state or federal court located within the State of Delaware as the exclusive forum for substantially all disputes between Zymeworks and its stockholders, and also provide that the federal district courts are the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, each of which could limit our stockholders' ability to choose the judicial forum for disputes with Zymeworks or its directors, officers, stockholders or employees.

Our amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, stockholders, officers or other employees to Zymeworks or our stockholders, (3) any action arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws or (4) any other action asserting a claim that is governed by the internal affairs doctrine shall be the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, another State court in Delaware or the federal district court for the District of Delaware), except for any claim as to which such court determines that there is an indispensable party not subject to the jurisdiction of such court (and the indispensable party does not consent to the personal jurisdiction of such court within ten days following such determination), which is vested in the exclusive jurisdiction of a court or forum other than such court or for which such court does not have subject matter jurisdiction. This provision does not apply to any action brought to enforce a duty or liability created by the Exchange Act and the rules and regulations thereunder.

Section 22 of the Securities Act establishes concurrent jurisdiction for federal and state courts over Securities Act claims. Accordingly, both state and federal courts have jurisdiction to hear such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated bylaws provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States will be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

Any person or entity purchasing or otherwise acquiring or holding or owning (or continuing to hold or own) any interest in any of our securities shall be deemed to have notice of and consented to the foregoing bylaw provisions. Although we believe these exclusive forum provisions benefit us by providing increased consistency in the application of Delaware law and federal securities laws in the types of lawsuits to which each applies, the exclusive forum provisions may limit a stockholder's ability to bring a claim in a judicial forum of its choosing for disputes with us or our current or former directors, officers, stockholders or other employees, which may discourage such lawsuits against us and our current and former directors, officers, stockholders and other employees. Our stockholders will not be deemed to have waived its compliance with the federal securities laws and the rules and regulations thereunder as a result of our exclusive forum provisions.

The enforceability of similar exclusive forum provisions in other companies' organizational documents have been challenged in legal proceedings, and, while certain courts have determined these provisions are enforceable, it is possible that a court of law could rule that these types of provisions are inapplicable or unenforceable if they are challenged in a proceeding or otherwise. If a court were to find either exclusive forum provision contained in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur significant additional costs associated with resolving such action in other jurisdictions, which could harm our financial condition and results of operations.

General Risk Factors

We are at risk of securities class action litigation.

Securities class action litigation has often been brought against companies following a decline in the market price of their securities. This risk is especially relevant for us because biotechnology companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could materially harm our business.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. We cannot assure that analysts will cover us or provide accurate or favorable coverage. If one or more of the analysts who cover us downgrade our stock or change their opinion of our common stock negatively, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our stock price or trading volume to decline. Moreover, the research and reports that analysts publish may suggest a price for our common stock that does not fully or accurately reflect the true value of our company. Furthermore, even if such analyst publications are favorable, these reports could have negative consequences for us.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents incorporated by reference herein or therein, contain “forward-looking statements” or information within the meaning of applicable securities legislation, including Section 27A of the Securities Act, and Section 21E of the Exchange Act. Forward-looking statements include statements that may relate to our plans, objectives, goals, strategies, future events, future revenue or performance, capital expenditures, financing needs and other information that is not historical information. Forward-looking statements can often be identified by the use of terminology such as “subject to,” “believe,” “anticipate,” “plan,” “expect,” “intend,” “estimate,” “project,” “may,” “will,” “should,” “would,” “could,” “can,” the negatives thereof, variations thereon and similar expressions, or by discussions of strategy. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. In particular, forward-looking statements in this prospectus and the documents incorporated by reference herein and therein include, but are not limited to, statements about:

- the size of our addressable markets and our ability to commercialize product candidates;
- the achievement of advances in and expansion of our therapeutic platforms and antibody engineering expertise;
- the likelihood of product candidate development and clinical trial progression, initiation or success;
- our ability to predict and manage government regulation;
- the impact of the COVID-19 pandemic on our business and operations; and
- the expected benefits and other impacts of the Redomicile Transactions.

All forward-looking statements, including, without limitation, those related to our examination of historical operating trends, are based upon our current expectations and various assumptions. Certain assumptions made in preparing the forward-looking statements include:

- our ability to manage our growth effectively;
- the absence of material adverse changes in our industry or the global economy;
- our ability to understand and predict trends in our industry and markets;
- our ability to enter into and maintain good business relationships with strategic partners;
- our ability to comply with current and future regulatory standards;
- our ability to protect our intellectual property rights;
- our continued compliance with third-party license terms and the non-infringement of third-party intellectual property rights;
- our ability to manage and integrate any acquisitions we may pursue;
- our ability to retain key personnel; and
- our ability to raise sufficient debt or equity financing to support our continued growth.

[Table of Contents](#)

We believe there is a reasonable basis for our expectations and beliefs, but they are inherently uncertain. We may not realize our expectations, and our beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements. The following uncertainties and factors, among others (including those referred to in the section titled “Risk Factors” in this prospectus supplement and in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2022), could affect future performance and cause actual results to differ materially from those matters expressed in or implied by forward-looking statements:

- our or our partners’ ability to obtain regulatory approval for product candidates without significant delays;
- the predictive value of our current or planned clinical trials;
- delays with respect to the development and commercialization of our product candidates, which may cause increased costs or delay receipt of product revenue;
- our or any of our partners’ ability to enroll subjects in clinical trials and thereby complete trials on a timely basis;
- the design or our execution of clinical trials may not support regulatory approval, including where clinical trials are conducted outside the United States;
- our ability to achieve milestones and receive associated milestone payments pursuant to the terms of our collaboration agreements, including the Jazz Collaboration Agreement (as defined below);
- the extent to which our business may be adversely affected by the COVID-19 pandemic;
- global economic and political conditions, including as a result of the Russian invasion of Ukraine, as well as social and political unrest in the locations where our clinical trials are held, and the related impact on our business and the markets generally;
- expected benefits of the Redomicile Transactions may not materialize as expected or at all;
- unanticipated tax consequences in connection with the Redomicile Transactions;
- the Fast Track and Breakthrough Therapy designations for any of our product candidates may not expedite regulatory review or approval;
- the U.S. Food and Drug Administration, or the FDA, may not accept data from trials we conduct outside the United States;
- disruptions at the FDA and other government agencies caused by funding shortages or global health concerns;
- our discretion to discontinue or reprioritize the development of any of our product candidates;
- the potential for our product candidates to have undesirable side effects;
- no regulatory agency has made a determination that any of our product candidates are safe or effective for use by the general public or for any indication;
- our ability to face significant competition, including biosimilar products;
- the likelihood of broad market acceptance of our product candidates;
- our ability to obtain Orphan Drug Designation or exclusivity for some or all of our product candidates;
- our ability to commercialize products outside of the United States;

[Table of Contents](#)

- the outcome of reimbursement decisions by third-party payors relating to our products;
- our expectations with respect to the market opportunities for any product that we or our strategic partners develop;
- our ability to pursue product candidates that may be profitable or have a high likelihood of success;
- our ability to use and expand our therapeutic platforms to build a pipeline of product candidates;
- our ability to meet the requirements of ongoing regulatory review;
- the threat of product liability lawsuits against us or any of our strategic partners;
- changes in product candidate manufacturing or formulation that may result in additional costs or delay;
- the potential disruption of our business and dilution of our shareholdings associated with acquisitions and joint ventures;
- the potential for foreign governments to impose strict price controls;
- the risk of security breaches or data loss, which could compromise sensitive business or health information;
- current and future legislation that may increase the difficulty and cost of commercializing our product candidates;
- economic, political, regulatory and other risks associated with international operations;
- our exposure to legal and reputational penalties as a result of any of our current and future relationships with various third parties;
- our ability to comply with export control and import laws and regulations;
- our history of significant losses since inception;
- our ability to generate revenue from product sales and achieve profitability;
- our requirement for substantial additional funding;
- the potential dilution to our stockholders associated with future financings;
- restrictions on our ability to seek financing, which may be imposed by future debt;
- unstable market and economic conditions;
- currency fluctuations and changes in foreign currency exchange rates;
- our ability to maintain existing and future strategic partnerships;
- our ability to realize the anticipated benefits of our strategic partnerships;
- our ability to secure future strategic partners;
- our reliance on third-party manufacturers to produce our product candidate supplies and on other third parties to store, monitor and transport bulk drug substance and drug product;
- risk related to the manufacture of product candidates and difficulties in production;
- our reliance on third parties to oversee clinical trials of our product candidates and, in some cases, maintain regulatory files for those product candidates;

- our reliance on the performance of independent clinical investigators and contract research organizations, or CROs;
- our reliance on third parties for various operational and administrative aspects of our business including our reliance on third parties' cloud-based software platforms;
- our ability to operate without infringing the patents and other proprietary rights of third parties;
- our ability to obtain and enforce patent protection for our product candidates and related technology;
- our patents could be found invalid or unenforceable if challenged;
- our intellectual property rights may not necessarily provide us with competitive advantages;
- we may become involved in expensive and time-consuming patent lawsuits;
- the risk that the duration of our patents will not adequately protect our competitive position;
- our ability to obtain protection under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments, and similar foreign legislation;
- we may be unable to protect the confidentiality of our proprietary information;
- our ability to comply with procedural and administrative requirements relating to our patents;
- the risk of claims challenging the inventorship of our patents and other intellectual property;
- our intellectual property rights for some of our product candidates are dependent on the abilities of third parties to assert and defend such rights;
- patent reform legislation and court decisions can diminish the value of patents in general, thereby impairing our ability to protect our products;
- we may not be able to protect our intellectual property rights throughout the world;
- we will require FDA approval for any proposed product candidate names and any failure or delay associated with such approval may adversely affect our business;
- our election to rely on certain reduced reporting and disclosure requirements available to smaller reporting companies may make our common stock less attractive to investors;
- the risk of employee misconduct including noncompliance with regulatory standards and insider trading;
- our ability to market our products in a manner that does not violate the law and subject us to civil or criminal penalties;
- if we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected;
- our ability to retain key executives and attract and retain qualified personnel;
- our ability to manage organizational growth;
- our exposure to potential securities class action litigation; and
- if securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

[Table of Contents](#)

Consequently, forward-looking statements should be regarded solely as our current plans, estimates and beliefs. You should not place undue reliance on forward-looking statements. We cannot guarantee future results, events, levels of activity, performance or achievements. We do not undertake and specifically decline any obligation to update, republish or revise forward-looking statements to reflect future events or circumstances or to reflect the occurrences of unanticipated events, except as required by law. Our Risk Factors are not guarantees that no such conditions exist as of the date of this prospectus and should not be interpreted as an affirmative statement that such risks or conditions have not materialized, in whole or in part.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

USE OF PROCEEDS

We will not receive any proceeds from the issuance of our shares of common stock in exchange for Exchangeable Shares. We expect to receive nominal proceeds, if any, from the issuance of shares of our common stock upon the exercise of pre-funded warrants. We expect to use the net proceeds from the exercise of the pre-funded warrants, if any, for general corporate purposes.

Our management will have broad discretion in the application of the net proceeds, if any, from this offering, and the amounts and timing of our actual expenditures will depend on numerous factors, including those described in the section titled “Risk Factors” in this prospectus and the documents incorporated by reference herein and therein.

DESCRIPTION OF CAPITAL STOCK

The description of our capital stock, including our common stock, the preferred stock purchase rights associated with our common stock, and our preferred stock, is incorporated by reference to [Exhibit 99.1](#) to our Current Report on Form 8-K12B filed with the SEC on October 13, 2022 and in the Registration Statement on [Form 8-A](#) relating thereto, filed with the SEC on December 15, 2022.

PLAN OF DISTRIBUTION

The shares of our common stock issuable to holders of Exchangeable Shares may be issued using various legal mechanisms described in greater detail in the section titled “[Description of Exchangeable Shares and Related Agreements](#)” in our proxy statement/prospectus dated September 2, 2022, which we filed with the SEC on September 2, 2022 and which is incorporated herein by reference. The shares of our common stock underlying pre-funded warrants may be issued upon our receipt of a nominal cash exercise price or on a net exercise basis. No broker, dealer or underwriter has been engaged in connection with soliciting such exchange or exercise, and no commission or other compensation will be paid to any person in connection with solicitation of such exchange or exercise.

CERTAIN MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS

The following discussion is a general summary of certain material U.S. federal income tax consequences of the ownership and disposition of shares of our common stock acquired in exchange for Exchangeable Shares or pursuant to the exercise of a pre-funded warrant in this offering. It is not a comprehensive discussion of all tax considerations that may be relevant to a particular holder's decision to acquire shares of our common stock, including U.S. federal estate, gift and alternative minimum tax considerations, the Medicare contribution tax imposed on certain net investment income, the special accounting rules under Section 451(b) of the U.S. Internal Revenue Code of 1986, as amended, or the Code, and U.S. state and local or non-U.S. tax considerations, and is limited to holders that hold shares of our common stock as capital assets for U.S. federal income tax purposes (generally, property held for investment) and that acquire shares of our common stock in exchange for Exchangeable Shares or upon exercise of a pre-funded warrant.

Further, the following discussion is based on the Code and the U.S. Treasury Regulations promulgated thereunder, including administrative and judicial interpretations thereof, as of the date of this prospectus. These authorities may be replaced, revoked or modified, possibly with retroactive effect, and subject to differing interpretations so as to result in U.S. federal income tax consequences different from those discussed herein. Holders should consult their own tax advisors regarding the tax consequences of owning and disposing of shares of our common stock.

The term "U.S. Holder" means a beneficial owner of shares of our common stock that is, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation (or any other entity treated as a corporation for U.S. federal income tax purposes) created or organized in or under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if it (a) is subject to the primary supervision of a court within the United States and one or more U.S. persons have the authority to control all substantial decisions of the trust or (b) has a valid election in effect to be treated as a U.S. person.

The term "Non-U.S. Holder" means a beneficial owner of shares of our common stock that is, for U.S. federal income tax purposes, not a U.S. Holder or a partnership or pass-through entity (including any entity or arrangement treated as a partnership or other flow-through entity and the equity holders therein).

This summary does not describe all of the U.S. federal income tax consequences applicable to a U.S. Holder if such U.S. Holder is subject to special treatment under U.S. federal income tax laws, including if such U.S. Holder is:

- a dealer in securities or currencies;
- banks, broker dealers or other financial institutions;
- a regulated investment company;
- a real estate investment trust;
- an insurance company;
- a tax-exempt organization (including a private foundation);
- a pension plan;

- a cooperative;
- a governmental organization;
- a person holding shares of our common stock as part of a hedging, integrated or conversion transaction, a constructive sale or a straddle;
- a trader in securities that has elected the mark-to-market method of accounting for its securities;
- a person who owns, directly, indirectly or constructively, 5% or more of our total combined voting power or value;
- a partnership or other pass-through entity for U.S. federal income tax purposes or its partner in or member of such entity;
- certain former U.S. citizens or long-term residents;
- a person whose “functional currency” is not the U.S. dollar; or
- a person that received shares of our common stock pursuant to the exercise of any employee stock option or otherwise as compensation.

If a partnership (or any other entity or arrangement treated as a partnership for U.S. federal income tax purposes) holds shares of our common stock, the tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership. Partners of a partnership holding shares of our common stock should consult their own tax advisors regarding the tax consequences applicable to their particular circumstances.

All holders should consult their own tax advisors regarding the tax consequences applicable to their particular circumstances of purchasing, owning and disposing of shares of our common stock.

U.S. Federal Income Tax Considerations of the Exercise of Pre-Funded Warrants for Shares of Common Stock

The U.S. federal income tax characterization of the exercise of pre-funded warrants to obtain our shares of common stock is uncertain. Although it is not entirely free from doubt, a pre-funded warrant should be treated as a share of our common stock for U.S. federal income tax purposes. Accordingly, no gain or loss should be recognized upon the exercise of a pre-funded warrant and, upon exercise, the holding period of a pre-funded warrant should carry over to the shares of common stock received. Similarly, the tax basis of a pre-funded warrant should carry over to the shares of common stock received upon exercise, increased by the exercise price (if applicable). Holders of pre-funded warrants should consult their own tax advisors regarding the U.S. federal income tax consequences applicable to the exercise of pre-funded warrants for shares of our common stock.

U.S. Federal Income Tax Considerations of the Exchange of Exchangeable Shares for Shares of Common Stock

The U.S. federal income tax characterization of the Exchangeable Shares for U.S. tax purposes is uncertain. If the Exchangeable Shares are treated as shares of our common stock for U.S. tax purposes, an exchange of Exchangeable Shares for shares of our common stock should not be a taxable event for U.S. federal income tax purposes, in which case holders should not recognize any gain or loss for U.S. income tax purposes upon the exchange and, upon exercise, the holding period of an exchangeable share should carry over to the shares of common stock received. Similarly, the tax basis of an exchangeable share should carry over to the shares of common stock received upon exercise. However, if the Exchangeable Shares are not treated as shares of our common stock for U.S. tax purposes, the tax treatment of an exchange could vary, and the tax treatment described in the sections titled “—U.S. Federal Income Tax Considerations Applicable to the Ownership of Our Shares of Common Stock—U.S. Holders—Gain on

Disposition of Our Common Stock” and “—U.S. Federal Income Tax Considerations Applicable to the Ownership of Our Shares of Common Stock—Non-U.S. Holders—Gain on Disposition of Our Common Stock” could apply. Holders of Exchangeable Shares should consult their own tax advisors regarding the U.S. federal income tax consequences applicable to the tax treatment of the Exchangeable Shares and the exercise of Exchangeable Shares for shares of our common stock for U.S. federal income tax purposes.

U.S. Federal Income Tax Considerations Applicable to the Ownership of Our Shares of Common Stock

U.S. Holders

Distributions

We do not currently anticipate declaring or paying cash dividends on our common stock in the foreseeable future. However, if we do make distributions on our common stock, those payments will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, the excess will constitute a return of capital and will first reduce a U.S. Holder’s basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock as described in the section titled “—U.S. Federal Income Tax Considerations Applicable to the Ownership of Our Shares of Common Stock—U.S. Holders—Gain on Disposition of Our Common Stock.” Dividends paid to non-corporate U.S. Holders who meet certain requirements are generally eligible for a preferential U.S. federal income tax rate if certain holding period requirements are met.

Corporate stockholders that are U.S. Holders may be eligible for the dividends received deduction, or DRD, on distributions constituting dividends for U.S. federal income tax purposes. No assurance can be given that we will have sufficient earnings and profits (as determined under U.S. federal income tax principles) to cause any distributions to be eligible for a DRD. In addition, a DRD is available only if certain holding periods and other taxable income requirements are satisfied.

Gain on Disposition of Our Common Stock

Upon a sale or other taxable disposition of our common stock, U.S. Holders generally will recognize capital gain or loss in an amount equal to the difference between the amount realized and such U.S. Holder’s adjusted tax basis in the common stock. Capital gain or loss will constitute long-term capital gain or loss if the U.S. Holder’s holding period for the common stock exceeds one year. The deductibility of capital losses is subject to certain limitations. U.S. Holders who recognize losses with respect to a disposition of our common stock should consult their own tax advisors regarding the tax treatment of such losses.

Information Reporting and Backup Withholding

Information reporting requirements generally will apply to payments of dividends (including constructive dividends) on the common stock and to the proceeds of a sale or other disposition of common stock paid by us to a U.S. Holder unless such U.S. Holder is an exempt recipient, such as certain corporations. Backup withholding will apply to payments made to a U.S. Holder if such U.S. Holder fails to provide its taxpayer identification number, or certification of exempt status, or if otherwise fails to comply with applicable requirements to establish an exemption.

Backup withholding is not an additional tax. Rather, any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against your U.S. federal income tax liability, if any, provided the required information is timely furnished to the IRS. U.S. Holders should consult their own tax advisors regarding their qualification for exemption from information reporting and backup withholding and the procedure for obtaining such exemption.

Non-U.S. Holders

Distributions

We do not currently anticipate declaring or paying cash dividends on our common stock in the foreseeable future. However, if we make distributions on our common stock (including constructive distributions, but not including certain distributions of stock or rights to acquire our common stock), those payments will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed our current and accumulated earnings and profits, the excess will constitute a return of capital and will first reduce Non-U.S. Holder's basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock as described in the section titled "—U.S. Federal Income Tax Considerations Applicable to the Ownership of Our Shares of Common Stock— Non-U.S. Holders—Gain on Disposition of Our Common Stock."

Subject to the discussions below regarding effectively connected income, backup withholding and Foreign Account Tax Compliance Act, or FATCA, withholding, any dividend paid to Non-U.S. Holders generally will be subject to U.S. federal withholding tax either at a rate of 30% of the gross amount of the dividend or such lower rate as may be specified by an applicable income tax treaty between the United States and a Non-U.S. Holder's country of residence. In order to receive a reduced treaty rate, a Non-U.S. Holder must provide us or the applicable paying agent with an IRS Form W-8BEN or W-8BEN-E or other appropriate version of IRS Form W-8 certifying qualification for the reduced rate. Under applicable Treasury Regulations, we may withhold up to 30% of the gross amount of the entire distribution even if the amount constituting a dividend, as described above, is less than the gross amount. Non-U.S. Holders may obtain a refund of any excess amounts withheld by filing an appropriate claim for refund with the IRS. If Non-U.S. Holders hold our common stock through a financial institution or other agent acting on Non-U.S. Holder's behalf, such Non-U.S. Holders will be required to provide appropriate documentation to the agent, which then will be required to provide certification to us or our paying agent, either directly or through other intermediaries. Special certification and other requirements apply to certain Non-U.S. Holders that are pass-through entities rather than corporations or individuals.

Dividends received by a Non-U.S. Holder that are treated as effectively connected with Non-U.S. Holder's conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, that are attributable to a permanent establishment or fixed base maintained by a Non-U.S. Holder in the United States) are generally exempt from the 30% U.S. federal withholding tax, subject to the discussions below regarding backup withholding and FATCA withholding. In order to obtain this exemption, a Non-U.S. Holder must provide us with a properly executed IRS Form W-8ECI or other applicable IRS Form W-8 or a successor form properly certifying such exemption. Such effectively connected dividends, although not subject to U.S. federal withholding tax, generally are taxed at the U.S. federal income tax rates applicable to U.S. persons, net of certain deductions and credits. In addition, if Non-U.S. Holder is a corporate non-U.S. Holder, dividends such Non-U.S. Holder receives that are effectively connected with Non-U.S. Holder's conduct of a U.S. trade or business may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty between the United States and Non-U.S. Holder's country of residence. Non-U.S. Holders should consult their own tax advisors regarding the tax consequences of the ownership and disposition of our common stock, including the application of any applicable tax treaties that may provide for different rules.

Gain on Disposition of Our Common Stock

Subject to the discussions below regarding backup withholding and FATCA withholding, Non-U.S. Holders generally will not be required to pay U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with a Non-U.S. Holder's conduct of a U.S. trade or business (and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by a Non-U.S. Holder in the United States);

- Non-U.S. Holder is an individual who is present in the United States for a period or periods aggregating 183 days or more during the calendar year in which the sale or disposition occurs and certain other conditions are met; or
- Our common stock constitutes a United States real property interest by reason of Parent's status as a "United States real property holding corporation," or a USRPHC, for U.S. federal income tax purposes at any time within the shorter of the five-year period preceding Non-U.S. Holder's disposition of, or holding period for, our common stock.

