Filed Pursuant to Rule 424(b)(5)
Registration No. 333-259970

CALCULATION OF REGISTRATION FEE

Title Of Each Class of Securities to be Registered	Number of Securities to be Registered	Maximum Offering Price Per Security	Maximum Aggregate Offering Price	Amount of Registration Fee
Common Shares, no par value	14,375,000(1)	$8.00	$115,000,000.00	$10,660.50
Pre-Funded Warrants to Purchase Common Shares(2)	3,340,000	$8.00(3)	—(3)	—(3)
Total	—	—	$115,000,000.00	$10,660.50(4)

(1) Includes 1,875,000 common shares that may be purchased by the underwriters upon exercise of the underwriters' option to purchase additional shares and 3,340,000 common shares that are issuable upon the exercise of the pre-funded warrants referenced below.

(2) Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), the pre-funded warrants to purchase common shares being registered hereunder include such indeterminate number of additional common shares as may be issued after the date hereof as a result of share splits, share dividends or similar transactions.

(3) Represents the sum of the per-warrant sales price of $7.9999 and the exercise price of $0.0001 per common share issuable pursuant to the warrants. Pursuant to Securities and Exchange Commission staff interpretation, the entire fee is allocated to the common shares underlying the warrants.

(4) The filing fee is calculated and being paid pursuant to Rule 457(r) under the Securities Act and relates to the Registration Statement on Form S-3ASR (File No. 333-259970) filed by the Registrant on October 1, 2021.

PROSPECTUS SUPPLEMENT
(To Prospectus dated October 1, 2021)

9,160,000 Common Shares
Pre-Funded Warrants to Purchase 3,340,000 Common Shares

We are offering 9,160,000 of our common shares and, in lieu of common shares to certain investors, pre-funded warrants to purchase up to 3,340,000 of our common shares pursuant to this prospectus supplement and the accompanying prospectus. The purchase price of each pre-funded warrant equals the price per share at which common shares are being sold to the public in this offering minus US$0.0001, which represents the exercise price of each pre-funded warrant. This prospectus supplement also relates to the offering of the common shares issuable upon the exercise of such pre-funded warrants.

Our common shares are listed on the New York Stock Exchange (the "NYSE"), under the symbol "ZYME." The last reported sale price of our common shares on the NYSE on January 26, 2022 was US$9.32 per share. There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on the NYSE or any other national securities exchange or nationally recognized trading system.

Investing in our securities involves a high degree of risk. Please read "Risk Factors" on page S-10 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.

	PER COMMON SHARE	PER PRE-FUNDED WARRANT	TOTAL
Public offering price	US$ 8.00	US$ 7.9999	US$99,999,666
Underwriting discounts and commissions (1)	US$ 0.48	US$ 0.48	US$ 6,000,000
Proceeds to Zymeworks Inc. (before expenses) (2)	US$ 7.52	US$ 7.5199	US$93,999,666

(1) See "Underwriting" for a description of the compensation payable to the underwriters.
(2) The amount of the offering proceeds to Zymeworks Inc. presented in this table does not give effect to any exercise of the pre-funded warrants being issued in this offering.

Delivery of the common shares and pre-funded warrants is expected to be made on or about January 31, 2022. We have granted the underwriters an option for a period of 30 days to purchase an additional 1,875,000 of our common shares. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be $6,900,000, and the total proceeds to us, before expenses, will be $108,099,666.

Joint Book-Running Managers

Jefferies **Evercore ISI** **Stifel** **Wells Fargo Securities**

Lead Co-Manager

Raymond James

Prospectus Supplement dated January 26, 2022

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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 shares and pre-funded warrants being offered and other information you should know before investing. You should read this prospectus supplement and the accompanying base shelf prospectus together with the additional information described under the heading "Where You Can Find More Information" before investing in our common shares and pre-funded warrants.

Neither we nor the underwriters 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 the underwriters are 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. See "Exchange Rate Information."

In this prospectus supplement and 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 Inc., either alone or together with our wholly-owned subsidiary, Zymeworks Biopharmaceuticals Inc. Furthermore, except as otherwise indicated, references to "Merck," "Lilly," "BMS," "GSK," "Daiichi Sankyo," "Janssen," "LEO," "BeiGene," "Iconic" and "Pfizer" refer to Merck Sharp & Dohme Research Ltd., Eli Lilly and Company, 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. and Pfizer Inc., respectively.

The names Azymetric, Zymeworks, ZymeCAD, EFECT, ZymeLink and the phrase "Building Better Biologics" are our registered trademarks. Other trademarks, product names and company names 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" within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and "forward-looking information" within the meaning of Canadian securities laws, or collectively, forward-looking statements. 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 anticipated use of proceeds of this offering and our existing cash, cash equivalents and short-term investments.

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 implement our restructuring announced in January 2022 and to manage the size of our organization 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 maintain good business relationships with our 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 acquisitions;
- 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 (including those referred to under "Risk Factors" in this prospectus supplement, the accompanying base shelf prospectus and in our Quarterly Report on Form 10-Q for the three months ended September 30, 2021), could affect future performance and cause actual results to differ materially from those matters expressed in or implied by forward-looking statements:

- our ability to obtain regulatory approval for our 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;
- the extent to which our business may be adversely affected by the COVID-19 pandemic;
- 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 (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;
- 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 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 and incidents 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 shareholders associated with future financings;
- restrictions on our ability to seek financing, which may be imposed by future debt;
- 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 provide supplies and store, monitor and transport bulk drug substance and drug product;
- 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 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 (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;
- 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 expected use of the net proceeds from this offering and our existing cash, cash equivalents and short-term investments;
- our estimated cash, cash equivalents and short-term investments as of December 31, 2021;
- 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.

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

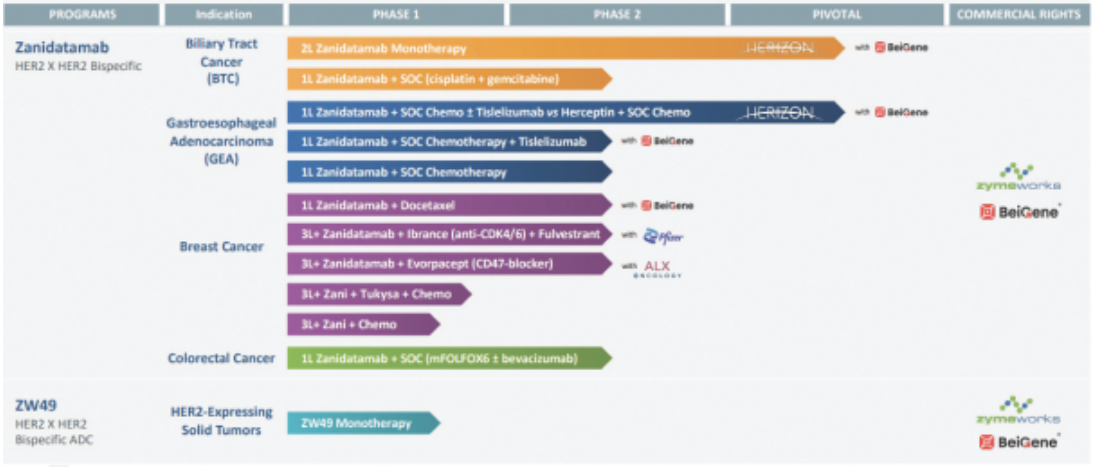
This summary highlights key aspects of this offering and certain information contained elsewhere in this prospectus supplement and the documents incorporated by reference. This summary is not complete and does not contain all of the information that may be important to you or that you should consider before investing in our common shares and pre-funded warrants. 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 shares and pre-funded warrants. You should pay special attention to the risks and uncertainties identified under the captions "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, 2021, when determining whether an investment in our common shares and pre-funded warrants is appropriate for you.

Company Overview

Zymeworks is a clinical-stage biopharmaceutical company dedicated to the development of next-generation multifunctional biotherapeutics. Our suite of complementary therapeutic platforms and our fully integrated drug development engine provide the flexibility and compatibility to precisely engineer and develop highly differentiated product candidates. These capabilities have resulted in multiple product candidates with the potential to drive positive outcomes in large underserved and unaddressed patient populations.

Our lead product candidate, zanidatamab, is a novel bispecific antibody that targets two distinct domains of the human epidermal growth factor receptor 2 ("HER2"). Zanidatamab's unique binding properties result in multiple mechanisms of action that may enable it to address unmet need in patient populations with HER2-expressing cancers. In clinical trials, zanidatamab monotherapy and zanidatamab in combination with chemotherapy have been well tolerated with promising antitumor activity in patients with treatment-naive and heavily pretreated HER2-expressing cancers, including individuals whose disease had progressed on multiple prior treatment regimens that included HER-targeted agents. Based on these data, a number of global multicenter clinical trials have been initiated to evaluate zanidatamab in specific indications and lines of therapy. These include pivotal clinical trials in (i) previously-treated HER2 gene amplified biliary tract cancer ("BTC") and (ii) first-line locally advanced or metastatic HER2-positive gastroesophageal adenocarcinomas ("GEA") in combination with chemotherapy with or without BeiGene's tislelizumab, as well as proof of concept trials in (iii) first-line locally advanced or metastatic HER2-positive colorectal cancer, GEA, or BTC in combination with standard of care chemotherapy, (iv) first-line locally advanced or metastatic HER2-positive GEA in combination with tislelizumab and chemotherapy, (v) first-line locally advanced or metastatic HER2-positive breast cancer in combination with docetaxel, (vi) previously-treated locally advanced or metastatic HER2-positive, hormone receptor-positive breast cancer in combination with Pfizer's Ibrance (palbociclib) and fulvestrant, (vii) previously-treated locally advanced or metastatic HER2-expressing cancers (including HER2-positive and HER2-low breast cancer) in combination with ALX Oncology Inc.'s ("ALX Oncology") evorpacept (ALX148), and (viii) previously-treated locally advanced or metastatic HER2-expressing breast cancer in combination with Seagen, Inc.'s ("Seagen") Tukysa (tucatinib) and chemotherapy.

Our second product candidate, ZW49, combines the unique design of zanidatamab with our ZymeLink antibody-drug conjugate ("ADC") platform, comprised of our proprietary cytotoxin (cancer cell-killing compound) and cleavable linker. We designed ZW49 to be a best-in-class HER2-targeting ADC to further address unmet need across a range of HER2-expressing cancers. A Phase 1 clinical trial to establish safety and antitumor activity of ZW49 is currently ongoing. The table below summarizes our current product candidate pipeline.



We are also advancing a deep pipeline of preclinical product candidates and discovery-stage programs in oncology (including immuno-oncology agents) and other therapeutic areas.

Our proprietary capabilities and technologies include several modular, complementary therapeutic platforms that can be used in combination with each other and with existing approaches. This ability to layer technologies without compromising manufacturability enables us to engineer next-generation biotherapeutics with synergistic activity, which we believe will result in improved patient outcomes. Our platforms include:

- *Azymetric*, our bispecific platform, which enables therapeutic antibodies to simultaneously bind multiple distinct locations on a target (known as an epitope) or to multiple targets. This is achieved by tailoring multiple configurations of the antibody's Fab regions (locations on the antibody to which epitopes bind);
- *ZymeLink*, our ADC platform, comprised of cytotoxins and the linker technology used to couple these cytotoxins to tumor-targeting antibodies or proteins. This platform can be used in conjunction with our other therapeutic platforms to increase safety and efficacy as compared to existing ADC technologies;
- *EFECT*, which enables finely tuned modulation (both up and down) of immune cell recruitment and function; and
- *ProTECT*, which enables tumor-specific activity that may reduce systemic toxicity, and simultaneously enhances localized immune co-stimulation or checkpoint modulation that may increase efficacy.

Our protein engineering expertise and proprietary structure-guided molecular modeling capabilities enable these therapeutic platforms. Together with our internal antibody discovery and generation technologies, we have established a fully integrated drug development engine and toolkit capable of rapidly delivering a steady pipeline of next-generation product candidates in oncology and other therapeutic areas.

Our Azymetric, EFECT and ZymeLink therapeutic platforms have been further leveraged through multiple revenue-generating strategic partnerships and collaborations with the following global pharmaceutical companies: Merck, Lilly, BMS, GSK, Daiichi Sankyo, Janssen, LEO, BeiGene, and Exelixis.

Our goal is to leverage our next-generation therapeutic platforms and proprietary protein engineering capabilities to become a leader in the discovery, development and commercialization of best-in-class multifunctional biotherapeutics for the treatment of cancer and other diseases with high unmet medical need.

Recent Developments

Zanidatamab Clinical Program

1L HER2-positive GEA Clinical Data from European Society for Medical Oncology ("ESMO") Annual Congress

In September 2021, we presented Phase 2 clinical data for zanidatamab in combination with chemotherapy in first-line locally advanced or metastatic HER2-positive GEA at the ESMO Annual Congress. The data presented are from a clinical study of 36 patients with HER2-expressing GEA who received zanidatamab in combination with either CAPOX (capecitabine/oxaliplatin; n=14), FP (5FU/cisplatin; n=2), or mFOLFOX6 (5FU/leucovorin/oxaliplatin; n=20). None of the patients had received prior HER2-targeted therapies.

In 28 response-evaluable patients with locally advanced or metastatic HER2-positive GEA, zanidatamab plus chemotherapy resulted in a confirmed objective response rate ("cORR") of 75% and disease control rate ("DCR") of 89% overall, with a cORR of 93% and a disease control rate ("DCR") of 100% in the announced Phase 3 regimen of zanidatamab + CAPOX/FP. All patients except one experienced a decrease in their tumor size. The median duration of response ("mDOR") is 16.4 months and the median progression-free survival ("mPFS") is 12.0 months across all treatment regimens with 61% of patients still on study at the time of data cutoff. In addition, the data demonstrated that zanidatamab plus chemotherapy is generally well tolerated, with the majority of treatment-related adverse events ("TRAE"s) considered mild to moderate in severity (Grade 1 or 2). The most common grade ³ 3 TRAE is diarrhea, which was manageable in the outpatient setting; introduction of prophylactic loperamide reduced the incidence in cycle 1 from 44% to 18%. No severe (grade ³ 3) infusion-related reactions or cardiac events were observed. The data presented compare favorably to current standard of care and support initiation of the global, randomized Phase 3 trial, HERIZON-GEA-01.

First Patient Dosed In Phase 1b/2 Clinical Trial Of Zanidatamab And Evorpacept (ALX148)

In October 2021, we announced the first patient dosed in the Phase 1b/2 clinical trial of zanidatamab in combination with ALX Oncology's CD47 blocker, evorpacept (ALX148), in patients with advanced HER2-expressing breast cancer and other solid tumors.

3L+ HER2-positive Breast Cancer Clinical Data from the San Antonio Breast Cancer Symposium ("SABCS")

In December 2021, we announced new clinical data for zanidatamab in heavily pretreated HER2-positive breast cancer. The data presented at SABCS are from a clinical study of 24 patients with heavily pretreated HER2-positive locally advanced or metastatic breast cancer who received zanidatamab in combination with either vinorelbine (n=12), capecitabine (n=8), or paclitaxel (n=4). Patients received multiple prior regimens containing HER2-targeted agents including trastuzumab (96%), pertuzumab (96%), and T-DM1 (96%), and many also received a tyrosine kinase inhibitor.

In 22 efficacy-evaluable patients, treatment with zanidatamab and chemotherapy resulted in a cORR of 36.4% and DCR of 86.4%, and the majority of patients experienced a decrease in their tumor size. The mPFS is 7.3 months across all treatment regimens with 42% of patients still on study at the time of data cutoff. Zanidatamab in combination with single agent chemotherapy is well tolerated, with the majority of TRAEs considered mild to moderate in severity (Grade 1 or 2).

HERIZON-GEA-01 Clinical Trial

In December 2021, we announced that our partner, BeiGene, had dosed the first patient in the HERIZON-GEA-01 trial, a global, randomized, Phase 3 clinical trial [NCT05152147] designed to evaluate the efficacy and safety of zanidatamab in combination with physician's choice chemotherapy (CAPOX or FP) with or without the PD-1 inhibitor, tislelizumab, compared to trastuzumab plus physician's choice chemotherapy for

first-line treatment in subjects with locally advanced or metastatic HER2-positive gastroesophageal adenocarcinomas. Primary endpoints are progression-free survival per RECIST 1.1 criteria, as assessed by blinded independent central review, and overall survival. The trial is expected to enroll approximately 700 patients at approximately 300 sites across 38 countries. BeiGene will oversee trial sites in Asia (excluding Japan), Australia and New Zealand, and we will oversee trial sites in the rest of the world, including North and South America, Japan, Europe, Middle East and Africa.

Strategic Priorities for 2022 and 2023

Effective January 15, 2022, Mr. Kenneth Galbraith became Chair of the Board of Directors, President, and Chief Executive Officer. On January 19, 2022, we issued a press release announcing our key strategic priorities for 2022 and 2023, including:

- Fully recruit the HERIZON-BTC-01 pivotal clinical study for zanidatamab by mid-2022;
- Fully recruit the HERIZON-GEA-01 pivotal clinical study for zanidatamab expected by the end of 2023;
- Complete or close out other ongoing early-stage clinical studies for zanidatamab as data become available, and use these data to identify and support strategic decisions regarding future clinical development opportunities beyond the ongoing pivotal clinical studies;
- Finalize a clear clinical development path for ZW49 based on additional clinical data expected in 2022 from the ongoing Phase 1 clinical trial;
- Select and advance two new antibody-drug conjugate or multispecific product candidates leveraging Zymeworks' novel, therapeutic platforms (Azymetric, ZymeLink, EFECT and ProTECT™) to IND-enabling studies to provide the ability to submit two Investigational New Drug, or IND, applications expected by the end of 2024;
- Execute on new partnerships and collaborations to support the development and commercialization of zanidatamab and our early-stage R&D pipeline and technology platforms;
- Continue to support and advance our core technology platforms and collaborations; and
- Improve our financial position over 2022 and 2023 through a combination of alternatives, including forming additional partnerships and collaborations, monetizing existing assets and products and securing additional financing.

As part of our renewed focus on achieving these key strategic priorities, on January 15, 2022, we authorized a restructuring of our workforce with a target of reducing our employee headcount by at least 25% across the organization by the end of 2022.

Preliminary Estimate of Cash, Cash Equivalents and Short-term Investments as of December 31, 2021

We estimate that we had approximately $250.0 million in cash, cash equivalents and short-term investments as of December 31, 2021.

The above information reflects our preliminary results based on currently available information. Our internal closing procedures with respect to the period presented above are not complete. As a result, our final results may vary from the preliminary results presented above. Our actual results for the year ended December 31, 2021 will not be finalized until after this offering is completed and may differ materially from the above estimates. Further, these preliminary estimates are not a comprehensive statement or estimate of our financial results or financial condition as of and for the year ended December 31, 2021. Accordingly, you should not place undue reliance upon these preliminary estimates and these preliminary estimates should not be viewed as a substitute for audited annual financial statements. See "Cautionary Note Regarding Forward-Looking Statements" and "Risk Factors."

Risk Factors Summary

Our business is subject to numerous risks and uncertainties, including those highlighted in the section of this prospectus supplement captioned “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 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 business has been and may continue to be adversely affected by the COVID-19 pandemic.
- 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.
- 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.
- 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.
- 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.

- 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.
- Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties.
- 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.
- We may become involved in lawsuits to protect or enforce our patents and trade secrets, which could be expensive, time consuming and unsuccessful.
- If we are unable to protect the confidentiality of our proprietary information, the value of our technology and products could be adversely affected.
- Our share price is likely to be volatile and the market price of our common shares after this offering may drop below the price you paid.
- We are governed by the corporate laws of Canada, which in some cases have a different effect on shareholders than the corporate laws of the United States.
- U.S. civil liabilities may not be enforceable against us, our directors, our officers or certain experts named in this prospectus supplement.
- Our principal shareholders, in aggregate, could exert substantial control over us which could delay or prevent a change in corporate control or result in the entrenchment of management or the board of directors.
- Provisions in our corporate charter documents and Canadian law could make an acquisition of us, which may be beneficial to our shareholders, more difficult and may prevent attempts by our shareholders to replace or remove our current management and/or limit the market price of our common shares.

Our Corporate Information

We were incorporated on September 8, 2003 under the *Canada Business Corporations Act*, under the name “Zymeworks Inc.” On October 22, 2003, we were registered as an extra-provincial company under the Company Act (British Columbia), the predecessor to the Business Corporations Act (British Columbia), or the BCBCA. Zymeworks continued to the BCBCA on May 2, 2017. Our current principal office is located at 1385 West 8th Avenue, Suite 540, Vancouver, British Columbia, Canada V6H 3V9, and our telephone number is (604) 678-1388. As of February 1, 2022, our principal office will be located at 114 East 4th Avenue, Suite 800, Vancouver, BC V5T 1G4. 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 shares and pre-funded warrants.

THE OFFERING

The following summary contains basic information about the offering and is not intended to be complete. It does not contain all the information that is important to you. You should carefully read the entire prospectus supplement, the accompanying base shelf prospectus and the documents incorporated by reference herein and therein before making an investment decision. Unless otherwise indicated, the information in this prospectus supplement assumes that the underwriters do not exercise their option to purchase additional common shares.