We believe that we are not currently and will not become a USRPHC for U.S. federal income tax purposes, and the remainder of this discussion so assumes. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our U.S. and worldwide real property interests plus our other assets used or held for use in a trade or business, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, however, as long as our common stock is regularly traded on an established securities market, a Non-U.S. Holder's common stock will be treated as U.S. real property interests only if a Non-U.S. Holder actually (directly or indirectly) or constructively holds more than five percent of our regularly traded common stock at any time during the shorter of the five-year period preceding Non-U.S. Holder's disposition of, or holding period for, our common stock.

Non-U.S. Holders described in the first bullet above generally will be required to pay tax on the gain derived from the sale (net of certain deductions and credits) at U.S. federal income tax rates applicable to U.S. persons, and a corporate Non-U.S. Holder described in the first bullet above also may be subject to the branch profits tax at a 30% rate, or such lower rate as may be specified by an applicable income tax treaty. Non-U.S. Holders described in the second bullet above will be subject to tax at 30% (or such lower rate specified by an applicable income tax treaty) on the gain derived from the sale, which gain may be offset by U.S. source capital losses for the year, provided a Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses. Non-U.S. Holders should consult their tax advisors regarding any applicable income tax or other treaties that may provide for different rules.

Backup Withholding and Information Reporting

Generally, we must report annually to the IRS the amount of dividends paid to a Non-U.S. Holder, the name and address of such Non-U.S. holder, and the amount of tax withheld, if any. A similar report will be sent to the Non-U.S. Holder. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in the Non-U.S. Holder's country of residence.

Payments of dividends on or of proceeds from the disposition of our common stock made to Non-U.S. Holders may be subject to backup withholding at the applicable statutory rate unless a Non-U.S. Holder establishes an exemption, for example, by properly certifying Non-U.S. holder's non-U.S. status on a properly completed IRS Form W-8BEN or W-8BEN-E or another appropriate version of IRS Form W-8. Notwithstanding the foregoing, backup withholding and information reporting may apply if either we or our paying agent has actual knowledge, or reason to know, that a Non-U.S. Holder is a U.S. person.

Backup withholding is not an additional tax; rather, the U.S. federal income tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may generally be obtained from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Additional Withholding Requirements under the Foreign Account Tax Compliance Act

FATCA, including sections 1471 through 1474 of the Code and the Treasury Regulations and other official IRS guidance issued thereunder, generally imposes a U.S. federal withholding tax of 30% on dividends (including constructive dividends) on, and, subject to the proposed regulations discussed below, the gross proceeds from a sale or other disposition of, our common stock, paid to a "foreign financial institution" (as specially defined under these rules), unless such institution enters into an agreement with the U.S. government to, among other things, withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding

[Table of Contents](#)

the U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are non-U.S. entities with U.S. owners) or otherwise establishes an exemption. FATCA also generally imposes a U.S. federal withholding tax of 30% on dividends (including constructive dividends) on, and the gross proceeds from a sale or other disposition of, our common stock paid to a “non-financial foreign entity” (as specially defined under these rules) unless such entity provides the withholding agent with a certification identifying the substantial direct and indirect U.S. owners of the entity, certifies that it does not have any substantial U.S. owners, or otherwise establishes an exemption.

The withholding obligations under FATCA generally apply to dividends (including constructive dividends) on our common stock and to the payment of gross proceeds of a sale or other disposition of our common stock. However, the U.S. Treasury Department has issued proposed regulations that, if finalized in their present form, would eliminate FATCA withholding on gross proceeds of the sale or other disposition of our common stock (but not on payments of dividends). The preamble of such proposed regulations states that they may be relied upon by taxpayers until final regulations are issued or until such proposed regulations are rescinded. The withholding tax will apply regardless of whether the payment otherwise would be exempt from withholding tax, including under the exemptions described in the section titled “—U.S. Federal Income Tax Considerations Applicable to the Ownership of Our Shares of Common Stock— Non-U.S. Holders—Distributions.” Under certain circumstances, Non-U.S. Holders might be eligible for refunds or credits of such taxes. An intergovernmental agreement between the United States and Non-U.S. Holder’s country of residence may modify the requirements described in this section. Each Non-U.S. Holder should consult with its own tax advisors regarding the application of FATCA withholding to ownership and disposition of our common stock.

THE PRECEDING DISCUSSION OF U.S. FEDERAL INCOME TAX CONSIDERATIONS IS FOR GENERAL INFORMATION ONLY. IT IS NOT TAX ADVICE TO HOLDERS OF OUR COMMON STOCK IN THEIR PARTICULAR CIRCUMSTANCES. ALL HOLDERS SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING THE PARTICULAR U.S. FEDERAL, STATE AND LOCAL AND NON-U.S. TAX CONSIDERATIONS OF OWNING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAWS.

CERTAIN CANADIAN INCOME TAX CONSIDERATIONS

The following is, as of the date of this prospectus, a summary of the principal Canadian federal income tax considerations under the *Income Tax Act* (Canada) and the regulations thereunder, or, collectively, the Tax Act, generally applicable to ownership and disposition of shares of our common stock purchased in this offering.

This summary applies only to a person who is a beneficial owner of shares of our common stock, and who, for the purposes of the Tax Act, and at all relevant times, deals at arm's length with us, is not affiliated with us, and who acquires and holds shares of our common stock as capital property, or a Holder. Generally, shares of our common stock will be considered to be capital property to a Holder thereof provided that the Holder does not acquire or hold shares of our common stock in the course of carrying on a business of trading or dealing in securities or as part of one or more transactions considered to be an adventure or concern in the nature of trade.

This summary is not applicable to a Holder: (i) if our company is or will be a "foreign affiliate," within the meaning of the Tax Act, of such Holder or of another corporation resident in Canada that does not deal at arm's length with the Holder for purposes of the Tax Act; (ii) that is a "financial institution" for the purposes of the mark-to-market rules under the Tax Act, (iii) an interest in which is a "tax shelter" or a "tax shelter investment" as defined in the Tax Act, (iv) that is a "specified financial institution" as defined in the Tax Act, (v) who has made a "functional currency" reporting election under section 261 of the Tax Act to report the Holder's "Canadian tax results" (as these terms are defined in the Tax Act) in a currency other than the Canadian currency, or (vi) that has entered or will enter into a "derivative forward agreement" or "synthetic disposition arrangement" (as defined in the Tax Act) with respect to shares of our common stock. Additional considerations, not discussed herein, may be applicable to a Holder that is a corporation that is, or becomes as part of a transaction or event or series of transaction or events that includes the acquisition of shares of our common stock, controlled by a non-resident person or group of non-resident persons for the purposes of the foreign affiliate dumping rules in section 212.3 of the Tax Act. Any such Holder should consult its own tax advisor with respect to the income tax considerations applicable to it in respect of acquiring, holding and disposing of shares of our common stock.

This summary is based on the assumption that our company will not be a resident of Canada for purposes of the Tax Act.

This summary is based on the facts set out in this prospectus, the current provisions of the Tax Act and an understanding of the current published administrative policies and assessing practices of the Canada Revenue Agency, or the CRA, made public prior to the date of this prospectus. This summary takes into account all proposed amendments to the Tax Act that have been publicly announced by or on behalf of the Minister of Finance (Canada), prior to the date of this prospectus, or the Proposed Amendments, and assumes that such Proposed Amendments will be enacted in the form proposed, although no assurance can be given that the Proposed Amendments will be enacted in their current form or at all. Except for the Proposed Amendments, this summary does not take into account or anticipate any other changes in law or any changes in the CRA's administrative policies and assessing practices, whether by judicial, governmental or legislative action or decision, nor does it take into account other federal or any provincial, territorial or foreign tax legislation or considerations, which may differ from the Canadian federal income tax considerations described herein. The provisions of provincial income tax legislation vary from province to province in Canada and in some cases differ from the Tax Act.

This summary is of a general nature only and is not intended to be, nor should it be construed to be, legal or tax advice to any particular Holder, and no representations with respect to the income tax considerations applicable to any particular Holder are made. This summary is not exhaustive of all Canadian federal income tax considerations. This summary does not address the deductibility of interest on any funds borrowed by a Holder to purchase common shares of our stock. The relevant tax considerations applicable to the acquiring, holding and disposing of shares of our common stock may vary according to the status of the purchaser, the jurisdiction in which the purchaser resides or carries on business and the purchaser's own particular circumstances. Accordingly, readers are urged to consult their own tax advisors about the specific tax consequences to them of acquiring, holding and disposing of shares of our common stock.

The shares of our common stock are not “Canadian securities” for the purpose of the irrevocable election under subsection 39(4) of the Tax Act to treat all “Canadian securities,” as defined in the Tax Act, owned by a Holder as capital property, and therefore such election will not apply to shares of our common stock. Holders who do not hold shares of our common stock as capital property should consult their own tax advisors regarding their particular circumstances.

For purposes of the Tax Act, all amounts relating to the acquisition, holding or disposition of shares of our common stock (including dividends, adjusted cost base and proceeds of disposition) must generally be expressed in Canadian dollars. Amounts denominated in any other currency must be converted into Canadian dollars generally based on the relevant exchange rate as determined in accordance with the Tax Act. The amount of dividends required to be included in the income of, and capital gains or capital losses realized by a Resident Holder (as defined below) may be affected by fluctuations in the Canadian/U.S. dollar exchange rate.

Holders Resident in Canada

The following portion of this summary is generally applicable to a Holder who, for the purposes of the Tax Act and any applicable income tax treaty or convention, is resident or deemed to be resident in Canada at all relevant times, which we refer to as a Resident Holder.

Dividends on Shares of Our Common Stock

A Resident Holder will be required to include in computing such Resident Holder’s income for a taxation year the amount of any dividends including amounts deducted for United States withholding tax, if any, received on shares of our common stock. Dividends received on shares of our common stock by a Resident Holder who is an individual will not be subject to the gross-up and dividend tax credit rules in the Tax Act normally applicable to taxable dividends received from “taxable Canadian corporations” as defined in the Tax Act. A Resident Holder that is a corporation will be required to include dividends received on shares of our common stock in computing its income and will generally not be entitled to deduct the amount of such dividends in computing its taxable income.

To the extent that United States withholding tax is payable by a Resident Holder in respect of any dividends received on shares of our common stock, the Resident Holder may be eligible for a foreign tax credit or deduction under the Tax Act to the extent and under the circumstances described in the Tax Act. Resident Holders should consult their own tax advisors regarding the availability of a foreign tax credit or deduction in their particular circumstances.

Disposition of Shares of Our Common Stock

A disposition or deemed disposition of shares of our common stock by a Resident Holder (including on a purchase of shares of our common stock for cancellation by our company) will generally result in a capital gain (or capital loss) to the extent that the proceeds of disposition, net of any reasonable costs of the disposition, exceed (or are less than) the adjusted cost base to the Resident Holder of such shares of our common stock immediately before the disposition. The adjusted cost base to a Resident Holder of a share of our common stock will be determined by averaging the cost of that share of our common stock with the adjusted cost base (determined immediately before the acquisition of the share of our common stock) of all other shares of our common stock held as capital property at that time by the Resident Holder. The tax treatment of capital gains and capital losses is discussed in greater detail in the section titled “—Taxation of Capital Gains and Capital Losses.”

Taxation of Capital Gains and Capital Losses

Generally, one-half of any capital gain, or a taxable capital gain, realized by a Resident Holder must be included in the Resident Holder’s income for the taxation year in which the disposition occurs. Subject to and in accordance with the provisions of the Tax Act, one-half of any capital loss incurred by a Resident Holder, or an allowable capital loss, must generally be deducted from taxable capital gains realized by the Resident Holder in the taxation year in which the disposition occurs. Allowable capital losses in excess of taxable capital gains for the taxation year of disposition generally may be carried back and deducted in any of the three preceding taxation years or carried forward and deducted in any subsequent year against taxable capital gains realized in such taxation years, in the circumstances and to the extent provided in the Tax Act.

Capital gains realized by a Resident Holder that is an individual or trust, other than certain specified trusts, may give rise to a liability for minimum tax under the Tax Act.

United States tax, if any, levied on any gain realized on a disposition of shares of our common stock may be eligible for a foreign tax credit under the Tax Act to the extent and under the circumstances described in the Tax Act. Resident Holders should consult their own tax advisors with respect to the availability of a foreign tax credit, having regard to their own particular circumstances.

Offshore Investment Fund Property Rules

The Tax Act contains provisions, or the OIF Rules, which, in certain circumstances, may require a Resident Holder to include an amount in income in each taxation year in respect of the acquisition and holding of shares of our common stock if (1) the value of such shares of our common may reasonably be considered to be derived, directly or indirectly, primarily from portfolio investments in: (i) shares of the capital stock of one or more corporations, (ii) indebtedness or annuities, (iii) interests in one or more corporations, trusts, partnerships, organizations, funds or entities, (iv) commodities, (v) real estate, (vi) Canadian or foreign resource properties, (vii) currency of a country other than Canada, (viii) rights or options to acquire or dispose of any of the foregoing, or (ix) any combination of the foregoing, or the Investment Assets, and (2) it may reasonably be concluded that one of the main reasons for the Resident Holder acquiring, holding or having shares of our common stock was to derive a benefit from portfolio investments in Investment Assets in such a manner that the taxes, if any, on the income, profits and gains from the Investment Assets for any particular year are significantly less than the tax that would have been applicable under Part I of the Tax Act if the income, profits and gains had been earned directly by the Resident Holder.

In making this determination, the OIF Rules provide that regard must be had to all of the circumstances, including (i) the nature, organization and operation of any non-resident entity, including our company, and the form of, and the terms and conditions governing, the Resident Holder's interest in, or connection with, any such non-resident entity, (ii) the extent to which any income, profit and gains that may reasonably be considered to be earned or accrued, whether directly or indirectly, for the benefit of any such non-resident entity, including our company, are subject to an income or profits tax that is significantly less than the income tax that would be applicable to such income, profits and gains if they were earned directly by the Resident Holder, and (iii) the extent to which any income, profits and gains of any such non-resident entity, including our company, for any fiscal period are distributed in that or the immediately following fiscal period.

If applicable, the OIF Rules can result in a Resident Holder being required to include in its income for each taxation year in which such Resident Holder owns shares of our common stock the amount, if any, by which (i) the total of all amounts each of which is the product obtained when the Resident Holder's "designated cost" (as defined in the Tax Act) of shares of our common stock at the end of a month in the year is multiplied by 1/12 of the aggregate of the prescribed rate of interest for the period including that month plus two percentage points exceeds (ii) the Resident Holder's income for the year (other than a capital gain) in respect of shares of our common stock determined without reference to the OIF Rules. Any amount required to be included in computing a Resident Holder's income under these provisions will be added to the adjusted cost base and the designated cost of shares of our common stock to the Resident Holder.

The CRA has taken the position that the term "portfolio investment" should be given a broad interpretation. If the term "portfolio investment" should be given a broad interpretation, and even if the value of the shares of our common stock may reasonably be considered to be derived, directly or indirectly, primarily from portfolio investments in Investment Assets, the OIF Rules will apply only if it is reasonable to conclude that one of the main reasons for a Resident Holder acquiring, holding or having shares of our common stock was to derive, either directly or indirectly, a benefit from Investment Assets in such a manner that the taxes, if any, on the income, profits and gains from such Investment Assets for any particular year are significantly less than the tax that would have been applicable under Part I of the Tax Act if the income, profits and gains had been earned directly by the Resident Holder.

The OIF Rules are complex and their application will potentially depend, in part, on the reasons for a Resident Holder acquiring, holding or having shares of our common stock. Resident Holders are urged to consult their own tax advisors regarding the application and consequences of the OIF Rules in their own particular circumstances.

Additional Refundable Tax

A Resident Holder that is, throughout the relevant taxation year, a “Canadian-controlled private corporation” (as defined in the Tax Act) may be subject to pay a refundable tax on its “aggregate investment income” (as defined in the Tax Act), including taxable capital gains and certain dividends. Proposed Amendments released on August 9, 2022, are intended to extend this additional tax and refund mechanism in respect of “aggregate investment income” to “substantive CCPCs” as defined in such Proposed Amendments. Resident Holders are advised to consult their own tax advisors regarding the possible implications of these Proposed Amendments in their particular circumstances.

Foreign Property Information Reporting

A Resident Holder who is a “specified Canadian entity” (as defined in the Tax Act) for a taxation year or a fiscal period and whose total “cost amount” of “specified foreign property” (each as defined in the Tax Act), including shares of our common stock, at any time in the year or fiscal period exceeds C\$100,000 will be required to file an information return with the CRA for the taxation year or fiscal period disclosing certain prescribed information in respect of such property. Subject to certain exceptions, a taxpayer resident in Canada, other than a corporation or trust exempt from tax under Part I of the Tax Act, will be a “specified Canadian entity,” as will certain partnerships. Penalties may apply where a Resident Holder fails to file the required information return in respect of such Resident Holder’s “specified foreign property” (as defined in the Tax Act) on a timely basis in accordance with the Tax Act. The reporting requirements with respect to “specified foreign property” were expanded so that more detailed information is required to be provided to the CRA.

The reporting rules in the Tax Act are complex and this summary does not purport to address all circumstances in which reporting may be required by a Resident Holder. Resident Holders should consult their own tax advisors regarding the reporting rules contained in the Tax Act.

Non-Residents of Canada

The following portion of this summary is applicable to a Holder who: (i) has not been, is not, and will not be resident or deemed to be resident in Canada for purposes of the Tax Act or any applicable tax treaty or convention; and (ii) does not and will not use or hold, and is not and will not be deemed to use or hold, shares of our common stock in connection with, or in the course of, carrying on a business in Canada, which we refer to as a Non-Resident Holder. Special rules, which are not discussed in this summary, may apply to a Non-Resident Holder that is an insurer carrying on business in Canada and elsewhere. Such Non-Resident Holders should consult their own tax advisors.

Dividends on Shares of Our Common Stock

Dividends paid in respect of shares of our common stock to a Non-Resident Holder will not be subject to Canadian withholding tax or other income tax under the Tax Act.

Disposition of Shares of Our Common Stock

A Non-Resident Holder who disposes or is deemed to dispose of shares of our common stock will not be subject to Canadian income tax in respect of any capital gain realized on the disposition unless such shares of our common stock constitute “taxable Canadian property” of the Non-Resident Holder for the purposes of the Tax Act and no exemption is available under an applicable income tax treaty or convention between Canada and the jurisdiction in which the Non-Resident Holder is resident.

Provided the shares of our common stock are listed on a “designated stock exchange”, as defined in the Tax Act (which currently includes The Nasdaq Stock Market LLC), at the time of disposition, shares of our common stock generally will not constitute taxable Canadian property of a Non-Resident Holder at that time, unless at any time during the 60 month period immediately preceding the disposition the following two conditions are met concurrently: (i) one or any combination of the Non-Resident Holder, persons with whom the Non-Resident Holder did not deal at arm’s length or partnerships in which the Non-Resident Holder or such non-arm’s length person holds a membership interest (either directly or indirectly through one or more partnerships), owned 25% or more of the issued shares of any class of the capital stock of our company; and (ii) more than 50% of the fair market value of the shares of our common stock was derived directly or indirectly from one or any combination of real or immovable property situated in Canada, “Canadian resource properties” (as defined in the Tax Act), “timber resource properties” (as defined in the Tax Act) or an option, an interest or right in such property, whether or not such property exists. Notwithstanding the foregoing, a share of our common stock may otherwise be deemed to be taxable Canadian property to a Non-Resident Holder for purposes of the Tax Act in certain circumstances. Non-Resident Holders whose shares of our common stock are taxable Canadian property should consult their own tax advisors for advice having regard to their particular circumstances.

Eligibility for Investment

Based on the provisions of the Tax Act on the date hereof, the shares of our common stock will be “qualified investments” under the Tax Act for trusts governed by registered retirement savings plans, or RRSPs, registered retirement income funds, or RRIFs, deferred profit sharing plans, or DPSPs, registered education savings plans, or RESPs, registered disability savings plans, or RDSPs, and tax-free savings accounts, or TFSA; collectively, RRSPs, RRIFs, RESPs, RDSPs and TFSA are referred to as Registered Plans, provided that the shares of our common stock are listed on a “designated stock exchange” for the purposes of the Tax Act (which currently includes The Nasdaq Stock Market LLC).

The annuitant, holder or subscriber, as applicable of a Registered Plan will be subject to a penalty tax in respect of the shares of our common stock held by a trust governed by such Registered Plan, as the case may be, if such shares of our common are a “prohibited investment” for such Registered Plan for the purposes of the Tax Act. The shares of our common stock will not be a prohibited investment for a Registered Plan, provided that the annuitant, holder or subscriber of such a Registered Plan, as the case may be: (1) deals at arm’s length with us for purposes of the Tax Act and (ii) does not have a “significant interest” within the meaning of the Tax Act in us. In addition, the shares of our common stock will not be a prohibited investment if the shares of our common stock are “excluded property” as defined in the Tax Act for trusts governed by a Registered Plan. Resident Holders who intend to hold shares of our common stock in a Registered Plan should consult their own tax advisors with respect to the application of the prohibited investment rules.

Pursuant to recent amendments to the Tax Act, provided that the offered shares are listed on a designated stock exchange, such shares would also be qualified investments for trusts governed by first home savings accounts (“FHSA”), and holders of FHSAs would also be subject to the prohibited investment rules described above. The amendments relating to FHSAs come into force on April 1, 2023.

LEGAL MATTERS

The validity of the shares offered hereby will be passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California.

EXPERTS

The consolidated financial statements of Zymeworks as of December 31, 2021 and 2020, and for each of the years in the three-year period ended December 31, 2021, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2021, have been incorporated by reference herein in reliance upon the reports of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.zymeworks.com. Information accessible on or through our website is not a part of this prospectus.

This prospectus and any prospectus supplement is part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. You should review the information and exhibits in the registration statement for further information on us and our consolidated subsidiaries and the securities that we are offering. Forms of any indenture or other documents establishing the terms of the offered securities are filed as exhibits to the registration statement of which this prospectus forms a part or under cover of a Current Report on Form 8-K and incorporated in this prospectus by reference. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should read the actual documents for a more complete description of the relevant matters.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference much of the information that we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated by reference in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents furnished pursuant to Items 2.02 or 7.01 of any Current Report on Form 8-K and, except as may be noted in any such Form 8-K, exhibits filed on such form that are related to such information), until the offering of the securities under the registration statement of which this prospectus forms a part is terminated or completed:

- Zymeworks BC's [Annual Report on Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on February 24, 2022;
- Zymeworks BC's [Amendment No. 1 to Annual Report on Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on May 2, 2022;
- Zymeworks BC's Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2022 and June 30, 2022, filed with the SEC on [May 4, 2022](#) and [August 4, 2022](#), respectively;
- our Quarterly Report on [Form 10-Q](#) for the quarterly period ended September 30, 2022, filed with the SEC on November 8, 2022;
- Zymeworks BC's Current Reports on Form 8-K filed with the SEC on [January 5, 2022](#); [January 19, 2022](#); [January 27, 2022](#); [January 31, 2022](#); [February 25, 2022](#); [March 9, 2022](#); [May 2, 2022](#) (Amendment No. 1 to Form 8-K originally filed with the SEC on January 19, 2022); [May 26, 2022](#); [June 10, 2022](#); [July 15, 2022](#); [August 5, 2022](#); [August 12, 2022](#); [August 19, 2022](#); [August 26, 2022](#); [September 2, 2022](#); [September 8, 2022](#); [September 22, 2022](#); [October 11, 2022](#); [October 12, 2022](#); [October 18, 2022](#); [October 19, 2022](#) and [October 21, 2022](#);
- our Current Reports on Form 8-K filed with the SEC on [October 13, 2022](#); [October 19, 2022](#); [October 21, 2022](#); [October 28, 2022](#); [November 9, 2022](#); [November 18, 2022](#); [November 29, 2022](#); [December 5, 2022](#); [December 9, 2022](#); [December 19, 2022](#); [December 19, 2022](#); [December 21, 2022](#); [December 30, 2022](#); [January 4, 2023](#); and [January 19, 2023](#);

[Table of Contents](#)

- our Form 8-K12B, filed with the SEC on [October 13, 2022](#);
- the description of our common stock and the preferred stock purchase rights associated with our common stock contained in the Registration Statement on [Form 8-A](#) relating thereto, filed with the SEC on December 15, 2022, including any amendment or report filed for the purpose of updating such description; and
- all other documents filed by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after December 31, 2022 but before the date of this prospectus.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address and telephone number:

Zymeworks Inc.
108 Patriot Drive, Suite A
Middletown, Delaware 19709
Attn: Corporate Secretary
Phone: (302) 274-8744



zymeworks

Up to 2,737,836 Shares

Common Stock

PROSPECTUS

March 7, 2023

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth fees and expenses to be paid by us in connection with the issuance and distribution of the securities being registered, other than discounts and commissions to be paid to agents or underwriters. All amounts shown are estimates except for the Securities and Exchange Commission, or the SEC, registration fee:

	Amount to be Paid
SEC registration fee	\$ 38,570 [†]
Stock exchange listing fee	*
Printing and engraving expenses	*
Accounting fees and expenses	*
Legal fees and expenses	*
Transfer agent and registrar fees and expenses	*
Trustee's fees and expenses	*
Miscellaneous expenses	*
Total	<u>\$ *</u>

[†] Represents the SEC registration fee for newly registered securities with a maximum aggregate offering price of \$350,000,000. Excludes fees previously paid by the registrant for the registration of the issuance of the following securities that are carried forward to this registration statement pursuant to Rule 415(a)(6) under the Securities Act of 1933, as amended, or the Securities Act: (i) \$150,000,000 of shares of common stock under that certain sales agreement, dated as of November 9, 2022, by and between the registrant and Cantor Fitzgerald & Co., which fee was previously paid by the registrant upon filing the related prospectus supplement with the SEC on November 9, 2022; (ii) 658,612 shares of common stock issuable upon exchange of exchangeable shares, which fee was previously paid by the registrant upon filing of the related prospectus supplement with the SEC on October 13, 2022; and (iii) 2,079,224 shares of common stock issuable upon exercise of pre-funded warrants, which fee was previously paid by the registrant upon filing of the related prospectus supplement with the SEC on October 13, 2022. See Exhibit 107 to this registration statement for additional detail.

* These fees and expenses are calculated based on the securities offered and the number of issuances and accordingly cannot be estimated at this time.

Item 15. Indemnification of Directors and Officers

Section 145 of the Delaware General Corporation Law authorizes a corporation's board of directors to grant, and authorizes a court to award, indemnity to officers, directors and other corporate agents.

Our certificate of incorporation contains provisions that limit the liability of our directors and certain of our officers for monetary damages to the fullest extent permitted by the Delaware General Corporation Law. Consequently, our directors will not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for the following:

- any breach of their duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or
- any transaction from which they derived an improper personal benefit.

Similarly, our officers who at the time of an act or omission as to which liability is asserted consented to or are deemed to have consented to certain service of process rules under Delaware law will not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as officers, except for liability in connection with:

- any breach of their duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any transaction from which they derived an improper personal benefit; or
- any action by or in the right of the corporation.

Any amendment, repeal or elimination of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to that amendment, repeal or elimination. If the Delaware General Corporation Law is amended to provide for further limitations on the personal liability of directors or officers of corporations, then the personal liability of our directors and officers will be further limited to the greatest extent permitted by the Delaware General Corporation Law.

Table of Contents

In addition, our bylaws provide that we will indemnify our directors and officers, and may indemnify our employees, agents and any other persons, to the fullest extent permitted by the Delaware General Corporation Law. Our bylaws also provide that we must advance expenses incurred by or on behalf of a director or officer in advance of the final disposition of any action or proceeding, subject to limited exceptions.

Further, we have entered into indemnification agreements with each of our directors and executive officers that may be broader than the specific indemnification provisions contained in the Delaware General Corporation Law. These indemnification agreements require us to, among other things, indemnify our directors and executive officers against liabilities that may arise by reason of their status or service. These indemnification agreements also generally require us to advance all expenses reasonably and actually incurred by our directors and executive officers in investigating or defending any such action, suit or proceeding. We believe that these agreements are necessary to attract and retain qualified individuals to serve as directors and executive officers.

The limitation of liability and indemnification provisions in our certificate of incorporation, bylaws and indemnification agreements may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against our directors and officers as required by these indemnification provisions.

We have obtained insurance policies under which, subject to the limitations of the policies, coverage is provided to our directors and officers against loss arising from claims made by reason of breach of fiduciary duty or other wrongful acts as a director or officer, including claims relating to public securities matters, and to us with respect to payments that may be made by us to our directors and officers pursuant to our indemnification obligations or otherwise as a matter of law.

The underwriting agreement to be filed as Exhibit 1.1 to this registration statement may provide for indemnification by the underwriters of us and our directors and officers for certain liabilities arising under the Securities Act, the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise.

Item 16. Exhibits

Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit Number	Filing Date	
1.1*	Form of Underwriting Agreement					
1.2	Sales Agreement, dated November 9, 2022, by and between Zymeworks Inc. and Cantor Fitzgerald & Co.	8-K	001-41535	1.1	November 9, 2022	
3.1	Amended and Restated Certificate of Incorporation	8-K12B	001-41535	3.1	October 13, 2022	
3.2	Certificate of Designations of Special Voting Stock	8-K12B	001-41535	3.2	October 13, 2022	
3.3	Certificate of Designations of Series B Participating Preferred Stock	8-K12B	001-41535	3.3	October 13, 2022	
3.4	Amended and Restated Bylaws	8-K12B	001-41535	3.4	October 13, 2022	
4.1	Specimen Common Stock Certificate of Zymeworks Inc.	S-4/A	333-266160	4.1	August 19, 2022	
4.2	Preferred Stock Rights Agreement, dated October 12, 2022, between the Company and Computershare Trust Company, N.A., as rights agent	8-K12B	001-41535	4.2	October 13, 2022	
4.3*	Form of Preferred Stock Certificate					
4.4	Form of Indenture					X
4.5*	Form of Debt Security					
4.6*	Form of Deposit Agreement					
4.7*	Form of Warrant Agreement					
4.8*	Form of Subscription Agreement					
4.9*	Form of Purchase Contract Agreement					
4.10*	Form of Unit Agreement					

Table of Contents

<u>Exhibit Number</u>	<u>Exhibit Description</u>	<u>Incorporation by Reference</u>			<u>Filed Herewith</u>
		<u>Form</u>	<u>File Number</u>	<u>Exhibit Number</u>	
4.11*	Form of Unit				
5.1	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation				X
23.1	Consent of KPMG LLP				X
23.2	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation (included in the opinion filed as Exhibit 5.1 to this Registration Statement)				X
24.1	Power of Attorney (included on the signature page to this Registration Statement)				X
25.1**	Form T-1 Statement of Eligibility of Trustee for Indenture under the Trust Indenture Act of 1939				
107	Filing Fee Tables				X

* To be filed by amendment or as an exhibit to a Form 8-K and incorporated by reference herein.

** To be filed pursuant to Section 305(b)(2) of the Trust Indenture Act of 1939, as amended.

Item 17. Undertakings

(a) The undersigned registrant hereby undertakes:

(1) to file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) to include any prospectus required by Section 10(a)(3) of the Securities Act;

(ii) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) that, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) to remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) that, for the purpose of determining liability under the Securities Act to any purchaser:

(i) each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) that, for the purpose of determining liability of the registrant under the Securities Act to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) the portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(6) that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(7) to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act, in accordance with the rules and regulations prescribed by the Commission under Section 305(b)(2) of the Trust Indenture Act.

(b) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Post-Effective Amendment No. 2 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Middletown, State of Delaware, on March 7, 2023.

ZYMEWORKS INC.

By: /s/ Kenneth Galbraith
Kenneth Galbraith
Chair of the Board of Directors and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Kenneth Galbraith, Christopher Astle and Neil Klompas, and each of them, as his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this registration statement, including post-effective amendments, and registration statements filed pursuant to Rule 462 under the Securities Act, and to file the same, with all exhibits thereto, and all other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith and about the premises, as fully for all intents and purposes as they, he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent or any of them, or their, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Post-Effective Amendment No. 2 has been signed by the following persons in the capacities and on the dates indicated:

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Kenneth Galbraith</u> Kenneth Galbraith	Chair of the Board of Directors and Chief Executive Officer (Principal Executive Officer)	March 7, 2023
<u>/s/ Christopher Astle</u> Christopher Astle	Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	March 7, 2023
<u>/s/ Troy M. Cox</u> Troy M. Cox	Director	March 7, 2023
<u>/s/ Kenneth Hillan</u> Kenneth Hillan	Director	March 7, 2023
<u>/s/ Susan Mahony</u> Susan Mahony	Director	March 7, 2023
<u>/s/ Kelvin Neu</u> Kelvin Neu	Director	March 7, 2023
<u>/s/ Hollings C. Renton</u> Hollings C. Renton	Director	March 7, 2023
<u>/s/ Natalie Sacks</u> Natalie Sacks	Director	March 7, 2023
<u>/s/ Lota Zoth</u> Lota Zoth	Director	March 7, 2023

ZYMEWORKS INC.

INDENTURE

Dated as of , 20

Trustee

TABLE OF CONTENTS

	<u>Page</u>
ARTICLE I DEFINITIONS AND INCORPORATION BY REFERENCE	1
Section 1.1 Definitions	1
Section 1.2 Other Definitions	4
Section 1.3 Incorporation by Reference of Trust Indenture Act	5
Section 1.4 Rules of Construction	5
ARTICLE II THE SECURITIES	6
Section 2.1 Issuable in Series	6
Section 2.2 Establishment of Terms of Series of Securities	6
Section 2.3 Execution and Authentication	8
Section 2.4 Registrar and Paying Agent	9
Section 2.5 Paying Agent to Hold Money in Trust	10
Section 2.6 Securityholder Lists	10
Section 2.7 Transfer and Exchange	11
Section 2.8 Mutilated, Destroyed, Lost and Stolen Securities	11
Section 2.9 Outstanding Securities	12
Section 2.10 Treasury Securities	12
Section 2.11 Temporary Securities	13
Section 2.12 Cancellation	13
Section 2.13 Defaulted Interest	13
Section 2.14 Global Securities	13
Section 2.15 CUSIP Numbers	16
ARTICLE III REDEMPTION	16
Section 3.1 Notice to Trustee	16
Section 3.2 Selection of Securities to be Redeemed	16
Section 3.3 Notice of Redemption	17
Section 3.4 Effect of Notice of Redemption	18
Section 3.5 Deposit of Redemption Price	18
Section 3.6 Securities Redeemed in Part	18
ARTICLE IV COVENANTS	18
Section 4.1 Payment of Principal and Interest	18
Section 4.2 SEC Reports	18
Section 4.3 Compliance Certificate	19
Section 4.4 Stay, Extension and Usury Laws	19
ARTICLE V SUCCESSORS	19
Section 5.1 When Company May Merge, Etc	19
Section 5.2 Successor Corporation Substituted	20

TABLE OF CONTENTS
(continued)

	<u>Page</u>
ARTICLE VI DEFAULTS AND REMEDIES	20
Section 6.1 Events of Default	20
Section 6.2 Acceleration of Maturity; Rescission and Annulment	21
Section 6.3 Collection of Indebtedness and Suits for Enforcement by Trustee	22
Section 6.4 Trustee May File Proofs of Claim	23
Section 6.5 Trustee May Enforce Claims Without Possession of Securities	23
Section 6.6 Application of Money Collected	24
Section 6.7 Limitation on Suits	24
Section 6.8 Unconditional Right of Holders to Receive Principal and Interest	25
Section 6.9 Restoration of Rights and Remedies	25
Section 6.10 Rights and Remedies Cumulative	25
Section 6.11 Delay or Omission Not Waiver	25
Section 6.12 Control by Holders	25
Section 6.13 Waiver of Past Defaults	26
Section 6.14 Undertaking for Costs	26
ARTICLE VII TRUSTEE	27
Section 7.1 Duties of Trustee	27
Section 7.2 Rights of Trustee	28
Section 7.3 Individual Rights of Trustee	29
Section 7.4 Trustee's Disclaimer	29
Section 7.5 Notice of Defaults	30
Section 7.6 Reports by Trustee to Holders	30
Section 7.7 Compensation and Indemnity	30
Section 7.8 Replacement of Trustee	31
Section 7.9 Successor Trustee by Merger, Etc	32
Section 7.10 Eligibility; Disqualification	32
Section 7.11 Preferential Collection of Claims Against Company	32
ARTICLE VIII SATISFACTION AND DISCHARGE; DEFEASANCE	33
Section 8.1 Satisfaction and Discharge of Indenture	33
Section 8.2 Application of Trust Funds; Indemnification	34
Section 8.3 Legal Defeasance of Securities of any Series	34
Section 8.4 Covenant Defeasance	36
Section 8.5 Repayment to Company	37
Section 8.6 Reinstatement	37
ARTICLE IX AMENDMENTS AND WAIVERS	38
Section 9.1 Without Consent of Holders	38
Section 9.2 With Consent of Holders	39
Section 9.3 Limitations	39
Section 9.4 Compliance with Trust Indenture Act	40
Section 9.5 Revocation and Effect of Consents	40

TABLE OF CONTENTS
(continued)

	<u>Page</u>
Section 9.6 Notation on or Exchange of Securities	40
Section 9.7 Trustee Protected	41
ARTICLE X MISCELLANEOUS	41
Section 10.1 Trust Indenture Act Controls	41
Section 10.2 Notices	41
Section 10.3 Communication by Holders with Other Holders	42
Section 10.4 Certificate and Opinion as to Conditions Precedent	42
Section 10.5 Statements Required in Certificate or Opinion	43
Section 10.6 Rules by Trustee and Agents	43
Section 10.7 Legal Holidays	43
Section 10.8 No Recourse Against Others	43
Section 10.9 Counterparts	43
Section 10.10 Governing Law; Waiver of Jury Trial; Consent to Jurisdiction	44
Section 10.11 No Adverse Interpretation of Other Agreements	44
Section 10.12 Successors	44
Section 10.13 Severability	44
Section 10.14 Table of Contents, Headings, Etc.	45
Section 10.15 Securities in a Foreign Currency	45
Section 10.16 Judgment Currency	45
Section 10.17 Force Majeure	46
Section 10.18 U.S.A. Patriot Act	46
ARTICLE XI SINKING FUNDS	46
Section 11.1 Applicability of Article	46
Section 11.2 Satisfaction of Sinking Fund Payments with Securities	47
Section 11.3 Redemption of Securities for Sinking Fund	47

ZYMEWORKS INC.

Reconciliation and tie between Trust Indenture Act of 1939 and Indenture, dated as of , 20

§ 310(a)(1)	7.10
(a)(2)	7.10
(a)(3)	Not Applicable
(a)(4)	Not Applicable
(a)(5)	7.10
(b)	7.10
§ 311(a)	7.11
(b)	7.11
(c)	Not Applicable
§ 312(a)	2.6
(b)	10.3
(c)	10.3
§ 313(a)	7.6
(b)(1)	7.6
(b)(2)	7.6
(c)(1)	7.6
(d)	7.6
§ 314(a)	4.2, 10.5
(b)	Not Applicable
(c)(1)	10.4
(c)(2)	10.4
(c)(3)	Not Applicable
(d)	Not Applicable
(e)	10.5
(f)	Not Applicable
§ 315(a)	7.1
(b)	7.5
(c)	7.1
(d)	7.1
(e)	6.14
§ 316(a)	2.10
(a)(1)(A)	6.12
(a)(1)(B)	6.13
(b)	6.8
§ 317(a)(1)	6.3
(a)(2)	6.4
(b)	2.5
§ 318(a)	10.1

Note: This reconciliation and tie shall not, for any purpose, be deemed to be part of the Indenture.

Indenture dated as of _____, 20 between Zymeworks Inc., a company incorporated under the laws of Delaware (the “*Company*”), and _____, a national banking association organized under the laws of the United States, as trustee (the “*Trustee*”).

Each party agrees as follows for the benefit of the other party and for the equal and ratable benefit of the Holders of the Securities issued under this Indenture.

ARTICLE I
DEFINITIONS AND INCORPORATION BY REFERENCE

Section 1.1 Definitions.

“*Additional Amounts*” means any additional amounts which are required hereby or by any Security, under circumstances specified herein or therein, to be paid by the Company in respect of certain taxes imposed on Holders specified herein or therein and which are owing to such Holders.

“*Affiliate*” of any specified person means any other person directly or indirectly controlling or controlled by or under common control with such specified person. For the purposes of this definition, “control” (including, with correlative meanings, the terms “controlled by” and “under common control with”), as used with respect to any person, shall mean the possession, directly or indirectly, of the power to direct or cause the direction of the management or policies of such person, whether through the ownership of voting securities or by agreement or otherwise.

“*Agent*” means any Registrar, Paying Agent or Notice Agent.

“*Board of Directors*” means the board of directors of the Company or any duly authorized committee thereof.

“*Board Resolution*” means a copy of a resolution certified by the Secretary or an Assistant Secretary of the Company to have been adopted by the Board of Directors or pursuant to authorization by the Board of Directors and to be in full force and effect on the date of the certificate and delivered to the Trustee.

“*Business Day*” means, any day except a Saturday, Sunday or a Legal Holiday in The City of New York, New York (or in connection with any payment, the place of payment) on which banking institutions are authorized or required by law, regulation or executive order to close.

“*Capital Stock*” means any and all shares, interests, participations, rights or other equivalents (however designated) of corporate stock.

“*Common Stock*” means the common stock, par value \$0.00001 per share, of the Company.

“*Company*” means the party named as such above until a successor replaces it and thereafter means the successor.

“*Company Order*” means a written order signed in the name of the Company by an Officer.

“*Corporate Trust Office*” means the principal office of the Trustee at which at any time this Indenture shall be administered, which office as of the date hereof is located at the address specified in Section 10.2. With respect to presentation for transfer or exchange, conversions or principal payment, such address shall be at the address specified in Section 10.2, or such other address as the Trustee may designate from time to time by written notice to the Holders and the Company, or the principal corporate trust office of any successor Trustee (or such other address as such successor Trustee may designate from time to time by written notice to the Holders and the Company).

“*Default*” means any event which is, or after notice or passage of time or both would be, an Event of Default.

“*Depository*” means, with respect to the Securities of any Series issuable or issued in whole or in part in the form of one or more Global Securities, the person designated as Depository for such Series by the Company, which Depository shall be a clearing agency registered under the Exchange Act; and if at any time there is more than one such person, “*Depository*” as used with respect to the Securities of any Series shall mean the Depository with respect to the Securities of such Series.

“*Discount Security*” means any Security that provides for an amount less than the stated principal amount thereof to be due and payable upon declaration of acceleration of the maturity thereof pursuant to Section 6.2.

“*Dollars*” and “*\$*” means the currency of The United States of America.

“*Exchange Act*” means the Securities Exchange Act of 1934, as amended.

“*Foreign Currency*” means any currency or currency unit issued by a government other than the government of The United States of America.

“*Foreign Government Obligations*” means, with respect to Securities of any Series that are denominated in a Foreign Currency, direct obligations of, or obligations guaranteed by, the government that issued or caused to be issued such currency for the payment of which obligations its full faith and credit is pledged and which are not callable or redeemable at the option of the issuer thereof.

“*GAAP*” means accounting principles generally accepted in the United States of America set forth in the opinions and pronouncements of the Accounting Principles Board of the American Institute of Certified Public Accountants and statements and pronouncements of the Financial Accounting Standards Board or in such other statements by such other entity as have been approved by a significant segment of the accounting profession, which are in effect as of the date of determination.

“*Global Security*” or “*Global Securities*” means a Security or Securities, as the case may be, in the form established pursuant to Section 2.2 evidencing all or part of a Series of Securities, issued to the Depositary for such Series or its nominee, and registered in the name of such Depositary or nominee.

“*Holder*” or “*Securityholder*” means a person in whose name a Security is registered on the books of the Registrar.

“*Indenture*” means this Indenture as amended or supplemented from time to time and shall include the form and terms of particular Series of Securities established as contemplated hereunder.

“*interest*” with respect to any Discount Security which by its terms bears interest only after Maturity, means interest payable after Maturity.

“*Maturity*,” when used with respect to any Security, means the date on which the principal of such Security becomes due and payable as therein or herein provided, whether at the Stated Maturity or by declaration of acceleration, call for redemption or otherwise.

“*Officer*” means the Chief Executive Officer, President, the Chief Financial Officer, the Treasurer or any Assistant Treasurer, the Secretary or any Assistant Secretary, and any Vice President of the Company.

“*Officer’s Certificate*” means a certificate signed by any Officer that meets the requirements of Section 10.5.

“*Opinion of Counsel*” means a written opinion of legal counsel who is acceptable to the Trustee. The opinion may contain customary limitations, qualifications, conditions and exceptions. The counsel may be an employee of or counsel to the Company.

“*person*” means any individual, corporation, partnership, joint venture, association, limited liability company, joint-stock company, trust, unincorporated organization or government or any agency or political subdivision thereof.

“*principal*” of a Security means the principal of the Security plus, when appropriate, the premium, if any, on, and any Additional Amounts in respect of, the Security.

“*Responsible Officer*” means any officer of the Trustee in its Corporate Trust Office having direct responsibility for the administration of this Indenture and also means, with respect to a particular corporate trust matter, any other officer to whom any corporate trust matter is referred because of his or her knowledge of and familiarity with a particular subject.

“*SEC*” means the Securities and Exchange Commission.

“*Securities*” means the debentures, notes or other debt instruments of the Company of any Series authenticated and delivered under this Indenture.

“Series” or “Series of Securities” means each series of debentures, notes or other debt instruments of the Company created pursuant to Sections 2.1 and 2.2 hereof.

“Stated Maturity” when used with respect to any Security, means the date specified in such Security as the fixed date on which the principal of such Security or interest is due and payable.

“Subsidiary” of any specified person means any corporation, association or other business entity of which more than 50% of the total voting power of shares of Capital Stock entitled (without regard to the occurrence of any contingency) to vote in the election of directors, managers or trustees thereof is at the time owned or controlled, directly or indirectly, by such person or one or more of the other Subsidiaries of that person or a combination thereof.

“TIA” means the Trust Indenture Act of 1939 (15 U.S. Code §§ 77aaa-77bbb) as in effect on the date of this Indenture; provided, however, that in the event the Trust Indenture Act of 1939 is amended after such date, “TIA” means, to the extent required by any such amendment, the Trust Indenture Act as so amended.