Common shares offered by us	9,160,000 common shares (11,035,000 common shares if the underwriters' option to purchase additional common shares is exercised in full).
Pre-funded warrants offered by us	We are also offering, in lieu of common shares to certain investors, pre-funded warrants to purchase 3,340,000 common shares. The purchase price of each pre-funded warrant equals the price per share at which the common shares are being sold to the public in this offering, minus $0.0001, which represents the exercise price of each pre-funded warrant. Each pre-funded warrant will be exercisable from the date of issuance until the date the warrant is exercised in full, subject to an ownership limitation. See "Description of Pre-Funded Warrants." This prospectus supplement also relates to the offering of the common shares issuable upon the exercise of such pre-funded warrants.
Common shares to be outstanding after this offering	55,713,660 common shares (or 57,588,660 common shares if the underwriters' exercise in full their option to purchase additional common shares in this offering).
Option to purchase additional shares	We have granted the underwriters an option to purchase up to an additional 1,875,000 common shares to be sold by the Company at the public offering price. The underwriters can exercise this option at any time within 30 days from the date of this prospectus supplement. See "Underwriting."
Use of proceeds	We estimate that the net proceeds to us from this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately $93.5 million, or approximately $107.6 million if the underwriters exercise their option to purchase 1,875,000 additional common shares from us in full. We intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, (i) to execute on our global development plan for zanidatamab both as a single agent and in combination with other anti-cancer agents in a variety of HER2-expressing tumors, including gastroesophageal, biliary tract, and other underserved cancers; (ii) to complete our ongoing adaptive Phase 1 clinical trials of ZW49; (iii) to advance other novel preclinical programs utilizing our next-generation ADC and multispecific platforms; and (iv) for general corporate purposes. See "Use of Proceeds."

Risk factors	An investment in our common shares and pre-funded warrants involves a high degree of risk. See “Risk Factors” beginning on page S-9 of this prospectus supplement and the similarly titled sections in the documents incorporated by reference in this prospectus supplement.
New York Stock Exchange symbol	Our common shares are listed on the NYSE under the symbol “ZYME.” There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on the NYSE or any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited. See “Description of Pre-Funded Warrants.”

The number of our common shares to be outstanding immediately after this offering is based on 46,553,660 common shares outstanding as of September 30, 2021, does not include the common shares issuable upon the exercise of the pre-funded warrants being offered by us in this offering, and excludes as of that date:

- 1,690,271 common shares issuable upon the exercise of fully-vested outstanding options to issue common shares, as of September 30, 2021, at a weighted average exercise price of C$18.82 per common share;
- 2,156,032 common shares issuable upon the exercise of fully-vested outstanding options to issue common shares, as of September 30, 2021, at a weighted average exercise price of $19.36 per common share;
- 837,310 common shares issuable upon the exercise of unvested outstanding options to issue common shares, as of September 30, 2021, at a weighted average exercise price of C$40.80 per common share;
- 2,786,005 common shares issuable upon the exercise of unvested outstanding options to issue common shares, as of September 30, 2021, at a weighted average exercise price of $32.68 per common share;
- 170,921 common shares issuable upon vesting and settlement of outstanding restricted stock units as of September 30, 2021;
- 1,152,206 common shares reserved for future issuance under our stock option plan and 1,482,477 common shares reserved for future issuance under our employee stock purchase plan, in each case, as of September 30, 2021;
- 500,000 common shares issuable upon the exercise of unvested outstanding options to issue common shares, as of January 15, 2022, at a weighted average exercise price of $14.97 per common share;
- 250,000 common shares reserved for future issuance under our Inducement Stock Option and Equity Compensation Plan, as of January 15, 2022;
- 5,241,961 pre-funded warrants to purchase up to 5,241,961 of our common shares outstanding as of September 30, 2021;
- 423,950 common shares underlying option and RSU awards granted subsequent to September 30, 2021 (but excluding any exercises, cancellations or settlements of such awards); and
- up to $150.0 million of our common shares that may be sold from time to time pursuant to the prospectus supplement we filed on October 1, 2021 relating to our “at the market” equity offering program (“ATM Program”) that we entered into on November 5, 2019, as amended, with Jefferies LLC, of which no shares have been sold as of the date of this prospectus supplement.

Except as otherwise indicated herein, all information in this prospectus supplement, including the number of common shares that will be outstanding after the offering, assumes no exercise of pre-funded warrants offered in this offering and no exercise by the underwriters of their option to purchase additional common shares in this offering and assumes no exercise or settlement of the outstanding stock options, restricted stock units and warrants described above.

RISK FACTORS

Investing in our common shares and pre-funded warrants 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 statements relating to us, or our business, property or financial results, each of which could cause purchasers of our common shares and pre-funded warrants 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 set out under "Risk Factors" in the accompanying base shelf prospectus and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 and the factors set out below in evaluating Zymeworks and its business before making an investment in our common shares and pre-funded warrants. 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.

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 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 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 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 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.

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. Success in preclinical studies or early-stage clinical trials does not mean that future clinical trials or registration 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 registration 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.

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, 2, and registration-enabling clinical trials and ZW49 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 candidate 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;
- 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 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 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 practices (cGMPs) 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 CMOs. 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.

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 topline 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 topline 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 topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary or topline data previously published. As a result, interim, preliminary and topline data should be viewed with caution until the final data are available. Adverse differences between interim, preliminary or topline data and final data could significantly harm our reputation and business prospects. Moreover, preliminary, interim and topline 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.

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. As a result of COVID-19, in March 2020, we transitioned our workforce to a remote working arrangement to protect the health and safety of our employees. In June 2020, we implemented a program to facilitate the phased return of employees to our lab and office facilities pursuant to enhanced health and safety protocols consistent with guidelines issued by local health authorities. Our preclinical research activities were supplemented by support from external CROs to complement the temporarily reduced capacity at our lab facilities. Certain clinical trial activities, including patient enrollment and site activations, were delayed or otherwise impacted by COVID-19.

The extent to which COVID-19 may cause more significant disruptions to our business and greater impacts to our operations 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. A lack of coordinated response on risk mitigation and global vaccination deployment with respect to the COVID-19 pandemic could result in significant increases to the duration and severity of the pandemic and could have a corresponding negative impact on our business. 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.

If the COVID-19 pandemic worsens or continues 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 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 could result in the continued significant disruption of global financial markets, reducing our ability to access capital, which could negatively affect our liquidity. COVID-19 has resulted in heightened financial market volatility that may continue, which could adversely impact the value of our common shares.

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 refractory 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 in patients with previously-treated HER2 gene-amplified BTC. While we anticipate submitting a Biologics License Application ("BLA") to the FDA in 2023 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.

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, 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 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. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. 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. Additional policies or changes to current policies may be implemented in the future. 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 ZW49 continue to be evaluated in clinical trials, and the results of these and future clinical trials may show that zanidatamab, ZW49 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 next-generation antibody therapeutic platforms to address specific cancer targets. These companies include MacroGenics, Inc., AstraZeneca PLC/Daiichi Sankyo, Roche AG, Seagen and others.

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 (the “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 GEA, the European Medicines Agency ("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 we obtain orphan drug exclusivity for zanidatamab, or 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.

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 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;
- 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. In addition, the COVID-19 pandemic is still evolving, and it is impossible to predict the impact this pandemic may have on the development of our product candidates, our preclinical studies and clinical trials, and our business. 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 (“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. Congress is currently considering legislation that, if passed, could have significant impact on prices of prescription drugs covered by Medicare, including limitations on drug price increases and allowing Medicare to negotiate drug pricing for certain drugs. 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 share 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 current good manufacturing practices ("cGMP") and current good clinical practice ("cGCP"), 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 shareholders 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.

Foreign governments tend to impose strict price controls, which may adversely affect our future profitability.

In most foreign countries, particularly in those in the European Union (“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 foreign 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 (“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 (“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, as a result of the COVID-19 pandemic, we may face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working 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.

In addition, 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 ("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 ("CPRA"), effective January 1, 2023, will expand 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 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 ("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 ("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 ("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 ("CJEU") invalidated the European Union-U.S. Privacy Shield ("Privacy Shield") as a data transfer mechanism for transferring personal information from the EEA to the United States. While the standard contractual clauses ("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. 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 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 this Supreme Court decision, 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 to the statute, 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 3% 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 several recent 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, in 2020, the U.S. Department of Health and Human Services (“HHS”) and CMS issued various rules pertaining to price reductions from pharmaceutical manufacturers to plan sponsors under Part D, changes to the Stark Law and the safe harbor regulation under the Anti-Kickback Statute, and manufacturer price reporting requirements under the Medicaid Drug Rebate Program, among others. Multiple lawsuits have been brought against the HHS challenging various aspects of the rules implemented during the Trump administration. As a result, the Biden administration and HHS have delayed the implementation or published rules rescinding some of these Trump-era policies.

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. No legislation or administrative actions have been finalized to implement these principles. Further, Congress is considering legislation that, if passed, could have significant impact on prices of prescription drugs covered by Medicare, including limitations on drug price increases and allowing Medicare to negotiate pricing for certain drugs. 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. 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 recently 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.

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. 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;
- 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 United Kingdom'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 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 AKS 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 AKS, 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.

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 loss for the years ended December 31, 2019 and 2020 and for the nine months ended September 30, 2021 was $145.4 million, $180.6 million and $172.7 million, respectively. As of September 30, 2021, our accumulated deficit was approximately $644.0 million. We expect to continue to incur losses for the foreseeable future, and we expect these losses to increase 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. 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 shareholders' 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 shareholders 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. We will continue to require additional funding to complete the development and commercialization of our product candidates 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. 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. We anticipate that the reduction in workforce will impact at least 25% of our employees; however, we are still assessing the full scope and scale of this plan and the reductions may ultimately be more or less than we currently anticipate.

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 successfully implement the reduction in workforce and achieve the anticipated cost reductions;
- 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, 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, strategic partnerships and grant funding.

Raising additional capital may cause dilution to our shareholders, 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 shareholders' ownership interest will be diluted, and the terms of these new securities may include liquidation or

other preferences that adversely affect our shareholders' rights as common shareholders. 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 you 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

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 Merck, Lilly, BMS, GSK, Daiichi Sankyo, Janssen, LEO, BeiGene and Iconic. 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 Merck, Lilly, BMS, GSK, Daiichi Sankyo, Janssen, LEO, BeiGene and Iconic 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 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, contamination and 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, due in part to the impact of the ongoing 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. 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 cGCP 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 cGCP 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 cGCP 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 cGCP 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 (“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 shares.

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 ("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.

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 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 in recent years 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 Washington State and the Province of British Columbia 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 reduction in workforce initiated in January 2022 and the announcement of our key strategic priorities for 2022 and 2023.

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. The target of the reduction in workforce is to reduce employee headcount by at least 25% by the end of 2022. The full scope, scale and impact of the reduction in workforce is not yet known. In January 2022, we also announced our key strategic priorities for 2022 and 2023. For additional information, see the section titled "Prospectus Supplement Summary—Recent Developments—Strategic Priorities for 2022 and 2023."

We may fail to effectively execute on, or achieve the stated goals of, the reduction in workforce or our key strategic priorities. 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, the reduction in workforce may negatively impact employee morale for those that are not directly impacted, which may increase employee attrition and hinder our ability to achieve our key priorities. Furthermore, certain of our shareholders may not agree with our key strategic priorities or the decisions we have or may make to execute on those 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, as well as lead to shareholder complaints and litigation.

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, our President and Chief Executive Officer, Neil Klompas, our Chief Operating Officer and Chief Financial Officer, Neil

Josephson, our Chief Medical 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 may limit our ability to retain and motivate these 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 September 30, 2021, we had 455 full-time employees. As a result of the reduction in workforce announced in January 2022, we expect to reduce our workforce by at least 25% by the end of 2022. However, 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 Shares, the Pre-Funded Warrants and the Offering.

Our share price is likely to be volatile and the market price of our common shares after this offering may drop below the price you paid.