“Trustee” means the person named as the “Trustee” in the first paragraph of this instrument until a successor Trustee shall have become such pursuant to the applicable provisions of this Indenture, and thereafter “Trustee” shall mean or include each person who is then a Trustee hereunder, and if at any time there is more than one such person, “Trustee” as used with respect to the Securities of any Series shall mean the Trustee with respect to Securities of that Series.

“U.S. Government Obligations” means securities which are direct obligations of, or guaranteed by, The United States of America for the payment of which its full faith and credit is pledged and which are not callable or redeemable at the option of the issuer thereof, and shall also include a depository receipt issued by a bank or trust company as custodian with respect to any such U.S. Government Obligation or a specific payment of interest on or principal of any such U.S. Government Obligation held by such custodian for the account of the holder of a depository receipt, *provided* that (except as required by law) such custodian is not authorized to make any deduction from the amount payable to the holder of such depository receipt from any amount received by the custodian in respect of the U.S. Government Obligation evidenced by such depository receipt.

Section 1.2 Other Definitions.

<u>TERM</u>	<u>DEFINED IN SECTION</u>
“Bankruptcy Law”	6.1
“Custodian”	6.1
“Event of Default”	6.1
“Judgment Currency”	10.16
“Legal Holiday”	10.7
“mandatory sinking fund payment”	11.1
“New York Banking Day”	10.16
“Notice Agent”	2.4
“optional sinking fund payment”	11.1
“Paying Agent”	2.4

TERM	DEFINED IN SECTION
"Registrar"	2.4
"Required Currency"	10.16
"Specified Courts"	10.10
"successor person"	5.1

Section 1.3 Incorporation by Reference of Trust Indenture Act.

Whenever this Indenture refers to a provision of the TIA, the provision is incorporated by reference in and made a part of this Indenture. The following TIA terms used in this Indenture have the following meanings:

"Commission" means the SEC.

"indenture securities" means the Securities.

"indenture security holder" means a Securityholder.

"indenture to be qualified" means this Indenture.

"indenture trustee" or "institutional trustee" means the Trustee.

"obligor" on the indenture securities means the Company and any successor obligor upon the Securities.

All other terms used in this Indenture that are defined by the TIA, defined by TIA reference to another statute or defined by SEC rule under the TIA and not otherwise defined herein are used herein as so defined.

Section 1.4 Rules of Construction .

Unless the context otherwise requires:

- (a) a term has the meaning assigned to it;
- (b) an accounting term not otherwise defined has the meaning assigned to it in accordance with GAAP;
- (c) "or" is not exclusive;
- (d) words in the singular include the plural, and in the plural include the singular; and
- (e) provisions apply to successive events and transactions.

ARTICLE II
THE SECURITIES

Section 2.1 Issuable in Series.

The aggregate principal amount of Securities that may be authenticated and delivered under this Indenture is unlimited. The Securities may be issued in one or more Series. All Securities of a Series shall be identical except as may be set forth or determined in the manner provided in a Board Resolution, a supplemental indenture or an Officer's Certificate detailing the adoption of the terms thereof pursuant to authority granted under a Board Resolution. In the case of Securities of a Series to be issued from time to time, the Board Resolution, Officer's Certificate or supplemental indenture detailing the adoption of the terms thereof pursuant to authority granted under a Board Resolution may provide for the method by which specified terms (such as interest rate, maturity date, record date or date from which interest shall accrue) are to be determined. Securities may differ between Series in respect of any matters, provided that all Series of Securities shall be equally and ratably entitled to the benefits of the Indenture.

Section 2.2 Establishment of Terms of Series of Securities.

At or prior to the issuance of any Securities within a Series, the following shall be established (as to the Series generally, in the case of Subsection 2.2.1 and either as to such Securities within the Series or as to the Series generally in the case of Subsections 2.2.2 through 2.2.21) by or pursuant to a Board Resolution, and set forth or determined in the manner provided in a Board Resolution, supplemental indenture hereto or Officer's Certificate:

2.2.1. the title (which shall distinguish the Securities of that particular Series from the Securities of any other Series) and ranking (including the terms of any subordination provisions) of the Series;

2.2.2. the price or prices (expressed as a percentage of the principal amount thereof) at which the Securities of the Series will be issued, including the portion of the principal amount of such Securities that is convertible into another Security or the method by which any such portion will be determined;

2.2.3. any limit upon the aggregate principal amount of the Securities of the Series which may be authenticated and delivered under this Indenture (except for Securities authenticated and delivered upon registration of transfer of, or in exchange for, or in lieu of, other Securities of the Series pursuant to Section 2.7, 2.8, 2.11, 3.6 or 9.6);

2.2.4. the date or dates on which the principal of the Securities of the Series is payable;

2.2.5. the rate or rates (which may be fixed or variable) per annum or, if applicable, the method used to determine such rate or rates (including, but not limited to, any commodity, commodity index, stock exchange index or financial index) at which the Securities of the Series shall bear interest, if any, the date or dates from which such interest, if any, shall accrue, the date or dates on which such interest, if any, shall commence and be payable and any regular record date for the interest payable on any interest payment date;

2.2.6. the right, if any, to defer payments of interest and the maximum length of such deferral period;

2.2.7. the place or places where the principal of and interest, if any, on the Securities of the Series shall be payable, where the Securities of such Series may be surrendered for registration of transfer or exchange and where notices and demands to or upon the Company in respect of the Securities of such Series and this Indenture may be delivered, and the method of such payment, if by wire transfer, mail or other means;

2.2.8. if applicable, the period or periods within which, the price or prices at which and the terms and conditions upon which the Securities of the Series may be redeemed, in whole or in part, at the option of the Company, and the manner in which any election by the Company to redeem the Securities will be evidenced;

2.2.9. the obligation, if any, of the Company to repurchase the Securities of the Series pursuant to any sinking fund or analogous provisions or at the option of a Holder thereof and the period or periods within which, the price or prices at which and the terms and conditions upon which Securities of the Series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;

2.2.10. if other than denominations of \$1,000 and any integral multiple thereof, the denominations in which the Securities of the Series shall be issuable;

2.2.11. the provisions relating to conversion or exchange of any Securities of the Series into the Company's Common Stock or other securities and the terms and conditions upon which such Securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or such conversion or exchange price will be calculated and any adjustments thereto, any mandatory or optional (at the option of the Company or the Holders of the Securities of a Series) conversion or exchange provisions, the applicable conversion or exchange period and the manner of settlement for any such conversion or exchange;

2.2.12. the forms of the Securities of the Series and whether the Securities will be issuable as Global Securities (including the terms pertaining to the exchange of any such Securities);

2.2.13. if other than the principal amount thereof, the portion of the principal amount of the Securities of the Series that shall be payable upon declaration of acceleration of the maturity thereof pursuant to Section 6.2;

2.2.14. the designation of the currency, currencies or currency units in which payment of the principal of and interest, if any, on the Securities of the Series will be made and, if other than that or those in which such Securities are denominated, the manner in which the exchange rate with respect to such payments will be determined;

2.2.15. the manner in which the amounts of payment of principal of or interest, if any, on the Securities of the Series will be determined, if such amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;

2.2.16. the provisions, if any, relating to any security provided for the Securities of the Series;

2.2.17. any addition to, deletion of or change in the covenants set forth in Articles IV or V or the Events of Default that applies to any Securities of the Series and any change in the right of the Trustee or the requisite Holders of such Securities to declare the principal amount thereof due and payable pursuant to Section 6.2;

2.2.18. any Depositaries, interest rate calculation agents, exchange rate calculation agents, conversion agents or other agents with respect to Securities of such Series if other than those appointed herein;

2.2.19. if there is more than one Trustee or a different Trustee, the identity of the Trustee and, if not the Trustee, the identity of each Agent with respect to such Securities;

2.2.20. any other terms of the Series (which may supplement, modify or delete any provision of this Indenture insofar as it applies to such Series), including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of Securities of that Series; and

2.2.21. whether any of the Company's direct or indirect Subsidiaries will guarantee the Securities of that Series, including the terms of subordination, if any, of such guarantees.

All Securities of any one Series need not be issued at the same time and may be issued from time to time, consistent with the terms of this Indenture, if so provided by or pursuant to the Board Resolution, supplemental indenture hereto or Officer's Certificate referred to above. No Board Resolution, supplemental indenture hereto or Officer's Certificate may affect the Trustee's own rights, duties or immunities under this Indenture or otherwise with respect to any Series of Securities except as the Trustee may agree in writing.

Section 2.3 Execution and Authentication.

An Officer shall sign the Securities for the Company by manual or facsimile signature.

If an Officer whose signature is on a Security no longer holds that office at the time the Security is authenticated, the Security shall nevertheless be valid.

A Security shall not be valid until authenticated by the manual signature of the Trustee or an authenticating agent. The signature shall be conclusive evidence that the Security has been authenticated under this Indenture.

The Trustee shall at any time, and from time to time, authenticate Securities for original issue in the principal amount provided in the Board Resolution, supplemental indenture hereto or Officer's Certificate, upon receipt by the Trustee of a Company Order. Each Security shall be dated the date of its authentication.

The aggregate principal amount of Securities of any Series outstanding at any time may not exceed any limit upon the maximum principal amount for such Series set forth in the Board Resolution, supplemental indenture hereto or Officer's Certificate delivered pursuant to Section 2.2, except as provided in Section 2.8.

Prior to the issuance of Securities of any Series, the Trustee shall have received and (subject to Section 7.2) shall be fully protected in relying on: (a) the Board Resolution, supplemental indenture hereto or Officer's Certificate establishing the form of the Securities of that Series or of Securities within that Series and the terms of the Securities of that Series or of Securities within that Series, (b) an Officer's Certificate complying with Section 10.4, (c) an Opinion of Counsel complying with Section 10.4 and (d) an Opinion of Counsel (which may be the same Opinion of Counsel referred to in the preceding clause (c)) that such Securities, when they have been duly executed, issued, and authenticated in accordance with the terms of the Indenture and delivered against payment therefor in the circumstances described in such Opinion of Counsel, will be legally valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

The Trustee shall have the right to decline to authenticate and deliver any Securities of such Series: (a) if the Trustee, being advised by counsel, determines that such action may not be taken lawfully; or (b) if the Trustee in good faith shall determine that such action would expose the Trustee to personal liability to Holders of any then-outstanding Series of Securities.

The Trustee may appoint an authenticating agent acceptable to the Company to authenticate Securities. An authenticating agent may authenticate Securities whenever the Trustee may do so. Each reference in this Indenture to authentication by the Trustee includes authentication by such agent. An authenticating agent has the same rights as an Agent to deal with the Company or an Affiliate of the Company.

Section 2.4 Registrar and Paying Agent.

The Company shall maintain, with respect to each Series of Securities, at the place or places specified with respect to such Series pursuant to Section 2.2, an office or agency where Securities of such Series may be presented or surrendered for payment ("*Paying Agent*"), where Securities of such Series may be surrendered for registration of transfer or exchange ("*Registrar*") and where notices and demands to or upon the Company in respect of the Securities of such Series and this Indenture may be delivered ("*Notice Agent*"). The Registrar shall keep a register with respect to each Series of Securities and to their transfer and exchange. The Company will give prompt written notice to the Trustee of the name and address, and any change in the name or address, of each Registrar, Paying Agent or Notice Agent. If at any time the Company shall fail to maintain any such required Registrar, Paying Agent or Notice Agent or shall fail to furnish the Trustee with the name and address thereof, such presentations, surrenders, notices and demands may

be made or served at the Corporate Trust Office of the Trustee, and the Company hereby appoints the Trustee as its agent to receive all such presentations, surrenders, notices and demands; provided, however, that any appointment of the Trustee as the Notice Agent shall exclude the appointment of the Trustee or any office of the Trustee as an agent to receive the service of legal process on the Company.

The Company may also from time to time designate one or more co-registrars, additional paying agents or additional notice agents and may from time to time rescind such designations; provided, however, that no such designation or rescission shall in any manner relieve the Company of its obligations to maintain a Registrar, Paying Agent and Notice Agent in each place so specified pursuant to Section 2.2 for Securities of any Series for such purposes. The Company will give prompt written notice to the Trustee of any such designation or rescission and of any change in the name or address of any such co-registrar, additional paying agent or additional notice agent. The term "*Registrar*" includes any co-registrar; the term "*Paying Agent*" includes any additional paying agent; and the term "*Notice Agent*" includes any additional notice agent. The Company or any of its Affiliates may serve as Registrar or Paying Agent.

The Company hereby appoints the Trustee the initial Registrar, Paying Agent and Notice Agent for each Series unless another Registrar, Paying Agent or Notice Agent, as the case may be, is appointed prior to the time Securities of that Series are first issued.

Section 2.5 Paying Agent to Hold Money in Trust.

The Company shall require each Paying Agent other than the Trustee to agree in writing that the Paying Agent will hold in trust, for the benefit of Securityholders of any Series of Securities, or the Trustee, all money held by the Paying Agent for the payment of principal of or interest on the Series of Securities, and will notify the Trustee in writing of any default by the Company in making any such payment. While any such default continues, the Trustee may require a Paying Agent to pay all money held by it to the Trustee. The Company at any time may require a Paying Agent to pay all money held by it to the Trustee. Upon payment over to the Trustee, the Paying Agent (if other than the Company or a Subsidiary of the Company) shall have no further liability for the money. If the Company or a Subsidiary of the Company acts as Paying Agent, it shall segregate and hold in a separate trust fund for the benefit of Securityholders of any Series of Securities all money held by it as Paying Agent. Upon any bankruptcy, reorganization or similar proceeding with respect to the Company, the Trustee shall serve as Paying Agent for the Securities.

Section 2.6 Securityholder Lists.

The Trustee shall preserve in as current a form as is reasonably practicable the most recent list available to it of the names and addresses of Securityholders of each Series of Securities and shall otherwise comply with TIA § 312(a). If the Trustee is not the Registrar, the Company shall furnish to the Trustee at least ten days before each interest payment date and at such other times as the Trustee may request in writing a list, in such form and as of such date as the Trustee may reasonably require, of the names and addresses of Securityholders of each Series of Securities.

Section 2.7 Transfer and Exchange.

Where Securities of a Series are presented to the Registrar or a co-registrar with a request to register a transfer or to exchange them for an equal principal amount of Securities of the same Series, the Registrar shall register the transfer or make the exchange if its requirements for such transactions are met. To permit registrations of transfers and exchanges, the Trustee shall authenticate Securities at the Registrar's request. No service charge shall be made for any registration of transfer or exchange (except as otherwise expressly permitted herein), but the Company may require payment of a sum sufficient to cover any transfer tax or similar governmental charge payable in connection therewith (other than any such transfer tax or similar governmental charge payable upon exchanges pursuant to Sections 2.11, 3.6 or 9.6).

Neither the Company nor the Registrar shall be required (a) to issue, register the transfer of, or exchange Securities of any Series for the period beginning at the opening of business fifteen days immediately preceding the sending of a notice of redemption of Securities of that Series selected for redemption and ending at the close of business on the day such notice is sent, or (b) to register the transfer of or exchange Securities of any Series selected, called or being called for redemption as a whole or the portion being redeemed of any such Securities selected, called or being called for redemption in part.

Section 2.8 Mutilated, Destroyed, Lost and Stolen Securities.

If any mutilated Security is surrendered to the Trustee, the Company shall execute and the Trustee shall authenticate and deliver in exchange therefor a new Security of the same Series and of like tenor and principal amount and bearing a number not contemporaneously outstanding.

If there shall be delivered to the Company and the Trustee (i) evidence to their satisfaction of the destruction, loss or theft of any Security and (ii) such security or indemnity bond as may be required by each of them to hold itself and any of its agents harmless, then, in the absence of notice to the Company or the Trustee that such Security has been acquired by a bona fide purchaser, the Company shall execute and upon receipt of a Company Order the Trustee shall authenticate and make available for delivery, in lieu of any such destroyed, lost or stolen Security, a new Security of the same Series and of like tenor and principal amount and bearing a number not contemporaneously outstanding.

In case any such mutilated, destroyed, lost or stolen Security has become or is about to become due and payable, the Company in its discretion may, instead of issuing a new Security, pay such Security.

Upon the issuance of any new Security under this Section, the Company may require the payment of a sum sufficient to cover any tax or other governmental charge that may be imposed in relation thereto and any other expenses (including the fees and expenses of the Trustee) connected therewith.

Every new Security of any Series issued pursuant to this Section in lieu of any destroyed, lost or stolen Security shall constitute an original additional contractual obligation of the Company, whether or not the destroyed, lost or stolen Security shall be at any time enforceable by anyone, and shall be entitled to all the benefits of this Indenture equally and proportionately with any and all other Securities of that Series duly issued hereunder.

The provisions of this Section are exclusive and shall preclude (to the extent lawful) all other rights and remedies with respect to the replacement or payment of mutilated, destroyed, lost or stolen Securities.

Section 2.9 Outstanding Securities.

The Securities outstanding at any time are all the Securities authenticated by the Trustee except for those canceled by it, those delivered to it for cancellation, those reductions in the interest on a Global Security effected by the Trustee in accordance with the provisions hereof and those described in this Section as not outstanding.

If a Security is replaced pursuant to Section 2.8, it ceases to be outstanding until the Trustee receives proof satisfactory to it that the replaced Security is held by a bona fide purchaser.

If the Paying Agent (other than the Company, a Subsidiary of the Company or an Affiliate of the Company) holds on the Maturity of Securities of a Series money sufficient to pay such Securities payable on that date, then on and after that date such Securities of the Series cease to be outstanding and interest on them ceases to accrue.

The Company may purchase or otherwise acquire the Securities, whether by open market purchases, negotiated transactions or otherwise. A Security does not cease to be outstanding because the Company or an Affiliate of the Company holds the Security (but see Section 2.10 below).

In determining whether the Holders of the requisite principal amount of outstanding Securities have given any request, demand, authorization, direction, notice, consent or waiver hereunder, the principal amount of a Discount Security that shall be deemed to be outstanding for such purposes shall be the amount of the principal thereof that would be due and payable as of the date of such determination upon a declaration of acceleration of the Maturity thereof pursuant to Section 6.2.

Section 2.10 Treasury Securities.

In determining whether the Holders of the required principal amount of Securities of a Series have concurred in any request, demand, authorization, direction, notice, consent or waiver, Securities of a Series owned by the Company or any Affiliate of the Company shall be disregarded, except that for the purposes of determining whether the Trustee shall be protected in relying on any such request, demand, authorization, direction, notice, consent or waiver only Securities of a Series that a Responsible Officer of the Trustee actually knows are so owned shall be so disregarded.

Section 2.11 Temporary Securities.

Until definitive Securities are ready for delivery, the Company may prepare and the Trustee shall authenticate temporary Securities upon a Company Order. Temporary Securities shall be substantially in the form of definitive Securities but may have variations that the Company considers appropriate for temporary Securities. Without unreasonable delay, the Company shall prepare and the Trustee upon receipt of a Company Order shall authenticate definitive Securities of the same Series and date of maturity in exchange for temporary Securities. Until so exchanged, temporary securities shall have the same rights under this Indenture as the definitive Securities.

Section 2.12 Cancellation.

The Company at any time may deliver Securities to the Trustee for cancellation. The Registrar and the Paying Agent shall forward to the Trustee any Securities surrendered to them for registration of transfer, exchange or payment. The Trustee shall cancel all Securities surrendered for transfer, exchange, payment, replacement or cancellation in accordance with its customary procedures (subject to the record retention requirement of the Exchange Act and the Trustee) and deliver a certificate of such cancellation to the Company upon written request of the Company. The Company may not issue new Securities to replace Securities that it has paid or delivered to the Trustee for cancellation.

Section 2.13 Defaulted Interest.

If the Company defaults in a payment of interest on a Series of Securities, it shall pay the defaulted interest, plus, to the extent permitted by law, any interest payable on the defaulted interest, to the persons who are Securityholders of the Series on a subsequent special record date. The Company shall fix the record date and payment date. At least 10 days before the special record date, the Company shall send to the Trustee and to each Securityholder of the Series a notice that states the special record date, the payment date and the amount of interest to be paid. The Company may pay defaulted interest in any other lawful manner.

Section 2.14 Global Securities.

2.14.1. Terms of Securities. A Board Resolution, a supplemental indenture hereto or an Officer's Certificate shall establish whether the Securities of a Series shall be issued in whole or in part in the form of one or more Global Securities and the Depositary for such Global Security or Securities.

2.14.2. Transfer and Exchange. Notwithstanding any provisions to the contrary contained in Section 2.7 of the Indenture and in addition thereto, any Global Security shall be exchangeable pursuant to Section 2.7 of the Indenture for Securities registered in the names of Holders other than the Depositary for such Security or its nominee only if (i) such Depositary notifies the Company that it is unwilling or unable to continue as Depositary for such Global Security or if at any time such Depositary ceases to be a clearing agency registered under the Exchange Act, and, in either case, the Company fails to appoint a successor Depositary registered as a clearing agency under the Exchange Act within 90 days of such event or (ii) the Company executes and delivers to the Trustee an Officer's Certificate to the effect that such

Global Security shall be so exchangeable. Any Global Security that is exchangeable pursuant to the preceding sentence shall be exchangeable for Securities registered in such names as the Depositary shall direct in writing in an aggregate principal amount equal to the principal amount of the Global Security with like tenor and terms.

Except as provided in this Section 2.14.2, a Global Security may not be transferred except as a whole by the Depositary with respect to such Global Security to a nominee of such Depositary, by a nominee of such Depositary to such Depositary or another nominee of such Depositary or by the Depositary or any such nominee to a successor Depositary or a nominee of such a successor Depositary.

Neither the Trustee nor any Agent shall have any responsibility for any actions taken or not taken by the Depositary.

2.14.3. Legends. Any Global Security issued hereunder shall bear a legend in substantially the following form:

“THIS SECURITY IS A GLOBAL SECURITY WITHIN THE MEANING OF THE INDENTURE HEREINAFTER REFERRED TO AND IS REGISTERED IN THE NAME OF THE DEPOSITARY OR A NOMINEE OF THE DEPOSITARY. THIS SECURITY IS EXCHANGEABLE FOR SECURITIES REGISTERED IN THE NAME OF A PERSON OTHER THAN THE DEPOSITARY OR ITS NOMINEE ONLY IN THE LIMITED CIRCUMSTANCES DESCRIBED IN THE INDENTURE, AND MAY NOT BE TRANSFERRED EXCEPT AS A WHOLE BY THE DEPOSITARY TO A NOMINEE OF THE DEPOSITARY, BY A NOMINEE OF THE DEPOSITARY TO THE DEPOSITARY OR ANOTHER NOMINEE OF THE DEPOSITARY OR BY THE DEPOSITARY OR ANY SUCH NOMINEE TO A SUCCESSOR DEPOSITARY OR A NOMINEE OF SUCH A SUCCESSOR DEPOSITARY.”