Investors should consider an investment in our common shares or pre-funded warrants as risky and invest only if you can withstand a significant loss and wide fluctuations in the market value of their investment. You may be unable to sell your common shares (including those obtained by exercise of our pre-funded warrants) at or above the price you paid for such shares due to fluctuations in the market price of our common shares arising from changes in our operating performance or prospects. Some of the factors that may cause the market price of our common shares 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;
- 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;
- 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 shares;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- public concern over our product candidates or any future approved products;
- litigation;
- future sales of our common shares;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our common shares;
- additions or departures of key personnel, including developments relating to our reduction in workforce announced in January 2022;
- our ability to execute on our key strategic priorities announced in January 2022;
- 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, such as the COVID-19 pandemic;
- 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 shareholders;
- 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 ongoing 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 ongoing COVID-19 pandemic, may negatively affect the market price of our common shares, 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 shares.

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

An active trading market for our common shares may not be sustained. If an active market for our common shares does not continue, it may be difficult for our shareholders to sell their shares without depressing the market price for the common shares or sell their common shares at or above the prices at which they acquired their common shares or sell their common shares at the time they would like to sell. Any inactive trading market for our common shares may also impair our ability to raise capital to continue to fund our operations by selling common shares and may impair our ability to acquire other companies or technologies by using our common shares as consideration.

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

A large volume of sales of our common shares could decrease the prevailing market price of our common shares 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 shares does not occur, the mere perception of the possibility of these sales could depress the market price of our common shares and have a negative effect on our ability to raise capital in the future.

The pre-funded warrants are not listed on any exchange and the Company does not intend to list the pre-funded warrants on any exchange.

You may be unable to sell the pre-funded warrants at the prices desired or at all. There is no existing trading market for the pre-funded warrants and there can be no assurance that a liquid market will develop or be maintained for the pre-funded warrants, or that you will be able to sell any of the pre-funded warrants at a particular time (if at all). In addition, we do not intend to apply for listing of the pre-funded warrants on the NYSE or any other securities exchange or nationally recognized trading system. The liquidity of the trading market in the pre-funded warrants and the sale price, if any, for the pre-funded warrants, may be adversely affected by, among other things: (i) changes in the overall market for the pre-funded warrants; (ii) changes in our financial performance or prospects; (iii) changes or perceived changes in our creditworthiness; (iv) the prospects for companies in the industry generally; (v) the number of holders of the pre-funded warrants; and (vi) the interest of securities dealers in making a market for the pre-funded warrants.

Holders of pre-funded warrants will have no rights as a shareholder until such holders exercise their pre-funded warrants and acquire common shares.

Until holders of pre-funded warrants acquire common shares upon exercise of such pre-funded warrants, holders of the pre-funded warrants will have no rights with respect to the common shares underlying such pre-funded warrants. Upon exercise of the pre-funded warrants, the holders thereof will be entitled to exercise the rights of a shareholder only as to matters for which the record date occurs after the exercise date.

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

We have never paid any dividends on our common shares. 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 shares in the foreseeable future. See “Description of Share Capital—Dividend Policy” in the accompanying base shelf prospectus. As a result, capital appreciation, if any, of our common shares will be the sole source of gain on investment in our common shares for the foreseeable future. Investors seeking cash dividends should not invest in our common shares.

Our management team will have broad discretion to use the net proceeds from this offering and its investment of these proceeds may not yield a favorable return. They may invest the proceeds of this offering in ways with which investors disagree.

Our management team will have broad discretion in the application of the net proceeds from this offering and could spend or invest the proceeds in ways with which our shareholders disagree. Accordingly, investors will need to rely on our management team’s judgment with respect to the use of these proceeds. We intend to use the proceeds from this offering in the manner described under “Use of 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 this offering. In addition, the amount, allocation and timing of our actual expenditures will depend upon numerous factors, including 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.

Investors in this offering will pay a much higher price than the book value of our common shares and pre-funded warrants and therefore you will incur immediate and substantial dilution of your investment.

The public offering price per common share and pre-funded warrant will be substantially higher than the net tangible book value per common share. Therefore, if you purchase common shares or pre-funded warrants in this offering, you will experience immediate and substantial dilution, representing the difference between our pro forma as adjusted net tangible book value per share after giving effect to this offering. As of September 30, 2021, we have issued 7,469,618 outstanding stock options, certain of which have exercise prices below the public offering price, as well as 170,921 outstanding restricted stock units, which vest over time. To the extent these outstanding options are exercised or these outstanding restricted stock units vest, you will experience further dilution. See “Dilution.”

We are governed by the corporate laws of Canada, which in some cases have a different effect on shareholders than the corporate laws of the United States.

We are governed by the BCBCA and other relevant Canadian laws, which may affect the rights of shareholders differently than those of a company governed by the laws of a U.S. jurisdiction, and may, together with our charter documents, have the effect of delaying, deferring or discouraging another party from acquiring control of our company by means of a tender offer, a proxy contest or otherwise, or may affect the price an acquiring party would be willing to offer in such an instance. The material differences between the BCBCA and Delaware General Corporation Law (“DGCL”) that may have the greatest such effect include, but are not limited to, the following: (i) for certain corporate transactions (such as mergers and amalgamations or amendments to our articles) the BCBCA generally requires the voting threshold to be a special resolution approved by 66 2/3% of shareholders, or as set out in the articles, as applicable, whereas DGCL generally only requires a majority vote; and (ii) under the BCBCA a holder of 5% or more of our common shares can requisition a special meeting of shareholders, whereas such right does not exist under the DGCL. Investors may find our company and our common shares less attractive because we are governed by foreign laws.

U.S. civil liabilities may not be enforceable against us, our directors, our officers or certain experts named in this prospectus supplement.

We are governed by the BCBCA and our principal place of business is in Canada. Certain of our directors and officers, as well as certain experts named in this prospectus supplement, reside outside of the United States, and all or a substantial portion of their assets as well as all or a substantial portion of our assets are located outside the United States. As a result, it may be difficult for investors to effect service of process within the United States upon us and such directors, officers and experts or to enforce judgments obtained against us or such persons, in U.S. courts, in any action, including actions predicated upon the civil liability provisions of U.S. federal securities laws or any other laws of the United States. Additionally, rights predicated solely upon civil liability provisions of U.S. federal securities laws or any other laws of the United States may not be enforceable in original actions, or actions to enforce judgments obtained in U.S. courts, brought in Canadian courts, including courts in the Province of British Columbia. Furthermore, provisions in our articles provide that, unless we consent in writing to the selection of an alternative forum, the Supreme Court of British Columbia and the appellate courts therefrom, to the fullest extent permitted by law, will be the sole and exclusive forum for certain actions or proceedings brought against us, our directors and/or our officers. These provisions may limit our shareholders’ ability to bring a claim against us in a judicial forum that our shareholders consider favorable or convenient for such disputes and may discourage lawsuits with respect to such claims. See “Description of Share Capital.”

U.S. holders of our common shares or pre-funded warrants may suffer adverse U.S. federal income tax consequences if we are characterized as a passive foreign investment company.

Generally, we will be a “passive foreign investment company” (“PFIC”) for U.S. federal income tax purposes for any taxable year if either (i) at least 75% of our gross income is passive income or (ii) at least 50% of the average quarterly value of our assets is attributable to assets that produce passive income or are held for the production of passive income. For purposes of these tests, passive income generally includes dividends, interest, gains from the sale of investment property, and certain rents and royalties. If we are a PFIC for any taxable year during which a U.S. Holder (as defined under “Certain U.S. Federal Income Tax Considerations”) holds our common shares or pre-funded warrants, such U.S. Holder may suffer adverse U.S. federal income tax consequences. Additionally, if we are a PFIC

for any taxable year during which a U.S. Holder holds our common shares or pre-funded warrants, we will generally continue to be treated as a PFIC with respect to such U.S. Holder for all succeeding taxable years during which such U.S. Holder holds our common shares or pre-funded warrants (unless certain elections are made), even if we cease to satisfy the PFIC tests described above.

Based on a preliminary analysis, we do not believe that we will be classified as a PFIC for the taxable year ended December 31, 2021; however, we cannot be certain that our preliminary analysis is correct. Furthermore, even if we are not a PFIC for the taxable year ended December 31, 2021, whether we are a PFIC for the current taxable year or any future taxable year is a fact-intensive determination made on an annual basis and based on the application of complex U.S. federal income tax rules that are subject to differing interpretations. See "Certain U.S. Federal Income Tax Considerations – Passive Foreign Investment Company Consequences" for more information. U.S. Holders should consult their own tax advisors regarding the tax consequences if we are a PFIC for any taxable year.

Our principal shareholders, in aggregate, could exert substantial control 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 shareholders, being our shareholders that beneficially own (or upon exercise of convertible securities would own) 10% or more of our common shares, together with their affiliates and related persons, in aggregate, own or could acquire (contingent upon the exercise of convertible securities they own) approximately 13.5% of our outstanding common shares as of September 30, 2021 (3.7% excluding the exercise of convertible securities). Our directors and named executive officers beneficially own, in the aggregate, approximately 5.0% of our outstanding common shares as of September 30, 2021. Our principal shareholders, if acting together (with or without our directors and named executive officers), may have the ability to exert substantial control over the outcome of matters submitted to our shareholders 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 shareholders, if acting together (with or without our directors and named executive officers), may have the ability to exert substantial control over the management and affairs of our company. Accordingly, this concentration of ownership could harm the market price of our common shares 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.

Provisions in our corporate charter documents and Canadian law could make an acquisition of us, which may be beneficial to our shareholders, more difficult and may prevent attempts by our shareholders to replace or remove our current management and/or limit the market price of our common shares.

Provisions in our notice of articles and articles, as well as certain provisions under the BCBCA, and applicable Canadian securities laws, may discourage, delay or prevent a merger, acquisition or other change in control of us that shareholders may consider favorable, including transactions in which they might otherwise receive a premium for their common shares. These provisions include the establishment of a staggered board of directors, which divides the board into three groups, with directors in each group serving a three-year term. The existence of a staggered board can make it more difficult for shareholders to replace or remove incumbent members of our board of directors. As such, these provisions could also limit the price that investors might be willing to pay in the future for our common shares, thereby depressing the market price of our common shares. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our shareholders to replace or remove our current management by making it more difficult for shareholders to replace members of our board of directors. Among other things, these provisions include the following:

- shareholders cannot amend our articles unless such amendment is approved by shareholders holding at least a majority of the shares entitled to vote on such approval;
- our board of directors may, without shareholder approval, issue preferred shares having any terms, conditions, rights, preferences and privileges as the board of directors may determine; and

- shareholders must give advance notice to nominate directors or to submit proposals for consideration at shareholders' meetings.

General Risk Factors

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, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common shares.

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 or significant deficiencies 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. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common shares. Furthermore, if we cannot provide reliable financial reports or prevent fraud, including as a result of remote working by our employees in connection with COVID-19 and related public health safety measures, our business and results of operations would likely be materially and adversely affected.

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 share price and trading volume could decline.

The trading market for our common shares 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 shares negatively, our share 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 share price or trading volume to decline. Moreover, the research and reports that analysts publish may suggest a price for our common shares 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

We estimate that the net proceeds to us from the sale of our common shares and pre-funded warrants in this offering will be approximately $93.5 million, or approximately $107.6 million if the underwriters exercise in full their option to purchase additional common shares, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We will receive nominal proceeds, if any, from the exercise of the pre-funded warrants.

We intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, (i) to execute on our global development plan for zanidatamab both as a single agent and in combination with other anti-cancer agents in a variety of HER2-expressing tumors, including gastroesophageal, biliary tract, and other underserved cancers; (ii) to complete our ongoing adaptive Phase 1 clinical trials of ZW49; (iii) to advance other novel preclinical programs utilizing our next-generation ADC and multispecific platforms; and (iv) for general corporate purposes.

Pending these expected uses, we plan to invest these net proceeds in guaranteed investment certificates, term deposits and commercial paper acquired from financial institutions in accordance with the Company's cash investment policy. The goal with respect to the investment of these net proceeds is to preserve principal while also maintaining liquidity and maximizing investment returns without significantly increasing risk.

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 collaborations and the anticipated net proceeds from this offering, to fund our planned operations into the second half of 2023 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 (i) to execute on our global development plan for zanidatamab both as a single agent and in combination with other anti-cancer agents in a variety of HER2-expressing tumors, including gastroesophageal, biliary tract, and other underserved cancers; (ii) to complete our ongoing adaptive Phase 1 clinical trials of ZW49; and (iii) to advance other novel preclinical programs utilizing our next-generation ADC and multispecific platforms. These objectives will require additional capital exceeding our cash on hand resources even after giving effect to the offering and the exercise, if any, of the option to purchase additional common shares. 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.

If the underwriters’ option to purchase additional common shares is exercised in whole or in part, we will use the additional net proceeds from such exercise to support our key business objectives and 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 listed under the heading “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 our common shares or pre-funded warrants, your interest will be diluted to the extent of the difference between the public offering price per common share or pre-funded warrant you pay in this offering and the net tangible book value per common share immediately after you purchase securities in this offering.

As of September 30, 2021, our net tangible book value was approximately $245.6 million, or approximately $5.28 per common share, based on 46,553,660 common shares outstanding as of September 30, 2021. Our net tangible book value per common share represents the amount of our total tangible assets reduced by the amount of our total liabilities, divided by the total number of our common shares outstanding as of September 30, 2021.

After giving effect to the sale of approximately 9,160,000 common shares and pre-funded warrants to purchase up to 3,340,000 of our common shares in this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2021 would have been approximately $339.1 million, or $6.09 per common share. This represents an immediate increase in net tangible book value of $0.81 per share to our existing shareholders and an immediate dilution in net tangible book value of $1.91 per common share to new investors participating in this offering.

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

Public offering price per common share		$8.00
Net tangible book value per common share at September 30, 2021	$5.28	
Increase in net tangible book value per common share attributable to investors participating in this offering	$0.81	
As adjusted net tangible book value per common share after giving effect to this offering		$6.09
Dilution in net tangible book value per common share to new investors in this offering		$1.91

If holders of pre-funded warrants exercise the pre-funded warrants issued in this offering, but excluding any resulting accounting impact associated therewith, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, the as adjusted net tangible book value per common share would be $5.74 per common share, and the dilution in net tangible book value per common share to investors purchasing common shares in this offering would be $2.26 per common share.

If the underwriters fully exercise their option to purchase 1,875,000 additional common shares in full, the as adjusted net tangible book value per common share after giving effect to this offering would increase to $6.13 per common share, representing an immediate increase in net tangible book value (excluding common shares issuable upon the exercise of the pre-funded warrants and after deducting underwriting discounts and commissions and estimated offering expenses payable by us) of $0.85 per common share, and the dilution in net tangible book value per common share to investors purchasing common shares in this offering would be $1.87 per common share.

The discussion and tables (other than the net tangible book value calculation) above are based on 46,553,660 common shares outstanding as of September 30, 2021, does not include the common shares issuable upon the exercise of the pre-funded warrants being offered by us in this offering (except where otherwise noted), and excludes as of that date:

- 1,690,271 common shares issuable upon the exercise of fully-vested outstanding options to issue common shares, as of September 30, 2021, at a weighted average exercise price of C$18.82 per common share;
- 2,156,032 common shares issuable upon the exercise of fully-vested outstanding options to issue common shares, as of September 30, 2021, at a weighted average exercise price of $19.36 per common share;
- 837,310 common shares issuable upon the exercise of unvested outstanding options to issue common shares, as of September 30, 2021, at a weighted average exercise price of C$40.80 per common share;

- 2,786,005 common shares issuable upon the exercise of unvested outstanding options to issue common shares, as of September 30, 2021, at a weighted average exercise price of $32.68 per common share;
- 170,921 common shares issuable upon vesting and settlement of outstanding restricted stock units as of September 30, 2021;
- 1,152,206 common shares reserved for future issuance under our stock option plan and 1,482,477 common shares reserved for future issuance under our employee stock purchase plan, in each case, as of September 30, 2021;
- 500,000 common shares issuable upon the exercise of unvested outstanding options to issue common shares, as of January 21, 2022, at a weighted average exercise price of $14.97 per common share;
- 250,000 common shares reserved for future issuance under our Inducement Stock Option and Equity Compensation Plan, as of January 21, 2022;
- 5,241,961 pre-funded warrants to purchase up to 5,241,961 of our common shares outstanding as of September 30, 2021;
- 423,950 common shares underlying option and RSU awards granted subsequent to September 30, 2021 (but excluding any exercises, cancellations or settlements of such awards); and
- up to $150.0 million of our common shares that may be sold from time to time pursuant to the prospectus supplement we filed on October 1, 2021 relating to our “at the market” equity offering program (“ATM Program”) that we entered into on November 5, 2019, as amended, with Jefferies LLC, of which no shares have been sold as of the date of this prospectus supplement.

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

DIVIDEND POLICY

The Company has neither declared nor paid dividends on its common shares. The Company has no present intention of paying dividends on its common shares as it anticipates that all available funds will be invested to finance the growth of its business.

DESCRIPTION OF PRE-FUNDED WARRANTS

Pre-Funded Warrants

The following is a brief summary of certain terms and conditions of the pre-funded warrants being offered by this prospectus supplement. The following description is subject in all respects to the provisions contained in the pre-funded warrants.

Form

The pre-funded warrants will be issued as individual warrant agreements to certain investors. You should review the form of pre-funded warrant, which is filed as an exhibit to our Current Report on Form 8-K that we will file with the SEC on or about January 27, 2022 for a complete description of the terms and conditions applicable to the pre-funded warrants.

Exercisability

The pre-funded warrants are exercisable at any time after their original issuance. The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and by payment in full in immediately available funds for the number of common shares purchased upon such exercise. As an alternative to payment in immediately available funds, the holder may, in its sole discretion, elect to exercise the warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of common shares determined according to the formula set forth in the pre-funded warrant. No fractional common shares will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the fair market value of any fractional shares.

Exercise Limitations

Under the terms of the pre-funded warrants, we may not effect the exercise of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant, which, upon giving effect to such exercise, would cause (i) the aggregate number of our common shares beneficially owned by the holder (together with its affiliates) to exceed 9.99% of the number of our common shares outstanding immediately after giving effect to the exercise, or (ii) the combined voting power of our securities beneficially owned by the holder (together with its affiliates) to exceed 9.99% of the combined voting power of all of our securities then outstanding immediately after giving effect to the exercise, as such percentage to any ownership is determined in accordance with the terms of the pre-funded warrants. However, any holder may increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us.

Exercise Price

The exercise price per whole common share purchasable upon the exercise of the pre-funded warrants is $0.0001 per warrant share. The exercise price of the pre-funded warrants is subject to appropriate adjustment in the event of certain share dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common shares.

Transferability

Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent.

Exchange Listing

We do not intend to list the pre-funded warrants on the NYSE or any other national securities exchange or nationally recognized trading system.

Fundamental Transactions

In the event of a fundamental transaction, as described in the pre-funded warrants and generally including any reorganization, recapitalization or reclassification of our common shares, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common shares or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common shares, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash

or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction without regard to any limitations on exercised contained in the pre-funded warrants.

No Rights as a Shareholder

Except by virtue of such holder's ownership of our common shares, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our common shares, including any voting rights, until the holder exercises the pre-funded warrant.

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated January 26, 2022, among us and Jefferies LLC and Evercore Group L.L.C. as the representatives of the underwriters named below, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of common shares and pre-funded warrants, shown opposite its name below:

UNDERWRITER	NUMBER OF SHARES	NUMBER OF PRE-FUNDED WARRANTS
Jefferies LLC	3,572,400	1,302,600
Evercore Group L.L.C.	2,656,400	968,600
Stifel, Nicolaus & Company, Incorporated	1,648,800	601,200
Wells Fargo Securities, LLC	687,000	250,500
Raymond James (USA) Ltd.	595,400	217,100
Total	9,160,000	3,340,000

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the common shares and pre-funded warrants if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common shares as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common shares, that you will be able to sell any of the common shares held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the common shares and pre-funded warrants subject to their acceptance of the common shares and pre-funded warrants from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commission and Expenses

The underwriters have advised us that they propose to offer the common shares and pre-funded warrants to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers, which may include the underwriters, at that price less a concession not in excess of $0.288 per common share or pre-funded warrant. After the offering, the public offering price, concession and reallowance to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	PER SHARE			TOTAL	
	WITHOUT OPTION TO PURCHASE ADDITIONAL COMMON SHARES	WITH OPTION TO PURCHASE ADDITIONAL COMMON SHARES	PER PRE-FUNDED WARRANT	WITHOUT OPTION TO PURCHASE ADDITIONAL COMMON SHARES	WITH OPTION TO PURCHASE ADDITIONAL COMMON SHARES
Public offering price	$ 8.00	$ 8.00	$ 7.9999	$99,999,666	$114,999,666
Underwriting discounts and commissions, paid by us	$ 0.48	$ 0.48	$ 0.48	$ 6,000,000	$ 6,900,000
Proceeds to us, before expenses	$ 7.52	$ 7.52	$ 7.5199	$93,999,666	$108,099,666

We estimate expenses payable by us, in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $0.5 million. We have also agreed to reimburse the underwriters for up to $10,000 for their Financial Industry Regulatory Authority, Inc. ("FINRA") counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

Listing

Our common shares are listed on NYSE under the symbol "ZYME." We have applied to list the common shares offered by us pursuant to the offering (including the warrant shares) on the NYSE.

Listing on the NYSE is subject to us fulfilling all the listing requirements of the NYSE. We do not intend to list the pre-funded warrants on the NYSE or any other national securities exchange or any other nationally recognized trading system.

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase, from time to time, in whole or in part, up to an aggregate of 1,875,000 shares from us at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above. This option may be exercised only if the underwriters sell more shares than the total number set forth on the cover page of this prospectus supplement.