In addition, so long as the Depositary Trust Company (“DTC”) is the Depositary, each Global Note registered in the name of DTC or its nominee shall bear a legend in substantially the following form:

“UNLESS THIS GLOBAL NOTE IS PRESENTED BY AN AUTHORIZED REPRESENTATIVE OF THE DEPOSITARY TRUST COMPANY, A NEW YORK CORPORATION (“DTC”), TO THE COMPANY OR ITS AGENT FOR REGISTRATION OF TRANSFER, EXCHANGE OR PAYMENT, AND ANY GLOBAL NOTE ISSUED IS REGISTERED IN THE NAME OF CEDE & CO. OR IN SUCH OTHER NAME AS IS REQUESTED BY AN AUTHORIZED REPRESENTATIVE OF DTC (AND ANY PAYMENT IS MADE TO CEDE & CO. OR TO SUCH OTHER ENTITY AS IS REQUESTED BY AN AUTHORIZED REPRESENTATIVE OF DTC), ANY TRANSFER, PLEDGE OR OTHER USE HEREOF FOR VALUE OR OTHERWISE BY OR TO ANY PERSON IS WRONGFUL INASMUCH THE REGISTERED OWNER HEREOF, CEDE & CO., HAS AN INTEREST HEREIN.”

2.14.4. Acts of Holders. The Depositary, as a Holder, may appoint agents and otherwise authorize participants to give or take any request, demand, authorization, direction, notice, consent, waiver or other action which a Holder is entitled to give or take under the Indenture.

(a) Any request, demand, authorization, direction, notice, consent, waiver or other action provided by this Indenture to be given or taken by Holders may be embodied in and evidenced by one or more instruments of substantially similar tenor signed by such Holders in person or by agent duly appointed in writing; and, except as herein otherwise expressly provided, such action shall become effective when such instrument or instruments are delivered to the Trustee and, where it is hereby expressly required, to the Company. Such instrument or instruments (and the action embodied therein and evidenced thereby) are herein sometimes referred to as the "Act" of Holders signing such instrument or instruments. Proof of execution of any such instrument or of a writing appointing any such agent shall be sufficient for any purpose of this Indenture and conclusive in favor of the Trustee and the Company, if made in the manner provided in this Section.

(b) The fact and date of the execution by any Person of any such instrument or writing may be proved by the affidavit of a witness of such execution or by a certificate of a notary public or other officer authorized by law to take acknowledgments of deeds, certifying that the individual signing such instrument or writing acknowledged to such officer the execution thereof. Where such execution is by a signer acting in a capacity other than such signer's individual capacity, such certificate or affidavit shall also constitute sufficient proof of such signer's authority. The fact and date of the execution of any such instrument or writing, or the authority of the Person executing the same, may also be proved in any other manner which the Trustee deems sufficient.

(c) The ownership of Global Securities or any Securities issued in certificated form shall be proved by the Registrar.

(d) Any request, demand, authorization, direction, notice, consent, waiver or other Act of the Holder of any Security shall bind every future Holder of the same Security and the holder of every Security issued upon the registration of transfer thereof or in exchange therefor or in lieu thereof in respect of anything done, omitted or suffered to be done by the Trustee or the Company in reliance thereon, whether or not notation of such action is made upon such Security.

(e) If the Company shall solicit from the Holders any request, demand, authorization, direction, notice, consent, waiver or other Act, the Company may, at its option, by or pursuant to a Board Resolution, fix in advance a record date for the determination of Holders entitled to give such request, demand, authorization, direction, notice, consent, waiver or other Act, but the Company shall have no obligation to do so. If such a record date is fixed, such request, demand, authorization, direction, notice, consent, waiver or other Act may be given before or after such record date, but only the Holders of record at the close of business on such record date shall be deemed to be Holders for the purposes of determining whether Holders of the requisite proportion of Outstanding Securities have authorized or agreed or consented to such request, demand, authorization, direction, notice, consent, waiver or other Act, and for that purpose the Outstanding Securities shall be computed as of such record date; provided that no such authorization, agreement or consent by the Holders on such record date shall be deemed effective unless it shall become effective pursuant to the provisions of this Indenture not later than six months after the record date.

2.14.5. Payments. Notwithstanding the other provisions of this Indenture, unless otherwise specified as contemplated by Section 2.2, payment of the principal of and interest, if any, on any Global Security shall be made to the Holder thereof.

2.14.6. Consents, Declaration and Directions. The Company, the Trustee and any Agent shall treat a person as the Holder of such principal amount of outstanding Securities of such Series represented by a Global Security as shall be specified in a written statement of the Depository or by the applicable procedures of such Depository with respect to such Global Security, for purposes of obtaining any consents, declarations, waivers or directions required to be given by the Holders pursuant to this Indenture.

Section 2.15 CUSIP Numbers.

The Company in issuing the Securities may use "CUSIP" numbers (if then generally in use), and, if so, the Trustee shall use "CUSIP" numbers in notices of redemption as a convenience to Holders; provided that any such notice may state that no representation is made as to the correctness of such numbers either as printed on the Securities or as contained in any notice of a redemption and that reliance may be placed only on the other elements of identification printed on the Securities, and any such redemption shall not be affected by any defect in or omission of such numbers. The Company shall promptly notify the Trustee of any change that the Company is aware of in the CUSIP numbers.

**ARTICLE III
REDEMPTION**

Section 3.1 Notice to Trustee .

The Company may, with respect to any Series of Securities, reserve the right to redeem and pay the Series of Securities or may covenant to redeem and pay the Series of Securities or any part thereof prior to the Stated Maturity thereof at such time and on such terms as provided for in such Securities. If a Series of Securities is redeemable and the Company wants or is obligated to redeem prior to the Stated Maturity thereof all or part of the Series of Securities pursuant to the terms of such Securities, it shall notify the Trustee in writing of the redemption date and the principal amount of Series of Securities to be redeemed. The Company shall give the notice at least 5 days before the notice is delivered to the Holders, unless a shorter period is satisfactory to the Trustee.

Section 3.2 Selection of Securities to be Redeemed.

Unless otherwise indicated for a particular Series by a Board Resolution, a supplemental indenture hereto or an Officer's Certificate, if less than all the Securities of a Series are to be redeemed, the Securities of the Series to be redeemed will be selected as follows: (a) if the Securities are in the form of Global Securities, in accordance with the procedures of the Depository, (b) if the Securities are listed on any national securities exchange, in compliance with the requirements of the principal national securities exchange, if any, on which the Securities are listed, or (c) if not otherwise provided for under clause (a) or (b) in the manner that the Trustee deems fair and appropriate, including *pro rata*, by lot or other method, unless otherwise required by law or applicable stock exchange requirements, subject, in the case of Global Securities, to the applicable rules and procedures of the Depository. The Securities to be redeemed shall be selected from Securities of the Series outstanding not previously called for redemption. Portions of the principal of

Securities of the Series that have denominations larger than \$1,000 may be selected for redemption. Securities of the Series and portions of them it selected for redemption shall be in amounts of \$1,000 or whole multiples of \$1,000 or, with respect to Securities of any Series issuable in other denominations pursuant to Section 2.2.10, the minimum principal denomination for each Series and the authorized integral multiples thereof. Provisions of this Indenture that apply to Securities of a Series called for redemption also apply to portions of Securities of that Series called for redemption.

Section 3.3 Notice of Redemption.

Unless otherwise indicated for a particular Series by Board Resolution, a supplemental indenture hereto or an Officer's Certificate, at least 15 days but not more than 60 days before a redemption date, the Company shall send or cause to be sent by first-class mail or electronically, in accordance with the procedures of the Depository, a notice of redemption to each Holder whose Securities are to be redeemed.

The notice shall identify the Securities of the Series to be redeemed and shall state:

- (a) the redemption date;
- (b) the redemption price (or manner of calculation if not then known);
- (c) the name and address of the Paying Agent;
- (d) if any Securities are being redeemed in part, the portion of the principal amount of such Securities to be redeemed and that, after the redemption date and upon surrender of such Security, a new Security or Securities in principal amount equal to the unredeemed portion of the original Security shall be issued in the name of the Holder thereof upon cancellation of the original Security;
- (e) that Securities of the Series called for redemption must be surrendered to the Paying Agent to collect the redemption price;
- (f) that interest on Securities of the Series called for redemption ceases to accrue on and after the redemption date unless the Company defaults in the deposit of the redemption price;
- (g) the CUSIP number, if any; and
- (h) any other information as may be required by the terms of the particular Series or the Securities of a Series being redeemed.

At the Company's request, the Trustee shall give the notice of redemption in the Company's name and at its expense, provided, however, that the Company has delivered to the Trustee, at least 5 days (unless a shorter time shall be acceptable to the Trustee) prior to the notice date, an Officer's Certificate requesting that the Trustee give such notice and setting forth the information to be stated in such notice.

Section 3.4 Effect of Notice of Redemption.

Once notice of redemption is sent as provided in Section 3.3, Securities of a Series called for redemption become due and payable on the redemption date and at the redemption price. Except as otherwise provided in the supplemental indenture, Board Resolution or Officer's Certificate for a Series, a notice of redemption may not be conditional. Upon surrender to the Paying Agent, such Securities shall be paid at the redemption price plus accrued interest to the redemption date.

Section 3.5 Deposit of Redemption Price.

On or before 11:00 a.m., New York City time, on the redemption date, the Company shall irrevocably deposit with the Paying Agent money sufficient (as determined by the Company) to pay the redemption price of and accrued interest, if any, on all Securities to be redeemed on that date.

Section 3.6 Securities Redeemed in Part.

Upon surrender of a Security that is redeemed in part, the Trustee shall authenticate for the Holder a new Security of the same Series and the same maturity equal in principal amount to the unredeemed portion of the Security surrendered.

**ARTICLE IV
COVENANTS**

Section 4.1 Payment of Principal and Interest.

The Company covenants and agrees for the benefit of the Holders of each Series of Securities that it will duly and punctually pay the principal of and interest, if any, on the Securities of that Series in accordance with the terms of such Securities and this Indenture. On or before 11:00 a.m., New York City time, on the applicable payment date, the Company shall deposit with the Paying Agent money sufficient to pay the principal of and interest, if any, on the Securities of each Series in accordance with the terms of such Securities and this Indenture.

Section 4.2 SEC Reports.

To the extent any Securities of a Series are outstanding, the Company shall deliver to the Trustee within 15 days after it files them with the SEC copies of the annual reports and of the information, documents, and other reports (or copies of such portions of any of the foregoing as the SEC may by rules and regulations prescribe) which the Company is required to file with the SEC pursuant to Section 13 or 15(d) of the Exchange Act. The Company also shall comply with the other provisions of TIA § 314(a). Reports, information and documents filed with the SEC via the EDGAR system (or any successor system thereto) will be deemed to be delivered to the Trustee as of the time of such filing via EDGAR for purposes of this Section 4.2, it being understood that the Trustee shall have no responsibility whatsoever to determine if such filings have been made, and that the Trustee shall not be deemed to have knowledge of the information contained therein.

Delivery of reports, information and documents to the Trustee under this Section 4.2 are for informational purposes only and the Trustee's receipt of the foregoing shall not constitute constructive or actual notice of any information contained therein or determinable from information contained therein, including the Company's compliance with any of their covenants hereunder (as to which the Trustee is entitled to rely exclusively on Officer's Certificates).

Section 4.3 Compliance Certificate.

To the extent any Securities of a Series are outstanding, the Company shall deliver to the Trustee, within 120 days after the end of each fiscal year of the Company, an Officer's Certificate stating that a review of the activities of the Company and its Subsidiaries during the preceding fiscal year has been made under the supervision of the signing Officers with a view to determining whether the Company has kept, observed, performed and fulfilled its obligations under this Indenture, and further stating, as to each such Officer signing such certificate, that to the best of his/her knowledge the Company has kept, observed, performed and fulfilled each and every covenant contained in this Indenture and is not in default in the performance or observance of any of the terms, provisions and conditions hereof (or, if a Default or Event of Default shall have occurred, describing all such Defaults or Events of Default of which the Officer may have knowledge).

Section 4.4 Stay, Extension and Usury Laws.

The Company covenants (to the extent that it may lawfully do so) that it will not at any time insist upon, plead, or in any manner whatsoever claim or take the benefit or advantage of, any stay, extension or usury law wherever enacted, now or at any time hereafter in force, which may affect the covenants or the performance of this Indenture or the Securities; and the Company (to the extent it may lawfully do so) hereby expressly waives all benefit or advantage of any such law and covenants that it will not, by resort to any such law, hinder, delay or impede the execution of any power herein granted to the Trustee, but will suffer and permit the execution of every such power as though no such law has been enacted.

**ARTICLE V
SUCCESSORS**

Section 5.1 When Company May Merge, Etc.

The Company shall not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of its properties and assets to, any person (a "successor person") unless:

(a) the Company is the surviving corporation or the successor person (if other than the Company) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes, by a supplemental indenture, executed and delivered to the Trustee, the Company's obligations on the Securities and under this Indenture; and

(b) immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing.

Where the Company is not the surviving corporation, the Company shall deliver to the Trustee prior to the consummation of the proposed transaction an Officer's Certificate to the foregoing effect and an Opinion of Counsel stating that the proposed transaction and any supplemental indenture comply with this Indenture.

Notwithstanding the above, any Subsidiary of the Company may consolidate with, merge into or transfer all or part of its properties to the Company. Neither an Officer's Certificate nor an Opinion of Counsel shall be required to be delivered in connection therewith.

Section 5.2 Successor Corporation Substituted.

Upon any consolidation or merger, or any sale, lease, conveyance or other disposition of all or substantially all of the assets of the Company in accordance with Section 5.1, the successor corporation formed by such consolidation or into or with which the Company is merged or to which such sale, lease, conveyance or other disposition is made shall succeed to, and be substituted for, and may exercise every right and power of, the Company under this Indenture with the same effect as if such successor person has been named as the Company herein; provided, however, that the predecessor Company in the case of a sale, conveyance or other disposition (other than a lease) shall be released from all obligations and covenants under this Indenture and the Securities.

**ARTICLE VI
DEFAULTS AND REMEDIES**

Section 6.1 Events of Default.

"*Event of Default*," wherever used herein with respect to Securities of any Series, means any one of the following events, unless in the establishing Board Resolution, supplemental indenture or Officer's Certificate, it is provided that such Series shall not have the benefit of said Event of Default:

(a) default in the payment of any interest on any Security of that Series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of such payment is deposited by the Company with the Trustee or with a Paying Agent prior to 11:00 a.m., New York City time, on the 30th day of such period); or

(b) default in the payment of principal of any Security of that Series at its Maturity; or

(c) default in the performance or breach of any covenant or warranty of the Company in this Indenture (other than defaults pursuant to paragraphs (a) or (b) above or pursuant to a covenant or warranty that has been included in this Indenture solely for the benefit of Series of Securities other than that Series), which default continues uncured for a period of 60 days after there has been given, by registered or certified mail, to the Company by the Trustee or to the Company and the Trustee by the Holders of at least 25% in principal amount of the outstanding Securities of that Series a written notice specifying such default or breach and requiring it to be remedied and stating that such notice is a "Notice of Default" hereunder; or

(d) the Company pursuant to or within the meaning of any Bankruptcy Law:

(i) commences a voluntary case,

(ii) consents to the entry of an order for relief against it in an involuntary case,

(iii) consents to the appointment of a Custodian of it or for all or substantially all of its property,

(iv) makes a general assignment for the benefit of its creditors, or

(v) generally is unable to pay its debts as the same become due; or

(e) a court of competent jurisdiction enters an order or decree under any Bankruptcy Law that:

(i) is for relief against the Company in an involuntary case,

(ii) appoints a Custodian of the Company or for all or substantially all of its property, or

(iii) orders the liquidation of the Company, and the order or decree remains unstayed and in effect for 60 days; or

(f) any other Event of Default provided with respect to Securities of that Series, which is specified in a Board Resolution, a supplemental indenture hereto or an Officer's Certificate, in accordance with Section 2.2.18.

The term "*Bankruptcy Law*" means title 11, U.S. Code or any similar U.S. Federal or State law for the relief of debtors. The term "*Custodian*" means any receiver, trustee, assignee, liquidator or similar official under any Bankruptcy Law.

The Company will provide the Trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action the Company is taking or proposes to take in respect thereof.

Section 6.2 Acceleration of Maturity; Rescission and Annulment.

If an Event of Default with respect to Securities of any Series at the time outstanding occurs and is continuing (other than an Event of Default referred to in Section 6.1(d) or (e)) then in every such case the Trustee or the Holders of not less than 25% in principal amount of the outstanding Securities of that Series may declare the principal amount (or, if any Securities of that Series are Discount Securities, such portion of the principal amount as may be specified in the terms of such Securities) of and accrued and unpaid interest, if any, on all of the Securities of that Series to be due and payable immediately, by a notice in writing to the Company (and to the Trustee if given by Holders), and upon any such declaration such principal amount (or specified amount) and accrued and unpaid interest, if any, shall become immediately due and payable. If an Event of Default specified in Section 6.1(d) or (e) shall occur, the principal amount (or specified amount) of and accrued and unpaid interest, if any, on all outstanding Securities shall *ipso facto* become and be immediately due and payable without any declaration or other act on the part of the Trustee or any Holder.

At any time after such a declaration of acceleration with respect to any Series has been made and before a judgment or decree for payment of the money due has been obtained by the Trustee as hereinafter in this Article provided, the Holders of a majority in principal amount of the outstanding Securities of that Series, by written notice to the Company and the Trustee, may rescind and annul such declaration and its consequences if all Events of Default with respect to Securities of that Series, other than the non-payment of the principal and interest, if any, of Securities of that Series which have become due solely by such declaration of acceleration, have been cured or waived as provided in Section 6.13.

No such rescission shall affect any subsequent Default or impair any right consequent thereon.

Section 6.3 Collection of Indebtedness and Suits for Enforcement by Trustee.

The Company covenants that if

(a) default is made in the payment of any interest on any Security when such interest becomes due and payable and such default continues for a period of 30 days, or

(b) default is made in the payment of principal of any Security at the Maturity thereof, or

(c) default is made in the deposit of any sinking fund payment, if any, when and as due by the terms of a Security,

then, the Company will, upon demand of the Trustee, pay to it, for the benefit of the Holders of such Securities, the whole amount then due and payable on such Securities for principal and interest and, to the extent that payment of such interest shall be legally enforceable, interest on any overdue principal and any overdue interest at the rate or rates prescribed therefor in such Securities, and, in addition thereto, such further amount as shall be sufficient to cover the costs and expenses of collection, including the compensation, reasonable expenses, disbursements and advances of the Trustee, its agents and counsel.

If the Company fails to pay such amounts forthwith upon such demand, the Trustee, in its own name and as trustee of an express trust, may institute a judicial proceeding for the collection of the sums so due and unpaid, may prosecute such proceeding to judgment or final decree and may enforce the same against the Company or any other obligor upon such Securities and collect the moneys adjudged or deemed to be payable in the manner provided by law out of the property of the Company or any other obligor upon such Securities, wherever situated.

If an Event of Default with respect to any Securities of any Series occurs and is continuing, the Trustee may in its discretion proceed to protect and enforce its rights and the rights of the Holders of Securities of such Series by such appropriate judicial proceedings as the Trustee shall deem most effectual to protect and enforce any such rights, whether for the specific enforcement of any covenant or agreement in this Indenture or in aid of the exercise of any power granted herein, or to enforce any other proper remedy.

Section 6.4 Trustee May File Proofs of Claim.

In case of the pendency of any receivership, insolvency, liquidation, bankruptcy, reorganization, arrangement, adjustment, composition or other judicial proceeding relative to the Company or any other obligor upon the Securities or the property of the Company or of such other obligor or their creditors, the Trustee (irrespective of whether the principal of the Securities shall then be due and payable as therein expressed or by declaration or otherwise and irrespective of whether the Trustee shall have made any demand on the Company for the payment of overdue principal or interest) shall be entitled and empowered, by intervention in such proceeding or otherwise,

(a) to file and prove a claim for the whole amount of principal and interest owing and unpaid in respect of the Securities and to file such other papers or documents as may be necessary or advisable in order to have the claims of the Trustee (including any claim for the compensation, reasonable expenses, disbursements and advances of the Trustee, its agents and counsel) and of the Holders allowed in such judicial proceeding, and

(b) to collect and receive any moneys or other property payable or deliverable on any such claims and to distribute the same, and any custodian, receiver, assignee, trustee, liquidator, sequestrator or other similar official in any such judicial proceeding is hereby authorized by each Holder to make such payments to the Trustee and, in the event that the Trustee shall consent to the making of such payments directly to the Holders, to pay to the Trustee any amount due it for the compensation, reasonable expenses, disbursements and advances of the Trustee, its agents and counsel, and any other amounts due the Trustee under Section 7.7.

Nothing herein contained shall be deemed to authorize the Trustee to authorize or consent to or accept or adopt on behalf of any Holder any plan of reorganization, arrangement, adjustment or composition affecting the Securities or the rights of any Holder thereof or to authorize the Trustee to vote in respect of the claim of any Holder in any such proceeding.

Section 6.5 Trustee May Enforce Claims Without Possession of Securities.

All rights of action and claims under this Indenture or the Securities may be prosecuted and enforced by the Trustee without the possession of any of the Securities or the production thereof in any proceeding relating thereto, and any such proceeding instituted by the Trustee shall be brought in its own name as trustee of an express trust, and any recovery of judgment shall, after provision for the payment of the compensation, reasonable expenses, disbursements and advances of the Trustee, its agents and counsel, be for the ratable benefit of the Holders of the Securities in respect of which such judgment has been recovered.

Section 6.6 Application of Money Collected.

Any money or property collected by the Trustee pursuant to this Article shall be applied in the following order, at the date or dates fixed by the Trustee and, in case of the distribution of such money or property on account of principal or interest, upon presentation of the Securities and the notation thereon of the payment if only partially paid and upon surrender thereof if fully paid:

First: To the payment of all amounts due the Trustee under Section 7.7; and

Second: To the payment of the amounts then due and unpaid for principal of and interest on the Securities in respect of which or for the benefit of which such money has been collected, ratably, without preference or priority of any kind, according to the amounts due and payable on such Securities for principal and interest, respectively; and

Third: To the Company.

Section 6.7 Limitation on Suits.

No Holder of any Security of any Series shall have any right to institute any proceeding, judicial or otherwise, with respect to this Indenture, or for the appointment of a receiver or trustee, or for any other remedy hereunder, unless

(a) such Holder has previously given written notice to the Trustee of a continuing Event of Default with respect to the Securities of that Series;

(b) the Holders of not less than 25% in principal amount of the outstanding Securities of that Series shall have made written request to the Trustee to institute proceedings in respect of such Event of Default in its own name as Trustee hereunder;

(c) such Holder or Holders have offered to the Trustee indemnity or security satisfactory to the Trustee against the costs, expenses and liabilities which might be incurred by the Trustee in compliance with such request;

(d) the Trustee for 60 days after its receipt of such notice, request and offer of indemnity has failed to institute any such proceeding;

and

(e) no direction inconsistent with such written request has been given to the Trustee during such 60-day period by the Holders of a majority in principal amount of the outstanding Securities of that Series;

it being understood, intended and expressly covenanted by the Holder of every Security with every other Holder and the Trustee that no one or more of such Holders shall have any right in any manner whatever by virtue of, or by availing of, any provision of this Indenture to affect, disturb or prejudice the rights of any other of such Holders, or to obtain or to seek to obtain priority or preference over any other of such Holders or to enforce any right under this Indenture, except in the manner herein provided and for the equal and ratable benefit of all such Holders of the applicable Series.

Section 6.8 Unconditional Right of Holders to Receive Principal and Interest.