No Sales of Similar Securities

We have agreed, subject to specified exceptions, for a period of 60 days after the date of this prospectus supplement without the prior written consent of Jefferies LLC and Evercore Group L.L.C., not to directly or indirectly:

i. offer, sell, contract to sell, pledge, hedge, lend or otherwise dispose of, (or enter into any transaction which is designed to, or might reasonably be expected to, result in the disposition by us or any of our affiliates or any person in privity with us or our affiliate) directly or indirectly, including the submission or filing (or participation in the submission or filing) of a registration statement with the SEC in respect of, or establish or increase a put equivalent position or liquidate or decrease a call equivalent position within the meaning of the Exchange Act, any common shares or any securities convertible into, or exercisable, or exchangeable for, common shares; or publicly announce an intention to effect any such transaction; or

ii. enter into any swap, hedging or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of common shares or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of common shares or such other securities, in cash or otherwise).

The restrictions described in the immediately preceding paragraph do not apply to us with respect to:

1. issue and sell common shares pursuant to the underwriting agreement and issue the warrant shares upon exercise of the warrants,
2. issue and sell common shares pursuant to any employee stock option plan, stock ownership plan or dividend reinvestment plan of ours in effect at the execution of the underwriting agreement,
3. issue common shares issuable upon the conversion of securities or the exercise of warrants outstanding at the execution of the underwriting agreement,
4. file or amend one or more registration statements on Form S-8 relating to common shares granted pursuant to or reserved for issuance under any employee stock option plan, stock ownership plan or dividend reinvestment plan of ours in effect at the execution of the underwriting agreement and described in the Registration Statement, the Disclosure Package and the U.S. Final Prospectus,
5. enter into an agreement providing for the sale or issuance by us of, and sell and issue, common shares or any securities exercisable or exchangeable for, or convertible into, a number of common shares, in the aggregate amount of not more than 10% of our common shares issued and outstanding immediately following the closing date on a fully-diluted basis, pursuant to one or more strategic partnerships or collaborations, licensing transactions or business, product or technology acquisitions (in any event excluding transactions principally of a financing nature) without the prior written consent of Jefferies LLC and Evercore Group L.L.C.; provided, however, that any such issuance under clause (5) above shall be conditioned upon the execution of a lock-up agreement by any recipient thereof, and
6. offer and sell common shares under our at-the-market offering program pursuant to the Open Market Sale Agreement (the “Sale Agreement”), dated November 5, 2019, as amended, by and between the Company and Jefferies LLC, provided that no sales shall be made under the Sale Agreement until the earlier of (i) the exercise in full by the Underwriters of their option to purchase the Option Securities and (ii) 30 days after the date of this prospectus supplement.

Our executive officers and directors have agreed, subject to specified exceptions, for a period of 60 days after the date of this prospectus supplement (the “restricted period”) without the prior written consent of Jefferies LLC and Evercore Group L.L.C., not to directly or indirectly:

(i) offer, sell, contract to sell, pledge, hedge, lend or otherwise dispose of (or enter into any transaction which is designed to, or might reasonably be expected to, result in the disposition by the shareholder or any affiliate or any person in privity with the shareholder or affiliate, including the filing (or participation in the filing) of a registration statement with the SEC in respect of, or establish or increase a put equivalent position or liquidate or decrease a call equivalent position with the meaning of the Exchange Act any common shares or any securities convertible into, or exercisable or exchangeable for common shares or publicly announce an intention to effect any such transaction, or (ii) engage in any hedging or other transaction designed or intended, or which could reasonably be expected to lead to or result in, a sale or disposition or common shares or securities convertible into or exercisable or exchangeable for common shares, or (iii) make any demand for or exercise any right with respect to the registration of any of our common shares or any security convertible into or exercisable or exchangeable for our common shares.

The restrictions described in the immediately preceding paragraph do not apply with respect to:

a) transactions relating to securities acquired in open market transactions after completion of this offering;
b) transfer as a bona fide gift, including as a result of estate or intestate succession, or pursuant to a will or other testamentary document;
c) a member of the immediate family of the shareholder
d) any trust or other like entity for the direct or indirect benefit of the shareholder or immediate family of the shareholder;
e) a corporation, partnership, limited liability company or other entity of which the shareholder is the direct or indirect legal and beneficial owner;
f) any trust or other like entity for the direct or indirect benefit of the shareholder or any affiliate, wholly-owned subsidiary, limited partner, member or shareholder of the shareholder

g) any affiliate, wholly-owned subsidiary, limited partner, member or stockholder of the shareholder or to any investment fund or other entity controlled or managed by the shareholder;

h) the establishment or modification of a trading plan that complies with Rule 10b5-1 under the Exchange Act or similar plan under Canadian securities laws, provided such plan does not provide for the transfer of securities during the restricted period;

i) transfer of securities to us pursuant to agreements or rights under which we have the option to repurchase securities or a right of first refusal in connection with the termination of the shareholder's employment or other service relationship with us;

j) transfer of securities upon a vesting event of our securities or upon the exercise of securities to purchase securities by the shareholder, in each case on a "cashless" or "net exercise" basis, or to cover tax withholding obligations of the shareholder in connection with such vesting or exercise;

k) transfer of securities pursuant to a bona fide third party tender offer, merger, amalgamation, consolidation or other similar transaction involving a change of control of our company;

l) transfer of securities by operation of law pursuant to a qualified domestic order in connection with a divorce settlement or other court order; or

m) for certain of our executive officers, transfers of shares underlying restricted stock units that will vest and settle during the restricted period, but solely to the extent necessary to satisfy income tax withholding and remittance obligations in connection with such vesting or settlement of restricted stock units that are outstanding as of the date of this prospectus supplement, provided the shares received upon such vesting shall remain subject to the lock-up agreement;

provided that in the case of any transfer or distribution pursuant to clauses (b-g), (i) no public filing or public announcement under Section 16(a) of the Exchange Act, reporting a reduction in beneficial ownership of Subject Shares, or otherwise, shall be required or shall be voluntarily made during the restricted period and (ii) such transfer shall not involve a disposition for value; and further provided that in the case of any transfer or distribution pursuant to clause (b-g) or (l), each donee, distributee or transferee shall concurrently with such transfer or distribution sign and deliver a lock-up letter substantially in the form of this letter. For purposes of clause (k) of this paragraph, "change of control" shall mean the transfer (whether by tender offer, merger, consolidation or other similar transaction), after the closing of the Offering, to a person or group of affiliated persons, of our voting securities if, after such transfer, such person or group of affiliated persons would hold shares having more than 50% of the voting power of all outstanding voting shares of us (or the surviving entity).

These restrictions terminate after the close of trading of our common shares on and including the 60th day after the date of this prospectus supplement.

Jefferies LLC and Evercore Group L.L.C. may, in their sole discretion and at any time or from time to time before the termination of the 60-day period, release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the restricted period.

Stabilization

The underwriters have advised us that, pursuant to Regulation M under the Exchange Act, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common share at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either "covered" short sales or "naked" short sales.

"Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional common shares in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional common shares or purchasing common shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

"Naked" short sales are sales in excess of the option to purchase additional shares of our common shares. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common shares in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of common shares on behalf of the underwriters for the purpose of fixing or maintaining the price of the common shares. A syndicate covering transaction is the bid for or the purchase of common shares on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriter's purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common shares or preventing or retarding a decline in the market price of our common shares. As a result, the price of our common shares may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common shares originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common shares. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common shares on NYSE in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of our common shares in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

This prospectus supplement and the accompanying prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of common shares for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than this prospectus supplement and the accompanying prospectus in electronic format, the information on the underwriters' websites and any information contained in any other website maintained by any of the underwriters is not part of this prospectus supplement or the accompanying prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their affiliates are full-service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses. For example, in November 2019, we entered into our "at the market" sale agreement with Jefferies LLC, which was amended in October 2021.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit

default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common shares offered hereby. Any such short positions could adversely affect future trading prices of the common shares offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Selling Restrictions

Canada

The securities which are the subject of the offering contemplated by this Prospectus Supplement and the accompanying prospectus are not being offered or sold, directly or indirectly, in Canada or to any resident of Canada, and there has not been any advertisement or solicitation in furtherance of such offering of securities in Canada. Each underwriter has agreed that it will not, directly or indirectly, offer or sell any of the securities which are the subject of the offering contemplated by this prospectus supplement and the accompanying prospectus in Canada or to any resident of Canada, and that any selling agreement or similar agreement with respect to such securities will require each dealer or other party thereto to make an agreement to the same effect.

Australia

Neither this prospectus supplement nor the accompanying prospectus is a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, or has been lodged with the Australian Securities & Investments Commission, and each is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus supplement and the accompanying prospectus in Australia, you confirm and warrant that you are either:

(a) a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
(b) a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
(c) a person associated with the company under section 708(12) of the Corporations Act; or
(d) a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act, any offer made to you under this prospectus supplement and the accompanying prospectus is void and incapable of acceptance.

You warrant and agree that you will not offer any of the securities issued to you pursuant to this prospectus supplement and the accompanying prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant State"), no securities have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the securities which have been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that the securities may be offered to the public in that Relevant State at any time:

(a) to any legal entity which is a "qualified investor" as defined under Article 2 of the Prospectus Regulation;
(b) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the Prospectus Regulation), subject to obtaining the prior consent of representatives for any such offer; or
(c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of the securities shall require us or any of the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression “offer to the public” in relation to the securities in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase or subscribe for any securities, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell securities or debentures, whether as principal or agent; or to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong, or SFO, and any rules made under that Ordinance; or in other circumstances which do not result in the document being a “prospectus” as defined in the Companies Ordinance (Cap. 32) of Hong Kong, or CO, or which do not constitute an offer or invitation to the public for the purpose of the CO or the SFO. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the SFO and any rules made under that Ordinance.

Neither this prospectus supplement nor the accompanying prospectus have been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus supplement and the accompanying prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus supplement and the accompanying prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In Israel, this prospectus is being distributed only to, and is directed only at, and any offer of the securities is directed only at, (i) a limited number of persons in accordance with the Israeli Securities Law and (ii) investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and “qualified individuals,” each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case, purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors are required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended) (FIEL), and the underwriters will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

Neither this prospectus supplement nor the accompanying prospectus has been and neither will be lodged or registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and the accompanying prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person, which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the securities pursuant to an offer made under Section 275 of the SFA except:

(c) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(d) where no consideration is or will be given for the transfer;

(e) where the transfer is by operation of law;

(f) as specified in Section 276(7) of the SFA; or

(g) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (SIX), or on any other stock exchange or regulated trading facility in Switzerland. This prospectus supplement and the accompanying prospectus have been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus supplement, the accompanying prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus supplement, the accompanying prospectus nor any other offering or marketing material relating to the offering, us or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus supplement and the accompanying prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

United Kingdom

No securities have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the securities which has been approved by the Financial Conduct Authority, except that the securities may be offered to the public in the United Kingdom at any time:

(a) to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or

(c) in any other circumstances falling within Section 86 of the FSMA,

provided that no such offer of the securities shall require the Issuer or any Manager to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation. For the purposes of this provision, the expression an "offer to the public" in relation to the securities in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase or subscribe for any securities and the expression "UK Prospectus Regulation" means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

United Arab Emirates

The securities have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre) other than in compliance with the laws of the United Arab Emirates (and the Dubai International Financial Centre) governing the issue, offering and sale of securities. Further, this prospectus supplement does not constitute a public offer of securities in the United Arab Emirates (including the Dubai International Financial Centre) and is not intended to be a public offer. Neither this prospectus supplement nor the accompanying prospectus has been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

Dubai International Financial Centre

This document relates to an Exempt Offer in accordance with the Markets Rules of the Dubai Financial Services Authority. This document is intended for distribution only to Persons of a type specified in those rules to whom Exempt Offers can be made. It must not be delivered to, or relied on by, any other Person. The Dubai Financial Services Authority has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The Dubai Financial Services Authority has not approved this document nor taken steps to verify the information set out in it, and has no responsibility for it. The securities to which this document relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered hereby should conduct their own due diligence on the securities. If you do not understand the contents of this document you should consult an authorized financial adviser.

CERTAIN U.S. FEDERAL INCOME TAX CONSIDERATIONS

The following discussion is a general summary of certain U.S. federal income tax consequences of the ownership and disposition of the common shares and pre-funded warrants. It applies only to U.S. Holders (as defined below) that acquire and hold the common shares or pre-funded warrants as capital assets (generally, property held for investment purposes). This summary should not be construed to constitute legal or tax advice to any particular U.S. Holder.

This summary does not apply to or address U.S. Holders subject to special rules, including, without limitation, brokers, dealers in securities or currencies, traders in securities that elect to use a mark-to-market method of accounting for securities holdings, tax-exempt organizations, insurance companies, banks, thrifts and other financial institutions, persons liable for alternative minimum tax, persons that hold an interest in an entity that holds the common shares or pre-funded warrants, persons that will own, or will have owned, directly, indirectly or constructively 10% or more (by vote or value) of the Company's equity, persons that hold the common shares or pre-funded warrants as part of a hedging, integration, conversion or constructive sale transaction or a straddle, or persons whose functional currency is not the U.S. dollar.

This summary does not purport to be a complete analysis of all of the potential U.S. federal income tax considerations that may be relevant to U.S. Holders in light of their particular circumstances. Further, it does not address any aspect of foreign, state, local or estate or gift taxation or the 3.8% surtax imposed on certain net investment income. Each prospective investor should consult its own tax advisor as to the U.S. federal, state, local, foreign and any other tax consequences of the ownership and disposition of the common shares or pre-funded warrants.

This summary is based on the Internal Revenue Code of 1986, as amended (the "Code"), its legislative history, U.S. Treasury Regulations, Internal Revenue Service ("IRS"), rulings, published court decisions, and the income tax treaty between the United States and Canada (the "Convention") all as in effect as of the date hereof, and any of which may be repealed, revoked or modified (possibly with retroactive effect) so as to result in U.S. federal income tax consequences different from those discussed below. This summary is applicable to U.S. Holders who are residents of the United States for purposes of the Convention and who qualify for the full benefits of the Convention.

A "U.S. Holder" is a beneficial owner of the common shares or pre-funded warrants who, for U.S. federal income tax purposes, is a citizen or individual resident of the United States, a corporation (or other entity that is classified as a corporation for U.S. federal income tax purposes) that is created or organized in or under the laws of the United States or any State thereof or the District of Columbia, an estate whose income is subject to U.S. federal income tax regardless of its source, or a trust (i) if a U.S. court can exercise primary supervision over the trust's administration and one or more U.S. persons are authorized to control all substantial decisions of the trust, or (ii) that validly elects to be treated as a U.S. person for U.S. federal income tax purposes.

If a partnership or other pass-through entity holds the common shares or pre-funded warrants of the Company, the U.S. federal income tax treatment of a partner, beneficiary, or other stakeholder will generally depend on the status of that person and the tax treatment of the pass-through entity. A partner, beneficiary, or other stakeholder in a pass-through entity holding the common shares or pre-funded warrants should consult its own tax advisor with regard to the U.S. federal income tax treatment of its investment in the common shares or pre-funded warrants.

Pre-Funded Warrants

The U.S. federal income tax characterization of pre-funded warrants is uncertain. Although it is not entirely free from doubt, a pre-funded warrant should be treated as a share of our common shares for U.S. federal income tax purposes and a holder of pre-funded warrants should generally be taxed in the same manner as a holder of common shares as described below. 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 common shares received. Similarly, the tax basis of a pre-funded warrant should carry over to the common share received upon exercise, increased by the exercise price (if applicable). Prospective purchasers of pre-funded warrants should consult their own tax advisors regarding the U.S. federal income tax consequences applicable to the ownership and disposition of

the pre-funded warrants , including potential alternative characterizations and the effect of the PFIC rules (in particular, the uncertain treatment of any QEF election (as defined below)). The balance of this discussion generally assumes that the characterization described above is respected for U.S. federal income tax purposes and references to “common shares” below include the pre-funded warrants.

Distributions on the Common Shares

Subject to the PFIC rules discussed below, the gross amount of any distribution received by a U.S. Holder with respect to the common shares (including any amounts withheld to pay Canadian withholding taxes) will be included in the gross income of the U.S. Holder as a dividend to the extent attributable to the Company’s current or accumulated earnings and profits, as determined under U.S. federal income tax principles. The Company does not intend to calculate its earnings and profits under U.S. federal income tax rules. Accordingly, U.S. Holders should expect that a distribution generally will be treated as a dividend for U.S. federal income tax purposes. Unless the Company is treated as a PFIC for the taxable year in which it pays a distribution or in the preceding taxable year (see “Passive Foreign Investment Company Rules” below), the Company believes that it may qualify as a “qualified foreign corporation,” in which case, subject to certain requirements, including conditions relating to holding period and the absence of certain risk reduction transactions, distributions treated as dividends and received by non-corporate U.S. Holders may be eligible for a preferential tax rate. Distributions on the common shares generally will not be eligible for the dividends received deduction available to U.S. Holders that are corporations.

The amount of any distribution paid in Canadian dollars (including any amounts withheld to pay Canadian withholding taxes) will equal the U.S. dollar value of the Canadian dollars calculated by reference to the exchange rate in effect on the date the distribution is received by the U.S. Holder, regardless of whether the Canadian dollars are converted into U.S. dollars. A U.S. Holder will have a tax basis in the Canadian dollars equal to their U.S. dollar value on the date of receipt. If the Canadian dollars received are converted into U.S. dollars on the date of receipt, the U.S. Holder should generally not be required to recognize foreign currency gain or loss in respect of the distribution. If the Canadian dollars received are not converted into U.S. dollars on the date of receipt, a U.S. Holder may recognize foreign currency gain or loss on a subsequent conversion or other disposition of the Canadian dollars. Such gain or loss will be treated as U.S. source ordinary income or loss.

A U.S. Holder may be entitled to deduct or credit Canadian withholding tax imposed on dividends paid to a U.S. Holder, subject to applicable limitations in the Code. For purposes of calculating a U.S. Holder’s foreign tax credit, dividends received by such U.S. Holder with respect to the common shares of a foreign corporation generally constitute foreign source income. However, and subject to certain exceptions, a portion of the dividends paid by a foreign corporation will be treated as U.S. source income for U.S. foreign tax credit purposes, in proportion to its U.S. source earnings and profits, if U.S. persons collectively own, directly or indirectly, 50% or more of the voting power or value of the foreign corporation’s common shares. If a portion of any dividends paid with respect to the common shares are treated as U.S. source income under these rules, it may limit the ability of a U.S. Holder to claim a foreign tax credit for any Canadian withholding taxes imposed in respect of such dividend, although certain elections under the Code and the Convention may be available to mitigate these effects. The rules governing the foreign tax credit are complex. U.S. Holders are urged to consult their own tax advisors regarding the availability of the foreign tax credit under their particular circumstances, including the impact of, and any exception available to, the special income sourcing rule described in this paragraph.

Sale, Exchange or Other Taxable Disposition of the Common Shares

Subject to the PFIC rules discussed below, a U.S. Holder will recognize a capital gain or loss on the sale, exchange or other taxable disposition of the common shares in an amount equal to the difference between the amount realized for the common shares and the U.S. Holder’s adjusted tax basis in the common shares. Capital gains of non-corporate U.S. Holders derived with respect to capital assets held for more than one year are eligible for reduced rates of taxation. The deductibility of capital losses is subject to limitations. Any capital gain or loss recognized by a U.S. Holder generally will be treated as U.S. source gain or loss for U.S. foreign tax credit purposes.

Passive Foreign Investment Company Rules

A foreign corporation will be considered a PFIC for any taxable year in which (i) 75% or more of its gross income is “passive income” under the PFIC rules or (ii) 50% or more of the average quarterly value of its assets produce (or are held for the production of) “passive income.” For this purpose, “passive income” generally includes interest,

dividends, certain rents and royalties, and certain gains. Royalties derived from an unrelated person in the active conduct of a trade or business in the licensing of property developed or created through its own officers or staff of employees is generally excluded from passive income. Moreover, for purposes of determining if the foreign corporation is a PFIC, if the foreign corporation owns, directly or indirectly, at least 25%, by value, of the shares of another corporation, it will be treated as if it holds directly its proportionate share of the assets and receives directly its proportionate share of the income of such other corporation. If a corporation is treated as a PFIC with respect to a U.S. Holder for any taxable year, the corporation will continue to be treated as a PFIC with respect to that U.S. Holder in all succeeding taxable years, regardless of whether the corporation continues to meet the PFIC requirements in such years, unless certain elections are made.

The determination as to whether a foreign corporation is a PFIC is based on the application of complex U.S. federal income tax rules, which are subject to differing interpretations, and the determination will depend on the composition of the income, expenses and assets of the foreign corporation from time to time and the nature of the activities performed by its officers and employees. Based on a preliminary analysis, the Company does not believe that it will be classified as a PFIC for the taxable year ended December 31, 2021; however, the Company cannot be certain that its preliminary analysis is correct. Furthermore, even if the Company is not a PFIC for the taxable year ended December 31, 2021, whether the Company is a PFIC for the current taxable year or any future taxable year is a fact-intensive determination made on an annual basis and based on the application of complex U.S. federal income tax rules that are subject to differing interpretations. Neither the Company's U.S. counsel nor U.S. tax advisor expresses any opinion with respect to the Company's PFIC status or with respect to the Company's expectations regarding its PFIC status.

If the Company is classified as a PFIC, a U.S. Holder that does not make any of the elections described below would be required to report any gain on the disposition of common shares as ordinary income, rather than as capital gain, and to compute the tax liability on the gain and any "Excess Distribution" (as defined below) received in respect of common shares as if such items had been earned ratably over each day in the U.S. Holder's holding period (or a portion thereof) for the common shares. The amounts allocated to the taxable year during which the gain is realized or distribution is made, and to any taxable years in such U.S. Holder's holding period that are before the first taxable year in which the Company is treated as a PFIC with respect to the U.S. Holder, would be included in the U.S. Holder's gross income as ordinary income for the taxable year of the gain or distribution. The amount allocated to each other taxable year would be taxed as ordinary income in the taxable year during which the gain is realized or distribution is made at the highest tax rate in effect for the U.S. Holder in that other taxable year and would be subject to an interest charge as if the income tax liabilities had been due with respect to each such prior year. For purposes of these rules, gifts, exchanges pursuant to corporate reorganizations and use of common shares as security for a loan may be treated as a taxable disposition of the common shares. An "Excess Distribution" is the amount by which distributions during a taxable year in respect of a common share exceed 125% of the average amount of distributions in respect thereof during the three preceding taxable years (or, if shorter, the U.S. Holder's holding period for the common shares).