Notwithstanding any other provision in this Indenture, the Holder of any Security shall have the right, which is absolute and unconditional, to receive payment of the principal of and interest, if any, on such Security on the Maturity of such Security, including the Stated Maturity expressed in such Security (or, in the case of redemption, on the redemption date) and to institute suit for the enforcement of any such payment, and such rights shall not be impaired without the consent of such Holder.

Section 6.9 Restoration of Rights and Remedies.

If the Trustee or any Holder has instituted any proceeding to enforce any right or remedy under this Indenture and such proceeding has been discontinued or abandoned for any reason, or has been determined adversely to the Trustee or to such Holder, then and in every such case, subject to any determination in such proceeding, the Company, the Trustee and the Holders shall be restored severally and respectively to their former positions hereunder and thereafter all rights and remedies of the Trustee and the Holders shall continue as though no such proceeding had been instituted.

Section 6.10 Rights and Remedies Cumulative.

Except as otherwise provided with respect to the replacement or payment of mutilated, destroyed, lost or stolen Securities in Section 2.8, no right or remedy herein conferred upon or reserved to the Trustee or to the Holders is intended to be exclusive of any other right or remedy, and every right and remedy shall, to the extent permitted by law, be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law or in equity or otherwise. The assertion or employment of any right or remedy hereunder, or otherwise, shall not, to the extent permitted by law, prevent the concurrent assertion or employment of any other appropriate right or remedy.

Section 6.11 Delay or Omission Not Waiver.

No delay or omission of the Trustee or of any Holder of any Securities to exercise any right or remedy accruing upon any Event of Default shall impair any such right or remedy or constitute a waiver of any such Event of Default or an acquiescence therein. Every right and remedy given by this Article or by law to the Trustee or to the Holders may be exercised from time to time, and as often as may be deemed expedient, by the Trustee or by the Holders, as the case may be.

Section 6.12 Control by Holders.

The Holders of a majority in principal amount of the outstanding Securities of any Series shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the Trustee, or exercising any trust or power conferred on the Trustee, with respect to the Securities of such Series, provided that

- (a) such direction shall not be in conflict with any rule of law or with this Indenture,

(b) the Trustee may take any other action deemed proper by the Trustee which is not inconsistent with such direction,

(c) subject to the provisions of Section 7.1, the Trustee shall have the right to decline to follow any such direction if the Trustee in good faith shall, by a Responsible Officer of the Trustee, determine that the proceeding so directed would involve the Trustee in personal liability, and

(d) prior to taking any action as directed under this Section 6.12, the Trustee shall be entitled to indemnity satisfactory to it against the losses, costs, expenses and liabilities which might be incurred by it in compliance with such request or direction.

Section 6.13 Waiver of Past Defaults.

The Holders of not less than a majority in principal amount of the outstanding Securities of any Series may on behalf of the Holders of all the Securities of such Series, by written notice to the Trustee and the Company, waive any past Default hereunder with respect to such Series and its

consequences, except a Default in the payment of the principal of or interest on any Security of such Series (provided, however, that the Holders of a majority in principal amount of the outstanding Securities of any Series may rescind an acceleration and its consequences, including any related payment default that resulted from such acceleration). Upon any such waiver, such Default shall cease to exist, and any Event of Default arising therefrom shall be deemed to have been cured, for every purpose of this Indenture; but no such waiver shall extend to any subsequent or other Default or impair any right consequent thereon.

Section 6.14 Undertaking for Costs.

All parties to this Indenture agree, and each Holder of any Security by his acceptance thereof shall be deemed to have agreed, that any court may in its discretion require, in any suit for the enforcement of any right or remedy under this Indenture, or in any suit against the Trustee for any action taken, suffered or omitted by it as Trustee, the filing by any party litigant in such suit of an undertaking to pay the costs of such suit, and that such court may in its discretion assess reasonable costs, including reasonable attorneys' fees, against any party litigant in such suit, having due regard to the merits and good faith of the claims or defenses made by such party litigant; but the provisions of this Section shall not apply to any suit instituted by the Company, to any suit instituted by the Trustee, to any suit instituted by any Holder, or group of Holders, holding in the aggregate more than 10% in principal amount of the outstanding Securities of any Series, or to any suit instituted by any Holder for the enforcement of the payment of the principal of or interest on any Security on or after the Maturity of such Security, including the Stated Maturity expressed in such Security (or, in the case of redemption, on the redemption date).

ARTICLE VII
TRUSTEE

Section 7.1 Duties of Trustee.

(a) If an Event of Default has occurred and is continuing, the Trustee shall exercise the rights and powers vested in it by this Indenture and use the same degree of care and skill in their exercise as a prudent person would exercise or use under the circumstances in the conduct of such person's own affairs.

(b) Except during the continuance of an Event of Default:

(i) The Trustee need perform only those duties that are specifically set forth in this Indenture and no others, and no implied covenants or obligations shall be read into this Indenture against the Trustee.

(ii) In the absence of bad faith on its part, the Trustee may conclusively rely, as to the truth of the statements and the correctness of the opinions expressed therein, upon Officer's Certificates or Opinions of Counsel furnished to the Trustee and conforming to the requirements of this Indenture; however, in the case of any such Officer's Certificates or Opinions of Counsel which by any provisions hereof are specifically required to be furnished to the Trustee, the Trustee shall examine such Officer's Certificates and Opinions of Counsel to determine whether or not they conform to the form requirements of this Indenture (but need not confirm or investigate the accuracy of mathematical calculations or other facts stated therein).

(c) The Trustee may not be relieved from liability for its own negligent action, its own negligent failure to act or its own willful misconduct, except that:

(i) This paragraph does not limit the effect of paragraph (b) of this Section.

(ii) The Trustee shall not be liable for any error of judgment made in good faith by a Responsible Officer, unless it is proved in a court of competent jurisdiction that the Trustee was negligent in ascertaining the pertinent facts.

(iii) The Trustee shall not be liable with respect to any action taken, suffered or omitted to be taken by it with respect to Securities of any Series in good faith in accordance with the direction of the Holders of a majority in principal amount of the outstanding Securities of such Series relating to the time, method and place of conducting any proceeding for any remedy available to the Trustee, or exercising any trust or power conferred upon the Trustee, under this Indenture with respect to the Securities of such Series in accordance with Section 6.12.

(d) Every provision of this Indenture that in any way relates to the Trustee is subject to paragraph (a), (b) and (c) of this Section.

(e) The Trustee may refuse to perform any duty or exercise any right or power unless it receives indemnity satisfactory to it against the losses, costs, expenses and liabilities which might be incurred by it in performing such duty or exercising such right or power.

(f) The Trustee shall not be liable for interest or investment on any money received by it except as the Trustee may agree in writing with the Company. Money held in trust by the Trustee need not be segregated from other funds except to the extent required by law.

(g) No provision of this Indenture shall require the Trustee to expend or risk its own funds or otherwise incur any financial liability in the performance of any of its duties, or in the exercise of any of its rights or powers.

(h) The Paying Agent, the Registrar and any authenticating agent shall be entitled to the protections and immunities as are set forth in paragraphs (e), (f) and (g) of this Section and in Section 7.2, each with respect to the Trustee.

Section 7.2 Rights of Trustee.

(a) The Trustee may conclusively rely on and shall be protected in acting or refraining from acting upon any document (whether in its original or facsimile form) believed by it to be genuine and to have been signed or presented by the proper person. The Trustee need not investigate any fact or matter stated in the document.

(b) Before the Trustee acts or refrains from acting, it may require an Officer's Certificate or an Opinion of Counsel or both. The Trustee shall not be liable for any action it takes or omits to take in good faith in reliance on such Officer's Certificate or Opinion of Counsel.

(c) The Trustee may act through its attorneys and agents and shall not be responsible for the misconduct or negligence of any attorney or agent appointed with due care. No Depository shall be deemed an agent of the Trustee and the Trustee shall not be responsible for any act or omission by any Depository.

(d) The Trustee shall not be liable for any action it takes or omits to take in good faith which it believes to be authorized or within its rights or powers, provided that the Trustee's conduct does not constitute willful misconduct or negligence.

(e) The Trustee may consult with counsel and the advice of such counsel or any Opinion of Counsel shall be full and complete authorization and protection in respect of any action taken, suffered or omitted by it hereunder without willful misconduct or negligence, and in reliance thereon.

(f) The Trustee shall be under no obligation to exercise any of the rights or powers vested in it by this Indenture at the request or direction of any of the Holders of Securities unless such Holders shall have offered (and, if requested, provided) to the Trustee security or indemnity satisfactory to it against the losses, costs, expenses and liabilities which might be incurred by it in compliance with such request or direction.

(g) The Trustee shall not be bound to make any investigation into the facts or matters stated in any resolution, certificate, statement, instrument, opinion, report, notice, request, direction, consent, order, bond, debenture, note, other evidence of indebtedness or other paper or document, but the Trustee, in its discretion, may make such further inquiry or investigation into such facts or matters as it may see fit.

(h) The Trustee shall not be deemed to have notice of any Default or Event of Default unless a Responsible Officer of the Trustee has actual knowledge thereof or unless written notice of any event which is in fact such a default is received by the Trustee at the Corporate Trust Office of the Trustee, and such notice references the existence of a Default or Event of Default, the Securities generally or the Securities of a particular Series and this Indenture.

(i) In no event shall the Trustee be responsible or liable to any person for special, punitive, indirect, consequential or incidental loss or damage of any kind whatsoever (including but not limited to lost profits), even if the Trustee has been advised of the likelihood of such loss or damage and regardless of the form of action.

(j) The permissive right of the Trustee to take the actions permitted by this Indenture shall not be construed as an obligation or duty to do so.

(k) No bond or surety shall be required with respect to performance of Trustee's duties and powers.

(l) Under no circumstances shall the Trustee be liable in its individual capacity for the obligations evidenced by the Securities.

(m) Any request or direction of the Company mentioned herein shall be sufficiently evidenced by a Company Order and any resolution of the Board of Directors may be sufficiently evidenced by a Board Resolution.

(n) The Trustee may request that the Company deliver a certificate setting forth the names of individuals and/or titles of officers authorized at such time to take specified actions pursuant to this Indenture.

(o) The rights, privileges, protections, immunities and benefits given to the Trustee, including, without limitation, its right to be indemnified, are extended to, and shall be enforceable by, the Trustee in each of its capacities hereunder, and each agent, custodian and other Person employed to act hereunder.

Section 7.3 Individual Rights of Trustee.

The Trustee in its individual or any other capacity may become the owner or pledgee of Securities and may otherwise deal with the Company or an Affiliate of the Company with the same rights it would have if it were not Trustee. Any Agent may do the same with like rights. The Trustee is also subject to Sections 7.10 and 7.11.

Section 7.4 Trustee's Disclaimer.

The Trustee shall not be responsible for and makes no representation as to the validity or adequacy of this Indenture or the Securities, it shall not be accountable for the Company's use of the proceeds from the Securities, or any money paid to the Company or upon the Company's direction under any provision of this Indenture, it shall not be responsible for the use or application of any money received by any Paying Agent other than the Trustee, and it shall not be responsible for any statement herein or in the Securities or any other document in connection with the sale of the Securities other than its authentication. The recitals contained herein and in the Securities, except the Trustee's certificates of authentication, shall be taken as the statements of the Company, and the Trustee or any Authenticating Agent assumes no responsibility for their correctness.

Section 7.5 Notice of Defaults.

If a Default or Event of Default occurs and is continuing with respect to the Securities of any Series and if it is actually known to a Responsible Officer of the Trustee, the Trustee shall send to each Securityholder of the Securities of that Series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a Responsible Officer of the Trustee has knowledge of such Default or Event of Default. Except in the case of a Default or Event of Default in payment of principal of or interest on any Security of any Series, the Trustee may withhold the notice if and so long as it in good faith determines that withholding the notice is in the interests of Securityholders of that Series.

Section 7.6 Reports by Trustee to Holders.

Within 60 days after each , commencing , 20 , the Trustee shall transmit by mail to all Securityholders, as their names and addresses appear on the register kept by the Registrar, a brief report dated as of such anniversary date, in accordance with, and to the extent required under, TIA § 313.

A copy of each report at the time of its sending to Securityholders of any Series shall be filed with the SEC and each national securities exchange on which the Securities of that Series are listed. The Company shall promptly notify the Trustee in writing when Securities of any Series are listed on any national securities exchange or delisted from any national securities exchange.

Section 7.7 Compensation and Indemnity.

The Company shall pay to the Trustee from time to time compensation for its services as the Company and the Trustee shall from time to time agree upon in writing. The Trustee's compensation shall not be limited by any law on compensation of a trustee of an express trust. The Company shall reimburse the Trustee upon request for all reasonable out of pocket expenses incurred by it. Such expenses shall include the reasonable compensation and expenses of the Trustee's agents and counsel. The Company shall indemnify each of the Trustee and any predecessor Trustee (including for the cost of defending itself) against any cost, damages, losses, expense or liability, including taxes (other than taxes based upon, measured by or determined by the income of the Trustee)

incurred by it except as set forth in the next paragraph in the performance of its duties under this Indenture or in connection with its acceptance of its obligations hereunder, as Trustee or Agent. The Trustee shall notify the Company promptly of any claim for which it may seek indemnity. Failure by the Trustee to so notify the Company shall not relieve the Company of its obligations hereunder, unless and to the extent that the Company is materially prejudiced thereby. The Company shall defend the claim and the Trustee shall cooperate in the defense. The Trustee may have separate counsel and the Company shall pay the reasonable fees and expenses of such counsel. The Company need not pay for any settlement made without its consent, which consent will not be unreasonably withheld. This indemnification shall apply to officers, directors, employees, shareholders and agents of the Trustee.

The Company need not reimburse any expense or indemnify against any loss or liability incurred by the Trustee or by any officer, director, employee, shareholder or agent of the Trustee through willful misconduct or negligence, as finally adjudicated by a court of competent jurisdiction.

To secure the Company's payment obligations in this Section, the Trustee shall have a lien prior to the Securities of any Series on all money or property held or collected by the Trustee, except that held in trust to pay principal of and interest on particular Securities of that Series.

When the Trustee incurs expenses or renders services after an Event of Default specified in Section 6.1(d) or (e) occurs, the expenses and the compensation for the services are intended to constitute expenses of administration under any Bankruptcy Law.

The provisions of this Section shall survive the termination of this Indenture or the resignation or removal of the Trustee.

Section 7.8 Replacement of Trustee.

A resignation or removal of the Trustee and appointment of a successor Trustee shall become effective only upon the successor Trustee's acceptance of appointment as provided in this Section.

The Trustee may resign with respect to the Securities of one or more Series by so notifying the Company at least 30 days prior to the date of the proposed resignation. The Holders of a majority in principal amount of the Securities of any Series may remove the Trustee with respect to that Series by so notifying the Trustee and the Company in writing at least 30 days prior to such removal. The Company may remove the Trustee with respect to Securities of one or more Series with at least 30 days written notice if:

- (a) the Trustee fails to comply with Section 7.10;
- (b) the Trustee is adjudged a bankrupt or an insolvent or an order for relief is entered with respect to the Trustee under any Bankruptcy Law;
- (c) a Custodian or public officer takes charge of the Trustee or its property; or
- (d) the Trustee becomes incapable of acting.

If the Trustee resigns or is removed or if a vacancy exists in the office of Trustee for any reason, the Company shall promptly appoint a successor Trustee. Within one year after the successor Trustee takes office, the Holders of a majority in principal amount of the then-outstanding Securities may appoint a successor Trustee to replace the successor Trustee appointed by the Company.

If a successor Trustee with respect to the Securities of any one or more Series does not take office within 60 days after the retiring Trustee resigns or is removed, the retiring Trustee, the Company or the Holders of at least a majority in principal amount of the Securities of the applicable Series may petition any court of competent jurisdiction for the appointment of a successor Trustee.

A successor Trustee shall deliver a written acceptance of its appointment to the retiring Trustee and to the Company. Promptly after that, the retiring Trustee shall transfer all property held by it as Trustee to the successor Trustee subject to the lien provided for in Section 7.7, the resignation or removal of the retiring Trustee shall become effective, and the successor Trustee shall have all the rights, powers and duties of the Trustee with respect to each Series of Securities for which it is acting as Trustee under this Indenture. A successor Trustee shall send a notice of its succession to each Securityholder of each such Series. Notwithstanding replacement of the Trustee pursuant to this Section 7.8, the Company's obligations under Section 7.7 hereof shall continue for the benefit of the retiring Trustee with respect to expenses and liabilities incurred by it for actions taken or omitted to be taken in accordance with its rights, powers and duties under this Indenture prior to such replacement.

Section 7.9 Successor Trustee by Merger, Etc.

If the Trustee consolidates with, merges or converts into, or transfers all or substantially all of its corporate trust business to, another corporation, or national banking association, the successor corporation or national banking association without any further act shall be the successor Trustee, subject to Section 7.10.

Section 7.10 Eligibility; Disqualification.

This Indenture shall always have a Trustee who satisfies the requirements of TIA § 310(a)(1), (2) and (5). The Trustee shall always have a combined capital and surplus of at least \$50,000,000 as set forth in its most recent published annual report of condition. The Trustee shall comply with TIA § 310(b).

Section 7.11 Preferential Collection of Claims Against Company.

The Trustee is subject to TIA § 311(a), excluding any creditor relationship listed in TIA § 311(b). A Trustee who has resigned or been removed shall be subject to TIA § 311(a) to the extent indicated.

ARTICLE VIII
SATISFACTION AND DISCHARGE; DEFEASANCE

Section 8.1 Satisfaction and Discharge of Indenture.

This Indenture shall upon Company Order be discharged with respect to the Securities of any Series and cease to be of further effect as to all Securities of such Series (except as hereinafter provided in this Section 8.1), and the Trustee, at the expense of the Company, shall execute instruments acknowledging satisfaction and discharge of this Indenture, when

(a) either

(i) all Securities of such Series theretofore authenticated and delivered (other than Securities that have been destroyed, lost or stolen and that have been replaced or paid) have been delivered to the Trustee for cancellation; or

(ii) all such Securities of such Series not theretofore delivered to the Trustee for cancellation

(1) have become due and payable by reason of sending a notice of redemption or otherwise, or

(2) will become due and payable at their Stated Maturity within one year, or

(3) have been called for redemption or are to be called for redemption within one year under arrangements satisfactory to the Trustee for the giving of notice of redemption by the Trustee in the name, and at the expense, of the Company, or

(4) are deemed paid and discharged pursuant to Section 8.3, as applicable;

and the Company, in the case of (1), (2) or (3) above, shall have irrevocably deposited or caused to be deposited with the Trustee as trust funds in trust an amount of money or U.S. Government Obligations, which amount shall be sufficient (as determined by the Company) for the purpose of paying and discharging each installment of principal (including mandatory sinking fund or analogous payments) of and interest on all the Securities of such Series on the dates such installments of principal or interest are due;

(b) the Company has paid or caused to be paid all other sums payable hereunder by the Company; and

(c) the Company shall have delivered to the Trustee an Officer's Certificate and an Opinion of Counsel, each stating that all conditions precedent provided for relating to the satisfaction and discharge contemplated by this Section have been complied with.

Notwithstanding the satisfaction and discharge of this Indenture, the obligations of the Company to the Trustee under Section 7.7, and, if money shall have been deposited with the Trustee pursuant to clause (a) of this Section, the provisions of Sections 2.4, 2.7, 2.8, 8.2 and 8.5 shall survive.

Section 8.2 Application of Trust Funds; Indemnification.

(a) Subject to the provisions of Section 8.5, all money and U.S. Government Obligations or Foreign Government Obligations deposited with the Trustee pursuant to Section 8.1, 8.3 or 8.4 and all money received by the Trustee in respect of U.S. Government Obligations or Foreign Government Obligations deposited with the Trustee pursuant to Section 8.1, 8.3 or 8.4, shall be held in trust and applied by it, in accordance with the provisions of the Securities and this Indenture, to the payment, either directly or through any Paying Agent (including the Company acting as its own Paying Agent) as the Trustee may determine, to the persons entitled thereto, of the principal and interest for whose payment such money has been deposited with or received by the Trustee or to make mandatory sinking fund payments or analogous payments as contemplated by Sections 8.1, 8.3 or 8.4.

(b) The Company shall pay and shall indemnify the Trustee against any tax, fee or other charge imposed on or assessed against U.S. Government Obligations or Foreign Government Obligations deposited pursuant to Sections 8.1, 8.3 or 8.4 or the interest and principal received in respect of such obligations other than any payable by or on behalf of Holders.

(c) The Trustee shall deliver or pay to the Company from time to time upon Company Order any U.S. Government Obligations or Foreign Government Obligations or money held by it as provided in Sections 8.3 or 8.4 which, in the opinion of a nationally recognized firm of independent certified public accountants or investment bank expressed in a written certification thereof delivered to the Trustee, are then in excess of the amount thereof which then would have been required to be deposited for the purpose for which such U.S. Government Obligations or Foreign Government Obligations or money were deposited or received. This provision shall not authorize the sale by the Trustee of any U.S. Government Obligations or Foreign Government Obligations held under this Indenture.

Section 8.3 Legal Defeasance of Securities of any Series.

Unless this Section 8.3 is otherwise specified, pursuant to Section 2.2, to be inapplicable to Securities of any Series, the Company shall be deemed to have paid and discharged the entire indebtedness on all the outstanding Securities of any Series on the 91st day after the date of the deposit referred to in subparagraph (d) hereof, and the provisions of this Indenture, as it relates to such outstanding Securities of such Series, shall no longer be in effect (and the Trustee, at the expense of the Company, shall, upon receipt of a Company Order, execute instruments acknowledging the same), except as to:

(a) the rights of Holders of Securities of such Series to receive, from the trust funds described in subparagraph (d) hereof, (i) payment of the principal of and each installment of principal of and interest on the outstanding Securities of such Series on the Maturity of such principal or installment of principal or interest and (ii) the benefit of any mandatory sinking fund payments applicable to the Securities of such Series on the day on which such payments are due and payable in accordance with the terms of this Indenture and the Securities of such Series;

(b) the provisions of Sections 2.4, 2.5, 2.7, 2.8, 7.7, 8.2, 8.3, 8.5 and 8.6; and

(c) the rights, powers, trusts and immunities of the Trustee hereunder and the Company's obligations in connection therewith;

provided that, the following conditions shall have been satisfied:

(d) the Company shall have irrevocably deposited or caused to be deposited (except as provided in Section 8.2(c)) with the Trustee as trust funds specifically pledged as security for and dedicated solely to the benefit of the Holders of such Securities (i) in the case of Securities of such Series denominated in Dollars, cash in Dollars and/or U.S. Government Obligations, or (ii) in the case of Securities of such Series denominated in a Foreign Currency (other than a composite currency), money and/or Foreign Government Obligations, which through the payment of interest and principal in respect thereof in accordance with their terms, will provide (and without reinvestment and assuming no tax liability will be imposed on such Trustee), not later than one day before the due date of any payment of money, an amount in cash, sufficient, in the opinion of a nationally recognized firm of independent public accountants or investment bank expressed in a written certification thereof delivered to the Trustee, to pay and discharge each installment of principal of and interest, on and any mandatory sinking fund payments in respect of all the Securities of such Series on the dates such installments of principal or interest and such sinking fund payments are due;

(e) such deposit will not result in a breach or violation of, or constitute a default under, this Indenture or any other agreement or instrument to which the Company is a party or by which it is bound;

(f) no Default or Event of Default with respect to the Securities of such Series shall have occurred and be continuing on the date of such deposit or during the period ending on the 91st day after such date;

(g) the Company shall have delivered to the Trustee an Officer's Certificate and an Opinion of Counsel to the effect that (i) the Company has received from, or there has been published by, the Internal Revenue Service a ruling, or (ii) since the date of execution of this Indenture, there has been a change in the applicable Federal income tax law, in either case to the effect that, and based thereon such Opinion of Counsel shall confirm that, the Holders of the Securities of such Series will not recognize income, gain or loss for Federal income tax purposes as a result of such deposit, defeasance and discharge and will be subject to Federal income tax on the same amount and in the same manner and at the same times as would have been the case if such deposit, defeasance and discharge had not occurred;

(h) the Company shall have delivered to the Trustee an Officer's Certificate stating that the deposit was not made by the Company with the intent of defeating, hindering, delaying or defrauding any other creditors of the Company; and

(i) the Company shall have delivered to the Trustee an Officer's Certificate and an Opinion of Counsel, each stating that all conditions precedent provided for relating to the defeasance contemplated by this Section have been complied with.

Section 8.4 Covenant Defeasance.

Unless this Section 8.4 is otherwise specified pursuant to Section 2.2 to be inapplicable to Securities of any Series, the Company may omit to comply with respect to the Securities of any Series with any term, provision or condition set forth under Sections 4.2, 4.3, 4.4 and 5.1 and, unless otherwise specified therein, any additional covenants specified in a supplemental indenture for such Series of Securities or a Board Resolution or an Officer's Certificate delivered pursuant to Section 2.2 (and the failure to comply with any such covenants shall not constitute a Default or Event of Default with respect to such Series under Section 6.1) and the occurrence of any event specified in a supplemental indenture for such Series of Securities or a Board Resolution or an Officer's Certificate delivered pursuant to Section 2.2.18 and designated as an Event of Default shall not constitute a Default or Event of Default hereunder, with respect to the Securities of such Series, but, except as specified above, the remainder of this Indenture and such Securities will be unaffected thereby; provided that the following conditions shall have been satisfied:

(a) with reference to this Section 8.4, the Company has irrevocably deposited or caused to be irrevocably deposited (except as provided in Section 8.2(c)) with the Trustee as trust funds in trust for the purpose of making the following payments specifically pledged as security for, and dedicated solely to, the benefit of the Holders of such Securities (i) in the case of Securities of such Series denominated in Dollars, cash in Dollars and/or U.S. Government Obligations, or (ii) in the case of Securities of such Series denominated in a Foreign Currency (other than a composite currency), money and/or Foreign Government Obligations, which through the payment of interest and principal in respect thereof in accordance with their terms, will provide (and without reinvestment and assuming no tax liability will be imposed on such Trustee), not later than one day before the due date of any payment of money, an amount in cash, sufficient, in the opinion of a nationally recognized firm of independent certified public accountants or investment bank expressed in a written certification thereof delivered to the Trustee, to pay and discharge each installment of principal (including mandatory sinking fund or analogous payments) of and interest on all the Securities of such Series on the dates such installments of principal or interest are due;

(b) such deposit will not result in a breach or violation of, or constitute a default under, this Indenture or any other agreement or instrument to which the Company is a party or by which it is bound;

(c) no Default or Event of Default with respect to the Securities of such Series shall have occurred and be continuing on the date of such deposit;

(d) the Company shall have delivered to the Trustee an Officers' Certificate and an Opinion of Counsel to the effect that (i) the Company has received from, or there has been published by, the Internal Revenue Service a ruling, or (ii) since the date of execution of this Indenture, there has been a change in the applicable Federal income tax law, in either case to the effect that, and based thereon such Opinion of Counsel shall confirm, subject to customary exclusions, that the Holders of the Securities of such Series will not recognize income, gain or loss for Federal income tax purposes as a result of such deposit, covenant defeasance and discharge and will be subject to Federal income tax on the same amount and in the same manner and at the same times as would have been the case if such deposit, covenant defeasance and discharge had not occurred;

(e) The Company shall have delivered to the Trustee an Officer's Certificate stating the deposit was not made by the Company with the intent of defeating, hindering, delaying or defrauding any other creditors of the Company; and

(f) The Company shall have delivered to the Trustee an Officer's Certificate and an Opinion of Counsel, each stating that all conditions precedent herein provided for relating to the covenant defeasance contemplated by this Section have been complied with.

Section 8.5 Repayment to Company.

Subject to applicable abandoned property law, the Trustee and the Paying Agent shall pay to the Company upon request any money held by them for the payment of principal and interest that remains unclaimed for two years. After that, Securityholders entitled to the money must look to the Company for payment as general creditors unless an applicable abandoned property law designates another person, and the Trustee shall have no further liability with respect to such money.

Section 8.6 Reinstatement.

If the Trustee or the Paying Agent is unable to apply any money deposited with respect to Securities of any Series in accordance with Section 8.1 by reason of any legal proceeding or by reason of any order or judgment of any court or governmental authority enjoining, restraining or otherwise prohibiting such application, the obligations of the Company under this Indenture with respect to the Securities of such Series and under the Securities of such Series shall be revived and reinstated as though no deposit had occurred pursuant to Section 8.1 until such time as the Trustee or the Paying Agent is permitted to apply all such money in accordance with Section 8.1; provided, however, that if the Company has made any payment of principal or interest on or any Additional Amounts with respect to any Securities because of the reinstatement of its obligations, the Company shall be subrogated to the rights of the Holders of such Securities to receive such payment from the money or U.S. Government Obligations held by the Trustee or Paying Agent after payment in full to the Holders.

**ARTICLE IX
AMENDMENTS AND WAIVERS**

Section 9.1 Without Consent of Holders.

The Company and the Trustee may amend or supplement this Indenture or the Securities of one or more Series without the consent of any Securityholder:

- (a) to cure any ambiguity, defect or inconsistency as evidenced by an Officer Certificate;
- (b) to comply with Article V;
- (c) to provide for uncertificated Securities in addition to or in place of certificated Securities;
- (d) to add guarantees with respect to Securities of any Series or secure Securities of any Series;
- (e) to surrender any of the Company's rights or powers under this Indenture;
- (f) to add covenants or events of default for the benefit of the holders of Securities of any Series (and if such covenants or events of default are to be for the benefit of less than all Series of Securities, stating that such covenants or events of default, as applicable, are expressly being included solely for the benefit of such Series);
- (g) to comply with the applicable procedures of the applicable depository;
- (h) to make any change that does not adversely affect the rights of any Securityholder;
- (i) to provide for the issuance of and establish the form and terms and conditions of Securities of any Series as permitted by this Indenture;
- (j) to evidence and provide for the acceptance of appointment hereunder by a successor Trustee with respect to the Securities of one or more Series and to add to or change any of the provisions of this Indenture as shall be necessary to provide for or facilitate the administration of the trusts hereunder by more than one Trustee;
- (k) to comply with requirements of the SEC in order to effect or maintain the qualification of this Indenture under the TIA;
- (l) to add to, change or eliminate any provision of this Indenture or the Securities of such Series in accordance with the TIA, or to comply with the provisions of DTC, Euroclear or Clearstream or the Trustee with respect to provisions of this Indenture or the Securities of such Series relating to transfers or exchanges of the Securities of such Series or beneficial interests in the Securities of such Series; or

(m) to conform any provision of this Indenture, in so far as it relates to the Securities of such Series, to the description of the Securities of such Series in the prospectus supplement relation to the offering of the Securities of such Series.

Section 9.2 With Consent of Holders.

The Company and the Trustee may enter into a supplemental indenture with the written consent of the Holders of at least a majority in aggregate principal amount of the outstanding Securities of each Series affected by such supplemental indenture (including consents obtained in connection with a tender offer or exchange offer for the Securities of such Series), for the purpose of adding any provisions to or changing in any manner or eliminating any of the provisions of this Indenture or of any supplemental indenture or of modifying in any manner the rights of the Securityholders of each such Series. Except as provided in Section 6.13, the Holders of at least a majority in aggregate principal amount of the outstanding Securities of any Series by notice to the Trustee (including consents obtained in connection with a tender offer or exchange offer for the Securities of such Series) may waive compliance by the Company with any provision of this Indenture or the Securities with respect to such Series.

It shall not be necessary for the consent of the Holders of Securities under this Section 9.2 to approve the particular form of any proposed supplemental indenture or waiver, but it shall be sufficient if such consent approves the substance thereof. After a supplemental indenture or waiver under this section becomes effective, the Company shall send to the Holders of Securities affected thereby, a notice briefly describing the supplemental indenture or waiver. Any failure by the Company to send such notice, or any defect therein, shall not, however, in any way impair or affect the validity of any such supplemental indenture or waiver.

Section 9.3 Limitations.

Without the consent of each Securityholder affected, an amendment or waiver may not:

- (a) reduce the principal amount of Securities whose Holders must consent to an amendment, supplement or waiver;
- (b) reduce the rate of or extend the time for payment of interest (including default interest) on any Security;
- (c) reduce the principal or change the Stated Maturity of any Security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation;
- (d) reduce the principal amount of Discount Securities payable upon acceleration of the maturity thereof;
- (e) waive a Default or Event of Default in the payment of the principal of or interest, if any, on any Security (except a rescission of acceleration of the Securities of any Series by the Holders of at least a majority in principal amount of the outstanding Securities of such Series and a waiver of the payment default that resulted from such acceleration);

(f) make the principal of or interest, if any, on any Security payable in any currency other than that stated in the Security;

(g) make any change in Sections 6.8, 6.13 or 9.3 (this sentence); or

(h) waive a redemption payment with respect to any Security, provided that such redemption is made at the Company's option.

Section 9.4 Compliance with Trust Indenture Act.

Every amendment to this Indenture or the Securities of one or more Series shall be set forth in a supplemental indenture hereto that complies with the TIA as then in effect.

Section 9.5 Revocation and Effect of Consents.

Until an amendment is set forth in a supplemental indenture or a waiver becomes effective, a consent to it by a Holder of a Security is a continuing consent by the Holder and every subsequent Holder of a Security or portion of a Security that evidences the same debt as the consenting Holder's Security, even if notation of the consent is not made on any Security. However, any such Holder or subsequent Holder may revoke the consent as to his Security or portion of a Security if the Trustee receives the notice of revocation before the date of the supplemental indenture or the date the waiver becomes effective.

Any amendment or waiver once effective shall bind every Securityholder of each Series affected by such amendment or waiver unless it is of the type described in any of clauses (a) through (h) of Section 9.3. In that case, the amendment or waiver shall bind each Holder of a Security who has consented to it and every subsequent Holder of a Security or portion of a Security that evidences the same debt as the consenting Holder's Security.

The Company may, but shall not be obligated to, fix a record date for the purpose of determining the Holders entitled to give their consent or take any other action described above or required or permitted to be taken pursuant to this Indenture. If a record date is fixed, then notwithstanding the second immediately preceding paragraph, those Persons who were Holders at such record date (or their duly designated proxies), and only those persons, shall be entitled to give such consent or to revoke any consent previously given or take any such action, whether or not such Persons continue to be Holders after such record date. No such consent shall be valid or effective for more than 120 days after such record date.

Section 9.6 Notation on or Exchange of Securities.

The Company or the Trustee may place an appropriate notation about an amendment or waiver on any Security of any Series thereafter authenticated. The Company in exchange for Securities of that Series may issue and the Trustee shall authenticate upon receipt of a Company Order in accordance with Section 2.3 new Securities of that Series that reflect the amendment or waiver.

Section 9.7 Trustee Protected.

In executing, or accepting the additional trusts created by, any supplemental indenture permitted by this Article or the modifications thereby of the trusts created by this Indenture, the Trustee shall be entitled to receive, and (subject to Section 7.1) shall be fully protected in relying upon, an Officer's Certificate or an Opinion of Counsel or both complying with Section 10.4 and stating that the supplemental indenture is authorized or permitted by this Indenture and constitutes a legal valid and binding obligation of the Company, enforceable against it in accordance with its terms. The Trustee shall sign all supplemental indentures upon delivery of such an Officer's Certificate or Opinion of Counsel or both, except that the Trustee need not sign any supplemental indenture that adversely affects its rights, duties, liabilities or immunities under this Indenture.

**ARTICLE X
MISCELLANEOUS**

Section 10.1 Trust Indenture Act Controls.

If any provision of this Indenture limits, qualifies, or conflicts with another provision which is required or deemed to be included in this Indenture by the TIA, such required or deemed provision shall control.

Section 10.2 Notices.

Any notice or communication by the Company or the Trustee to the other, or by a Holder to the Company or the Trustee, is duly given if in writing and delivered in person or mailed by first-class mail (registered or certified, return receipt requested), facsimile transmission, email or overnight air courier guaranteeing next day delivery, to the others' address:

if to the Company:

Zymeworks Inc.
108 Patriot Drive, Suite A
Middletown, Delaware 19709
Attention: General Counsel and Corporate Secretary

with a copy to:

Wilson Sonsini Goodrich & Rosati, Professional Corporation
650 Page Mill Road
Palo Alto, CA 94304
Attention: Tony Jeffries, Esq. and Bryan King, Esq.
Email: tjeffries@wsgr.com; bking@wsgr.com

if to the Trustee:

Trustee:
Address:
Attention:
Email:

The Company or the Trustee by notice to the other may designate additional or different addresses for subsequent notices or communications. Any notice or communication delivered to the Trustee shall be deemed effective upon actual receipt thereof.

Any notice or communication to a Securityholder shall be sent electronically or by first-class mail to his address shown on the register kept by the Registrar, in accordance with the procedures of the Depository. Failure to send a notice or communication to a Securityholder of any Series or any defect in it shall not affect its sufficiency with respect to other Securityholders of that or any other Series.

If a notice or communication is sent or published in the manner provided above, within the time prescribed, it is duly given, whether or not the Securityholder receives it.

If the Company sends a notice or communication to Securityholders, it shall send a copy to the Trustee and each Agent at the same time.

Notwithstanding any other provision of this Indenture or any Security, where this Indenture or any Security provides for notice of any event (including any notice of redemption) to a Holder of a Global Security (whether by mail or otherwise), such notice shall be sufficiently given to the Depository for such Security (or its designee) pursuant to the customary procedures of such Depository.

Section 10.3 Communication by Holders with Other Holders.

Securityholders of any Series may communicate pursuant to TIA § 312(b) with other Securityholders of that Series or any other Series with respect to their rights under this Indenture or the Securities of that Series or all Series. The Company, the Trustee, the Registrar and anyone else shall have the protection of TIA § 312(c).

Section 10.4 Certificate and Opinion as to Conditions Precedent.

Upon any request or application by the Company to the Trustee to take any action under this Indenture, the Company shall furnish to the Trustee:

(a) an Officer's Certificate stating that, in the opinion of the signers, all conditions precedent, if any, provided for in this Indenture relating to the proposed action have been complied with; and

(b) an Opinion of Counsel stating that, in the opinion of such counsel, all such conditions precedent have been complied with.

Section 10.5 Statements Required in Certificate or Opinion.

Each certificate or opinion with respect to compliance with a condition or covenant provided for in this Indenture (other than a certificate provided pursuant to TIA § 314(a)(4)) shall comply with the provisions of TIA § 314(e) and shall include:

(a) a statement that the person making such certificate or opinion has read such covenant or condition;

(b) a brief statement as to the nature and scope of the examination or investigation upon which the statements or opinions contained in such certificate or opinion are based;

(c) a statement that, in the opinion of such person, he has made such examination or investigation as is necessary to enable him to express an informed opinion as to whether or not such covenant or condition has been complied with; and

(d) a statement as to whether or not, in the opinion of such person, such condition or covenant has been complied with.

Section 10.6 Rules by Trustee and Agents.

The Trustee may make reasonable rules for action by or a meeting of Securityholders of one or more Series. Any Agent may make reasonable rules and set reasonable requirements for its functions.

Section 10.7 Legal Holidays.

A “*Legal Holiday*” is any day that is not a Business Day. If a payment date is a Legal Holiday at a place of payment, payment may be made at that place on the next succeeding day that is not a Legal Holiday, and no interest shall accrue for the intervening period.

Section 10.8 No Recourse Against Others.

A director, officer, employee or stockholder (past or present), as such, of the Company shall not have any liability for any obligations of the Company under the Securities or the Indenture or for any claim based on, in respect of or by reason of such obligations or their creation. Each Securityholder by accepting a Security waives and releases all such liability. The waiver and release are part of the consideration for the issue of the Securities.

Section 10.9 Counterparts.

This Indenture may be executed in any number of counterparts and by the parties hereto in separate counterparts, each of which when so executed shall be deemed to be an original and all of which taken together shall constitute one and the same agreement. The exchange of copies of this Indenture and of signature pages by facsimile or PDF transmission shall constitute effective execution and delivery of this Indenture as to the parties hereto and may be used in lieu of the original Indenture for all purposes. Signatures of the parties hereto transmitted by facsimile or PDF shall be deemed to be their original signatures for all purposes.

THIS INDENTURE AND THE SECURITIES, INCLUDING ANY CLAIM OR CONTROVERSY ARISING OUT OF OR RELATING TO THE INDENTURE OR THE SECURITIES, SHALL BE GOVERNED BY THE LAWS OF THE STATE OF NEW YORK. THE COMPANY, THE TRUSTEE AND THE HOLDERS (BY THEIR ACCEPTANCE OF THE SECURITIES) EACH HEREBY IRREVOCABLY WAIVE, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF OR RELATING TO THIS INDENTURE, THE SECURITIES OR THE TRANSACTIONS CONTEMPLATED HEREBY OR THEREBY.

Any legal suit, action or proceeding arising out of or based upon this Indenture or the transactions contemplated hereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York (collectively, the "*Specified Courts*"), and each party irrevocably submits to the nonexclusive jurisdiction of such courts in any such suit, action or proceeding. Service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party's address set forth above shall be effective service of process for any suit, action or other proceeding brought in any such court. The Company, the Trustee and the Holders (by their acceptance of the Securities) each hereby irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the Specified Courts and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum.

Section 10.11 No Adverse Interpretation of Other Agreements.

This Indenture may not be used to interpret another indenture, loan or debt agreement of the Company or a Subsidiary of the Company. Any such indenture, loan or debt agreement may not be used to interpret this Indenture.

Section 10.12 Successors.

All agreements of the Company in this Indenture and the Securities shall bind its successor. All agreements of the Trustee in this Indenture shall bind its successor.

Section 10.13 Severability.

In case any provision in this Indenture or in the Securities shall be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions shall not in any way be affected or impaired thereby.

Section 10.14 Table of Contents, Headings, Etc.

The Table of Contents, Cross Reference Table, and headings of the Articles and Sections of this Indenture have been inserted for convenience of reference only, are not to be considered a part hereof, and shall in no way modify or restrict any of the terms or provisions hereof.

Section 10.15 Securities in a Foreign Currency.

Unless otherwise specified in a Board Resolution, a supplemental indenture hereto or an Officer's Certificate delivered pursuant to Section 2.2 of this Indenture with respect to a particular Series of Securities, whenever for purposes of this Indenture any action may be taken by the Holders of a specified percentage in aggregate principal amount of Securities of all Series or all Series affected by a particular action at the time outstanding and, at such time, there are outstanding Securities of any Series which are denominated in more than one currency, then the principal amount of Securities of such Series which shall be deemed to be outstanding for the purpose of taking such action shall be determined by converting any such other currency into a currency that is designated upon issuance of any particular Series of Securities. Unless otherwise specified in a Board Resolution, a supplemental indenture hereto or an Officer's Certificate delivered pursuant to Section 2.2 of this Indenture with respect to a particular Series of Securities, such conversion shall be at the spot rate for the purchase of the designated currency as published in The Financial Times in the "Currency Rates" section (or, if The Financial Times is no longer published, or if such information is no longer available in The Financial Times, such source as may be selected in good faith by the Company) on any date of determination. The provisions of this paragraph shall apply in determining the equivalent principal amount in respect of Securities of a Series denominated in currency other than Dollars in connection with any action taken by Holders of Securities pursuant to the terms of this Indenture.

All decisions and determinations provided for in the preceding paragraph shall, in the absence of manifest error, to the extent permitted by law, be conclusive for all purposes and irrevocably binding upon the Trustee and all Holders.

Section 10.16 Judgment Currency.

The Company agrees, to the fullest extent that it may effectively do so under applicable law, that (a) if for the purpose of obtaining judgment in any court it is necessary to convert the sum due in respect of the principal of or interest or other amount on the Securities of any Series (the "Required Currency") into a currency in which a judgment will be rendered (the "Judgment Currency"), the rate of exchange used shall be the rate at which in accordance with normal banking procedures the Trustee could purchase in The City of New York the Required Currency with the Judgment Currency on the day on which final unappealable judgment is entered, unless such day is not a New York Banking Day, then the rate of exchange used shall be the rate at which in accordance with normal banking procedures the Trustee could purchase in The City of New York the Required Currency with the Judgment Currency on the New York Banking Day preceding the day on which final unappealable judgment is entered and (b) its obligations under this Indenture to make payments in the Required Currency (i) shall not be discharged or satisfied by any tender, any recovery pursuant to any judgment (whether or not entered in accordance with subsection (a)), in any

currency other than the Required Currency, except to the extent that such tender or recovery shall result in the actual receipt, by the payee, of the full amount of the Required Currency expressed to be payable in respect of such payments, (ii) shall be enforceable as an alternative or additional cause of action for the purpose of recovering in the Required Currency the amount, if any, by which such actual receipt shall fall short of the full amount of the Required Currency so expressed to be payable, and (iii) shall not be affected by judgment being obtained for any other sum due under this Indenture. For purposes of the foregoing, “*New York Banking Day*” means any day except a Saturday, Sunday or a Legal Holiday in The City of New York on which banking institutions are authorized or required by law, regulation or executive order to close.

Section 10.17 Force Majeure.

In no event shall the Trustee be responsible or liable for any failure or delay in the performance of its obligations hereunder arising out of or caused by, directly or indirectly, forces beyond its control, including, without limitation, strikes, work stoppages, accidents, acts of war or terrorism, civil or military disturbances, nuclear or natural catastrophes or acts of God, and interruptions, loss or malfunctions of utilities, communications or computer (software and hardware) services, it being understood that the Trustee shall use reasonable best efforts which are consistent with accepted practices in the banking industry to resume performance as soon as practicable under the circumstances.

Section 10.18 U.S.A. Patriot Act.

The parties hereto acknowledge that in accordance with Section 326 of the U.S.A. Patriot Act, the Trustee is required to obtain, verify, and record information that identifies each person or legal entity that establishes a relationship or opens an account with the Trustee. The parties to this Indenture agree that they will provide the Trustee with such information as it may request in order for the Trustee to satisfy the requirements of the U.S.A. Patriot Act.

ARTICLE XI
SINKING FUNDS

Section 11.1 Applicability of Article.

The provisions of this Article shall be applicable to any sinking fund for the retirement of the Securities of a Series if so provided by the terms of such Securities pursuant to Section 2.2 and except as otherwise permitted or required by any form of Security of such Series issued pursuant to this Indenture.

The minimum amount of any sinking fund payment provided for by the terms of the Securities of any Series is herein referred to as a “*mandatory sinking fund payment*” and any other amount provided for by the terms of Securities of such Series is herein referred to as an “*optional sinking fund payment*.” If provided for by the terms of Securities of any Series, the cash amount of any sinking fund payment may be subject to reduction as provided in Section 11.2. Each sinking fund payment shall be applied to the redemption of Securities of any Series as provided for by the terms of the Securities of such Series.

Section 11.2 Satisfaction of Sinking Fund Payments with Securities.

The Company may, in satisfaction of all or any part of any sinking fund payment with respect to the Securities of any Series to be made pursuant to the terms of such Securities (1) deliver outstanding Securities of such Series to which such sinking fund payment is applicable (other than any of such Securities previously called for mandatory sinking fund redemption) and (2) apply as credit Securities of such Series to which such sinking fund payment is applicable and which have been repurchased by the Company or redeemed either at the election of the Company pursuant to the terms of such Series of Securities (except pursuant to any mandatory sinking fund) or through the application of permitted optional sinking fund payments or other optional redemptions pursuant to the terms of such Securities, provided that such Securities have not been previously so credited. Such Securities shall be received by the Trustee, together with an Officer's Certificate with respect thereto, not later than 15 days prior to the date on which the Trustee begins the process of selecting Securities for redemption, and shall be credited for such purpose by the Trustee at the price specified in such Securities for redemption through operation of the sinking fund and the amount of such sinking fund payment shall be reduced accordingly. If as a result of the delivery or credit of Securities in lieu of cash payments pursuant to this Section 11.2, the principal amount of Securities of such Series to be redeemed in order to exhaust the aforesaid cash payment shall be less than \$100,000, the Trustee need not call Securities of such Series for redemption, except upon receipt of a Company Order that such action be taken, and such cash payment shall be held by the Trustee or a Paying Agent and applied to the next succeeding sinking fund payment, provided, however, that the Trustee or such Paying Agent shall from time to time upon receipt of a Company Order pay over and deliver to the Company any cash payment so being held by the Trustee or such Paying Agent upon delivery by the Company to the Trustee of Securities of that Series purchased by the Company having an unpaid principal amount equal to the cash payment required to be released to the Company.

Section 11.3 Redemption of Securities for Sinking Fund.

Not less than 45 days (unless otherwise indicated in the Board Resolution, supplemental indenture hereto or Officer's Certificate in respect of a particular Series of Securities) prior to each sinking fund payment date for any Series of Securities, the Company will deliver to the Trustee an Officer's Certificate specifying the amount of the next ensuing mandatory sinking fund payment for that Series pursuant to the terms of that Series, the portion thereof, if any, which is to be satisfied by payment of cash and the portion thereof, if any, which is to be satisfied by delivering and crediting of Securities of that Series pursuant to Section 11.2, and the optional amount, if any, to be added in cash to the next ensuing mandatory sinking fund payment, and the Company shall thereupon be obligated to pay the amount therein specified. Not less than 30 days (unless otherwise indicated in the Board Resolution, Officer's Certificate or supplemental indenture in respect of a particular Series of Securities) before each such sinking fund payment date the Securities to be redeemed upon such sinking fund payment date will be selected in the manner specified in Section 3.2 and the Company shall send or cause to be sent a notice of the redemption thereof to be given in the name of and at the expense of the Company in the manner provided in and in accordance with Section 3.3. Such notice having been duly given, the redemption of such Securities shall be made upon the terms and in the manner stated in Sections 3.4, 3.5 and 3.6.

IN WITNESS WHEREOF, the parties hereto have caused this Indenture to be duly executed as of the day and year first above written.

ZYMEWORKS INC.

By: _____
Name:
Title:

,

as Trustee

By: _____
Name:
Title:



Wilson Sonsini Goodrich & Rosati
Professional Corporation

650 Page Mill Road
Palo Alto, CA 94304

o: (650) 493-9300
f: (650) 493-6811

March 7, 2023

Zymeworks Inc.
108 Patriot Drive, Suite A
Middletown, Delaware 19709

Re: Post-Effective Amendment No. 2 to Registration Statement on Form S-3

Ladies and Gentlemen:

At your request, we have examined Post-Effective Amendment No. 2 to the Registration Statement on Form S-3 (File No. 333-259970-01) (as amended, the "Registration Statement"), filed by Zymeworks Inc., a Delaware corporation (the "Company"), with the Securities and Exchange Commission (the "Commission") in connection with the registration pursuant to the Securities Act of 1933, as amended (the "Act"), of the Shelf Securities (as defined below) and the Underlying Shares (as defined below).

The Registration Statement relates to (i) the proposed issuance and sale by the Company, from time to time, pursuant to Rule 415 under the Act, as set forth in the Registration Statement, the base prospectus contained therein relating to the offering of the Shelf Securities (the "Base Prospectus") and the supplements to the Base Prospectus referred to therein (each, including the ATM Prospectus Supplement (as defined below), a "Prospectus Supplement"), of up to an aggregate offering price of \$500,000,000, or the equivalent thereof, of (a) shares of the Company's common stock, \$0.00001 par value per share (the "Common Stock"); (b) preferred stock purchase rights (the "Rights") associated with the Common Stock pursuant to that certain Preferred Stock Rights Agreement, dated as of October 12, 2022 (the "Rights Agreement"), by and between the Company and Computershare Trust Company, N.A., as rights agent (the "Rights Agent"); (c) shares of the Company's preferred stock, \$0.00001 par value per share (the "Preferred Stock"); (d) the Company's debt securities (the "Debt Securities"); (e) depositary shares of the Company representing a fractional interest in a share of Preferred Stock (the "Depositary Shares"); (f) warrants to purchase Common Stock, Preferred Stock or Debt Securities (the "Warrants"); (g) subscription rights to purchase Common Stock, Preferred Stock, Debt Securities, Depositary Shares, Warrants or units consisting of some or all of these securities (the "Subscription Rights"); (h) purchase contracts of the Company with respect to the securities of the Company (the "Purchase Contracts"); (i) units consisting of two or more securities described above in any combination (the "Units"); and (j) up to \$150,000,000 of shares of Common Stock (including the associated Rights, the "ATM Shares" and, together with the Common Stock, the Rights, the Preferred Stock, the Debt Securities, the Depositary Shares, the Warrants, the Subscription Rights, the Purchase Contracts and the Units, the "Shelf Securities") pursuant to the Base Prospectus and the prospectus supplement dated March 7, 2023 relating to the ATM Shares contained in the Registration Statement (the "ATM Prospectus Supplement"); and (ii) the offering by the Company, from time to time, of up to 2,737,836 shares of Common Stock (including the associated Rights, the "Underlying Shares") pursuant to the prospectus contained therein covering the issuance of the Underlying Shares (the "Underlying Shares Prospectus"), consisting of (a) up to 658,612 shares of Common Stock issuable upon the exchange of exchangeable shares (the "Exchangeable Shares") in the capital of Zymeworks ExchangeCo Ltd., an indirect subsidiary of the Company, which issued the Exchangeable Shares to certain shareholders of Zymeworks BC Inc. ("Zymeworks BC") in connection with redomicile transactions completed on October 13, 2022

AUSTIN BEIJING BOSTON BRUSSELS HONG KONG LONDON LOS ANGELES NEW YORK PALO ALTO
SAN DIEGO SAN FRANCISCO SEATTLE SHANGHAI WASHINGTON, DC WILMINGTON, DE

pursuant to which the Company became the ultimate parent company of Zymeworks BC (the “Redomicile Transactions”); and (b) up to 2,079,224 shares of Common Stock issuable upon the exercise of pre-funded warrants (the “Pre-Funded Warrants”) that were originally issued by Zymeworks BC and assumed by the Company in connection with the Redomicile Transaction.

The Shelf Securities are to be sold from time to time as set forth in the Registration Statement, the Base Prospectus contained therein and the Prospectus Supplements. The Debt Securities are to be issued pursuant to a debt securities indenture (the “Indenture”), a form of which has been filed as an exhibit to the Registration Statement and is to be entered into between the Company and a trustee to be named in a Prospectus Supplement to the Registration Statement (the “Trustee”). The Shelf Securities are to be sold pursuant to a purchase, underwriting or similar agreement in substantially the form to be filed under a Current Report on Form 8-K and, in the case of the ATM Shares, pursuant to that certain sales agreement, dated as of November 9, 2022, by and between the Company and Cantor Fitzgerald & Co. (the “Sales Agreement”). The Debt Securities are to be issued in the form set forth in the Indenture. The Indenture may be supplemented in connection with the issuance of each such series of Debt Securities, by a supplemental indenture or other appropriate action of the Company creating such series of Debt Securities.

We have examined instruments, documents, certificates and records that we have deemed relevant and necessary for the basis of our opinions hereinafter expressed. In such examination, we have assumed: (a) the authenticity of original documents and the genuineness of all signatures; (b) the conformity to the originals of all documents submitted to us as copies; (c) the truth, accuracy and completeness of the information, representations and warranties contained in the instruments, documents, certificates and records we have reviewed; (d) that the Registration Statement, and any amendments thereto (including post-effective amendments), will have become effective under the Act; (e) that a Prospectus Supplement will have been filed with the Commission describing the Shelf Securities offered thereby; (f) that the Shelf Securities and the Underlying Shares will be issued and sold in compliance with applicable U.S. federal and state securities laws and in the manner stated in the Registration Statement, the applicable Prospectus Supplement and the Underlying Shares Prospectus, as applicable; (g) that a definitive purchase, underwriting or similar agreement with respect to any Shelf Securities offered will have been duly authorized and validly executed and delivered by the Company and the other parties thereto; (h) that any Shelf Securities issuable upon conversion, exchange, redemption or exercise of any Shelf Securities being offered will be duly authorized, created and, if appropriate, reserved for issuance upon such conversion, exchange, redemption or exercise; (i) with respect to shares of Common Stock or Preferred Stock offered by the Company, that there will be sufficient shares of Common Stock or Preferred Stock authorized under the Company’s organizational documents that are not otherwise reserved for issuance; and (j) the legal capacity of all natural persons. As to any facts material to the opinions expressed herein that were not independently established or verified, we have relied upon oral or written statements and representations of officers and other representatives of the Company. The term “Board” means the Board of Directors of the Company or a duly constituted and acting committee thereof.

In rendering this opinion, we have also assumed that the Rights Agreement has been duly authorized, executed and delivered by the Rights Agent and that the members of the Board have acted in a manner consistent with their fiduciary duties as required under applicable law in adopting the Rights Agreement. This opinion does not address the determination a court of competent jurisdiction may make regarding whether the Board may be required to redeem or terminate, or take other action with respect to, the Rights in the future based on the facts and circumstances existing at that time. It should be understood that our opinion addresses the Rights and Rights Agreement in their entirety and not any particular provision of the Rights or the Rights Agreement and that it is not settled whether the invalidity of any particular provision of a rights agreement or purchase rights issued thereunder would result in invalidating in their entirety such rights.

Based on such examination, we are of the opinion that:

1. With respect to the shares of Common Stock and the associated Rights to be offered pursuant to the Base Prospectus, when: (a) the Board has taken all necessary corporate action to approve the issuance and the terms of the offering of the shares of Common Stock and related matters; and (b) the shares of Common Stock have been duly delivered either (i) in accordance with the applicable definitive purchase, underwriting or similar agreement approved by the Board, or upon the exercise of Warrants to purchase Common Stock, upon payment of the consideration therefor (not less than the par value of the Common Stock) provided for therein or (ii) upon conversion or exercise of any other Shelf Security, in accordance with the terms of such Shelf Security or the instrument governing such Shelf Security providing for such conversion or exercise as approved by the Board, for the consideration approved by the Board, then the shares of Common Stock and the associated Rights will be validly issued, and such shares of Common Stock will be fully paid and nonassessable.

2. With respect to any particular series of shares of Preferred Stock, when: (a) the Board has taken all necessary corporate action to approve the issuance and terms of the shares of Preferred Stock, the terms of the offering thereof, and related matters, including the adoption of a certificate of designation (a "Certificate") relating to such Preferred Stock conforming to the General Corporation Law of the State of Delaware (the "DGCL") and the filing of the Certificate with the Secretary of State of the State of Delaware; and (b) the shares of Preferred Stock have been duly delivered either (i) in accordance with the applicable definitive purchase, underwriting or similar agreement approved by the Board, or upon the exercise of Warrants to purchase Preferred Stock, upon payment of the consideration therefor (not less than the par value of the Preferred Stock) provided for therein or (ii) upon conversion or exercise of any other Shelf Security, in accordance with the terms of such Shelf Security or the instrument governing such Shelf Security providing for such conversion or exercise as approved by the Board, for the consideration approved by the Board, then the shares of Preferred Stock will be validly issued, fully paid and nonassessable.

3. With respect to the Debt Securities to be issued under the Indenture, when: (a) the Trustee is qualified to act as Trustee under the Indenture and the Company has filed a Form T-1 for the Trustee with the Commission; (b) the Trustee has duly executed and delivered the Indenture; (c) the Indenture has been duly authorized and validly executed and delivered by the Company to the Trustee; (d) the Indenture has been duly qualified under the Trust Indenture Act of 1939, as amended; (e) the Board has taken all necessary corporate action to approve the issuance and terms of such Debt Securities, the terms of the offering thereof and related matters; and (f) such Debt Securities have been duly executed, authenticated, issued and delivered in accordance with the provisions of the Indenture and the applicable definitive purchase, underwriting or similar agreement approved by the Board, or upon the exercise of Warrants to purchase Debt Securities, upon payment of the consideration therefor provided for therein, such Debt Securities will constitute valid and binding obligations of the Company, enforceable against the Company in accordance with their terms, and entitled to the benefits of the Indenture.

4. With respect to the Depositary Shares, when: (a) the Board has taken all necessary corporate action to approve the issuance and terms of the Depositary Shares, the terms of the offering thereof, and related matters, including the adoption of a Certificate relating to the Preferred Stock underlying such Depositary Shares and the filing of the Certificate with the Secretary of State of the State of Delaware; (b) the Deposit Agreement (the "Deposit Agreement") or agreements relating to the Depositary Shares and the related Depositary Receipts (the "Depositary Receipts") have been duly authorized and validly executed and delivered by the Company and the depositary appointed by the Company; (c) the shares of Preferred Stock underlying such Depositary Shares have been deposited with a bank or trust company (which meets the requirements for the depositary set forth in the Registration Statement) under the applicable Deposit Agreement; and (d) the Depositary Receipts representing the Depositary Shares have been duly executed, countersigned, registered and delivered in accordance with the

appropriate Deposit Agreement and the applicable definitive purchase, underwriting or similar agreement approved by the Board upon payment of the consideration therefor provided for therein, the Depositary Shares will be validly issued, and will entitle their holders to the rights specified in the Deposit Agreement and the Depositary Receipts.

5. With respect to the Warrants, when: (a) the Board has taken all necessary corporate action to approve the issuance and terms of the Warrants and related matters; and (b) the Warrants have been duly executed and delivered against payment therefor, pursuant to the applicable definitive purchase, underwriting, warrant or similar agreement, as applicable, duly authorized, executed and delivered by the Company and a warrant agent and the certificates for the Warrants have been duly executed and delivered by the Company and such warrant agent, then the Warrants will constitute valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

6. With respect to the Subscription Rights, when: (a) the Board has taken all necessary corporate action to authorize the issuance and terms of the Subscription Rights, the terms of the offering thereof, and related matters and (b) the rights agreement under which the Subscription Rights are to be issued has been duly authorized and validly executed and delivered by the Company, and upon payment of the consideration for the Subscription Rights provided for in such rights agreement, if any, then the Subscription Rights will be valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

7. With respect to the Purchase Contracts, when: (a) the Board has taken all necessary corporate action to approve the issuance and terms of the Purchase Contracts and related matters and (b) the agreement under which the Purchase Contracts are to be issued has been duly authorized and validly executed and delivered by the Company, then the Purchase Contracts will be valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

8. With respect to the Units, when: (a) the Board has taken all necessary corporate action to approve the issuance and terms of the Units (including any Shelf Securities underlying the Units) and related matters; and (b) the Units (including any Shelf Securities underlying the Units) have been duly executed and delivered against payment therefor, pursuant to the applicable definitive purchase, underwriting, or similar agreement duly authorized, executed and delivered by the Company and any applicable unit or other agents, and the certificates for the Units (including any Shelf Securities underlying the Units) have been duly executed and delivered by the Company and any applicable unit or other agents, then the Units will constitute valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

9. The ATM Shares have been duly authorized by the Company and, when issued and delivered by the Company against payment therefor in accordance with the terms of the Sales Agreement, will be validly issued, fully paid and nonassessable.

10. The Underlying Shares issuable upon exchange of the Exchangeable Shares have been duly authorized by the Company and, when issued and delivered by the Company in accordance with the terms of the Exchangeable Shares and the agreements governing the Exchangeable Shares, such Underlying Shares will be validly issued, fully paid and nonassessable.

11. The Underlying Shares issuable upon exercise of the Pre-Funded Warrants have been duly authorized by the Company and, when issued and delivered by the Company in accordance with the terms of the Pre-Funded Warrants, such Underlying Shares will be validly issued, fully paid and nonassessable.

Zymeworks Inc.

March 7, 2023

Page 5

Our opinion that any document is legal, valid and binding is qualified as to:

(a) limitations imposed by bankruptcy, insolvency, reorganization, arrangement, fraudulent transfer, moratorium or other similar laws relating to or affecting the rights of creditors generally;

(b) rights to indemnification and contribution, which may be limited by applicable law or equitable principles; and

(c) the effect of general principles of equity, including without limitation concepts of materiality, reasonableness, good faith and fair dealing, and the possible unavailability of specific performance or injunctive relief, whether considered in a proceeding in equity or at law.

We express no opinion as to the laws of any other jurisdiction, other than the federal laws of the United States of America, the laws of the State of New York as to the enforceability of the Debt Securities and the DGCL.

* * *

Zymeworks Inc.

March 7, 2023

Page 6

We hereby consent to the filing of this opinion as an exhibit to the above-referenced Registration Statement and to the use of our name wherever it appears in the Registration Statement, the Base Prospectus, any Prospectus Supplement, the Underlying Shares Prospectus and in any amendment or supplement thereto. In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Act or the rules and regulations of the Commission thereunder.

Very truly yours,

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation

/s/ Wilson Sonsini Goodrich & Rosati, P.C.

Consent of Independent Registered Public Accounting Firm

We consent to the use of our report dated February 24, 2022, on the consolidated financial statements of Zymeworks Inc., which comprise the consolidated balance sheets as of December 31, 2021 and December 31, 2020, the related consolidated statements of loss and comprehensive loss, changes in shareholders' equity and cash flows for each of the years in the three-year period ended December 31, 2021, and the related notes, and our report dated February 24, 2022 on the effectiveness of internal control over financial reporting as of December 31, 2021, which are incorporated by reference and to the reference to our firm under the heading "Experts" in the prospectus.

/s/ KPMG LLP

Chartered Professional Accountants

March 7, 2023

Vancouver, Canada

CALCULATION OF FILING FEE TABLES

Post-Effective Amendment to Form S-3ASR
(Form Type)

Zymeworks Inc.

(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial Effective Date	Filing Precedence with Unregistered Securities
Newly Registered Securities												
Fees to Be Paid	Equity	Common Stock, \$0.00001 par value per share	457(o)	(1)	(1)	(1)	—	—				
	Other	Preferred Stock Purchase Rights (2)	457(o)	(1)	(1)	(1)	—	—				
	Equity	Preferred Stock	457(o)	(1)	(1)	(1)	—	—				
	Debt	Debt Securities	457(o)	(1)	(1)	(1)	—	—				
	Equity	Depository Shares	457(o)	(1)	(1)	(1)	—	—				
	Equity	Warrants	457(o)	(1)	(1)	(1)	—	—				
	Other	Subscription Rights	457(o)	(1)	(1)	(1)	—	—				
	Other	Purchase Contracts	457(o)	(1)	(1)	(1)	—	—				
	Other	Units	457(o)	(1)	(1)	(1)	—	—				
	Unallocated (Universal) Shelf	Unallocated (Universal) Shelf	457(o)	(1)	(1)	\$350,000,000	\$110.20 per \$1,000,000	\$38,570				
Carry Forward Securities												
Carry Forward Securities	Equity	Common Stock, \$0.00001 par value per share	415(a)(6)	—		\$150,000,000 (3)			424(b)(5)	333-259970-01	October 13, 2022	\$16
	Equity	Common Stock, \$0.00001 par value per share	415(a)(6)	658,612		\$3,381,972.62 (4)			424(b)(5)	333-259970-01	October 13, 2022	\$37
	Equity	Common Stock, \$0.00001 par value per share	415(a)(6)	2,079,224		\$10,677,023.16 (5)			424(b)(5)	333-259970-01	October 13, 2022	\$1.1
	Total Offering Amounts					\$514,058,996		\$38,570				
	Total Fees Previously Paid							—				
	Total Fee Offsets							—				
	3Net Fee Due							\$38,570				

- (1) An indeterminate aggregate initial offering price and number of securities of each identified class is being registered as may from time to time be offered, issued or sold at indeterminate prices. In addition, an indeterminate number of securities that may be issued upon exercise, settlement, conversion or exchange of any offered securities, or pursuant to anti-dilution adjustments, is being registered. Separate consideration may or may not be received for securities that are issuable on exercise, conversion or exchange of other securities.

- (2) Each share of common stock registered for issuance under this registration statement includes an associated right to purchase one one-thousandth of a share of the registrant's Series B Participating Preferred Stock, par value \$0.00001 per share. Until the occurrence of certain prescribed events, the preferred stock purchase rights are not exercisable and may be transferred only with the common stock. No separate consideration is payable for the preferred stock purchase rights.
- (3) Represents \$150,000,000 of shares of the registrant's common stock that may be issued and sold under that certain sales agreement, dated as of November 9, 2022, by and between the registrant and Cantor Fitzgerald & Co., which amount was previously registered by the registrant on the prospectus supplement filed by the registrant with Securities and Exchange Commission (the "SEC") on November 9, 2022 and all of which remains unsold. Pursuant to Rule 415(a)(6) under the Securities Act of 1933, as amended (the "Securities Act"), the previously paid filing fee will continue to be applied to such shares.
- (4) Represents shares of the registrant's common stock issuable upon the exchange of exchangeable shares (the "Exchangeable Shares") in the capital of Zymeworks ExchangeCo Ltd., a company existing under the laws of British Columbia and the registrant's indirect subsidiary. The registrant previously registered 1,424,533 shares of common stock issuable upon exchange of the Exchangeable Shares on the prospectus supplement filed by the registrant with the SEC on October 13, 2022, of which 658,612 shares remain issuable. Pursuant to Rule 415(a)(6) under the Securities Act, the previously paid filing fee for the remaining 658,612 shares will continue to be applied to such shares.
- (5) Represents shares of the registrant's common stock issuable upon the exercise of the registrant's pre-funded warrants (the "Pre-Funded Warrants"). The registrant previously registered 4,794,224 shares of common stock issuable upon exercise of the Pre-Funded Warrants on the prospectus supplement filed by the registrant with the SEC on October 13, 2022, of which 2,079,224 shares remain issuable. Pursuant to Rule 415(a)(6) under the Securities Act, the previously paid filing fee for the remaining 2,079,224 shares will continue to be applied to such shares.