Certain additional adverse tax rules will apply to a U.S. Holder for any taxable year in which the Company is treated as a PFIC with respect to such U.S. Holder and any of the Company's subsidiaries is also treated as a PFIC (a "Subsidiary PFIC"). In such a case, the U.S. Holder will generally be deemed to own its proportionate interest (by value) in any Subsidiary PFIC and be subject to the PFIC rules described above with respect to the Subsidiary PFIC regardless of such U.S. Holder's percentage ownership in the Company.

The adverse tax consequences described above may be mitigated if a U.S. Holder makes a timely "qualified electing fund" (a "QEF") election, with respect to its interest in the PFIC. Consequently, if the Company is classified as a PFIC, it may be advantageous for a U.S. Holder to elect to treat the Company as a QEF with respect to such U.S. Holder in the first year in which it holds common shares. If a U.S. Holder makes a timely QEF election with respect to the Company, the electing U.S. Holder would be required in each taxable year that the Company is considered a PFIC to include in gross income (i) as ordinary income, the U.S. Holder's pro rata share of the ordinary earnings of the Company and (ii) as capital gain, the U.S. Holder's pro rata share of the net capital gain (if any) of the Company, whether or not the ordinary

earnings or net capital gain are distributed. An electing U.S. Holder's basis in common shares will be increased to reflect the amount of any taxed but undistributed income. Distributions of income that had previously been taxed will result in a corresponding reduction of basis in the common shares and will not be taxed again as distributions to the U.S. Holder.

A QEF election made with respect to the Company will not apply to any Subsidiary PFIC; a QEF election must be made separately for each Subsidiary PFIC (in which case the treatment described above would apply to such Subsidiary PFIC). If a U.S. Holder makes a timely QEF election with respect to a Subsidiary PFIC, it would be required in each taxable year to include in gross income its pro rata share of the ordinary earnings and net capital gain of such Subsidiary PFIC, but may not receive a distribution of such income. Such a U.S. Holder may, subject to certain limitations, elect to defer payment of current U.S. federal income tax on such amounts, subject to an interest charge (which would not be deductible for U.S. federal income tax purposes if the U.S. Holder were an individual).

If the Company determines that it, and any subsidiary in which the Company owns, directly or indirectly, more than 50% of such subsidiary's total aggregate voting power, is likely a PFIC in any taxable year, the Company intends to make available to U.S. Holders, upon request and in accordance with applicable procedures, a "PFIC Annual Information Statement" with respect to the Company and any such subsidiary for such taxable year. The "PFIC Annual Information Statement" may be used by U.S. Holders for purposes of complying with the reporting requirements applicable to a QEF election with respect to the Company and any such Subsidiary PFIC.

Alternatively, if the Company were to be classified as a PFIC, a U.S. Holder could also avoid certain of the rules described above by making a mark-to-market election (instead of a QEF election), provided the common shares are treated as regularly traded on a qualified exchange or other market within the meaning of the applicable U.S. Treasury Regulations. However, a U.S. Holder will not be permitted to make a mark-to-market election with respect to a Subsidiary PFIC. U.S. Holders should consult their own tax advisers regarding the potential availability and consequences of a mark-to-market election, as well as the advisability of making a protective QEF election in case the Company is classified as a PFIC in any taxable year.

During any taxable year in which the Company or any Subsidiary PFIC is treated as a PFIC with respect to a U.S. Holder, that U.S. Holder generally must file IRS Form 8621, Information Return by a Shareholder of a Passive Foreign Investment Company or Qualified Electing Fund. U.S. Holders should consult their own tax advisers concerning annual filing requirements.

Required Disclosure with Respect to Foreign Financial Assets

Certain U.S. Holders are required to report information relating to an interest in the common shares, subject to certain exceptions (including an exception for common shares held in accounts maintained by certain financial institutions), by attaching a completed IRS Form 8938, Statement of Specified Foreign Financial Assets, with their tax return for each year in which they hold an interest in the common shares. U.S. Holders should consult their own tax advisors regarding information reporting requirements relating to their ownership of the common shares.

CERTAIN CANADIAN INCOME TAX CONSIDERATIONS

The following is, as of the date of this offering, a summary of the principal Canadian federal income tax considerations under the Income Tax Act (Canada) and the Regulations thereunder (collectively, the "Tax Act") generally applicable to an investor who acquires common shares or pre-funded warrants pursuant to this prospectus supplement (and warrant shares upon the exercise of pre-funded warrants) as beneficial owner and who, for the purposes of the Tax Act and any applicable income tax treaty or convention, at all relevant times: (i) is not, and is not deemed to be, resident in Canada; (ii) does not use or hold, and is not deemed to use or hold, the common shares or pre-funded warrants in carrying on a business in Canada, or otherwise in respect of a business carried on in Canada; (iii) deals at arm's length with the Company and the underwriters; (iv) is not affiliated with the Company or the underwriters; (v) is not exempt from tax under the Tax Act; (vi) has not entered into and will not enter into a "synthetic disposition arrangement" or "derivative forward agreement" (within the meaning of the Tax Act) with respect to the common shares or pre-funded warrants; and (vii) acquires and holds the common shares, any warrant shares acquired on the exercise of pre-funded warrants (for the purpose of this section, sometimes collectively referred to as "Shares") and pre-funded warrants as capital property (a "Non-Resident Holder"). Special rules, which are not discussed in this summary, may apply to a Non-Resident Holder that is an insurer that carries on an insurance business in Canada and elsewhere, and any such person should consult its own tax advisors. Generally, the Shares and pre-funded warrants will be considered to be capital property to a Non-Resident Holder unless the Non-Resident Holder holds or uses the Shares or pre-funded warrants in the course of carrying on a business or has acquired them or been deemed to have acquired them in one or more transactions considered to be an adventure or concern in the nature of trade.

This summary is based upon the current provisions of the Tax Act in force as of the date hereof, counsel's understanding of the current published administrative policies of the Canada Revenue Agency (the "CRA") and all specific proposals to amend the Tax Act publicly announced by or on behalf of the Minister of Finance (Canada) prior to the date hereof (the "Tax Proposals"). This summary assumes that the Tax Proposals will be enacted substantially as proposed; however, no assurance can be given that the Tax Proposals will be enacted as proposed or at all. This summary does not otherwise take into account or anticipate any changes in law or the CRA's administrative policies, whether by legislative, governmental or judicial decision or action, nor does it take into account any provincial, territorial or foreign income tax legislation or considerations.

This summary is of a general nature only, is not exhaustive of all possible Canadian federal income tax considerations and is not intended to be, nor should it be construed to be, legal or tax advice to any particular Non-Resident Holder, and no representation with respect to the income tax consequences to any Non-Resident Holder or other person are made. Accordingly, Non-Resident Holders should consult their own tax advisors with respect to the tax consequences applicable to them, having regard to their own particular circumstances.

Currency Conversion

For purposes of the Tax Act, all amounts relating to the acquisition, holding or disposition of Shares and pre-funded warrants (including dividends, adjusted cost base and proceeds of disposition) must be expressed in Canadian dollars. Amounts determined in another currency must be converted into Canadian dollars using the relevant rate of exchange as determined in accordance with the rules contained in the Tax Act.

Exercise of Pre-Funded Warrants

No gain or loss will be realized by a Non-Resident Holder on the exercise of a pre-funded warrant to acquire a warrant share of the Company. When a pre-funded warrant is exercised, the Non-Resident Holder's cost of the warrant share acquired thereby will be equal to the aggregate of the Non-Resident Holder's adjusted cost base of such pre-funded warrant and the exercise price paid for the warrant share. The Non-Resident Holder's adjusted cost base of the warrant share so acquired will be determined by averaging the cost of such warrant share with the adjusted cost base to the Non-Resident Holder of all common shares of the Company held as capital property immediately before the acquisition of the warrant share pursuant to the exercise of the pre-funded warrant.

Dividends on Shares

Dividends paid or credited or deemed to be paid or credited to a Non-Resident Holder by the Company will be subject to Canadian withholding tax at the rate of 25% on the gross amount of the dividend unless such rate is reduced by the terms of an applicable income tax treaty or convention. For example, under the Canada-United States Income Tax Convention (1980), as amended (the "Treaty"), the rate of withholding tax on dividends paid or credited to a Non-Resident Holder who is resident in the U.S. for purposes of the Treaty and entitled to the full benefits under the Treaty (a "U.S. Holder") and who is the beneficial owner of the dividend is generally limited to 15% of the gross amount of the dividend (or 5% in the case of a U.S. Holder that is also a corporation that beneficially owns at least 10% of the Company's voting shares). Non-Resident Holders should consult their own tax advisors to determine their entitlement to relief under an applicable income tax treaty or convention.

Dispositions of Shares and Pre-Funded Warrants

A Non-Resident Holder generally will not be subject to tax under the Tax Act in respect of a capital gain realized on the disposition or deemed disposition of a Share or a pre-funded warrant unless the Share or pre-funded warrant constitutes "taxable Canadian property" to the Non-Resident Holder for purposes of the Tax Act, and the Non-Resident Holder is not entitled to relief under the terms of an applicable income tax treaty or convention. In addition, capital losses arising on the disposition or deemed disposition of a Share or a pre-funded warrant will not be recognized under the Tax Act unless the Share or pre-funded warrant constitutes "taxable Canadian property" to the Non-Resident Holder for purposes of the Tax Act.

Provided the common shares of the Company are listed on a "designated stock exchange", as defined in the Tax Act (which includes the NYSE) at the time of disposition, the Shares and pre-funded warrants 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) the Non-Resident Holder, persons with whom the Non-Resident Holder did not deal at arm's length, partnerships in which the Non-Resident Holder or such non-arm's length persons hold a membership interest (either directly or indirectly through one or more partnerships), or the Non-Resident Holder together with all such persons, owned 25% or more of the issued shares of any class or series of shares of the Company, and (ii) more than 50% of the fair market value of the common shares of the Company 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 in respect of, or an interest in, or for civil law a right in such property, whether or not such property exists. Notwithstanding the foregoing, a Share 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 common shares may constitute taxable Canadian property should consult their own tax advisors.

LEGAL MATTERS

Certain legal matters in connection with the securities offered hereby will be passed upon on behalf of the Company by Blake, Cassels & Graydon LLP with respect to Canadian legal matters and by Wilson Sonsini Goodrich & Rosati, P.C. with respect to U.S. legal matters. The underwriters are being represented in connection with this offering by Cooley LLP, with respect to U.S. legal matters and McCarthy Tétrault LLP with respect to Canadian legal matters.

EXPERTS

The consolidated financial statements of Zymeworks Inc. as of December 31, 2020 and 2019 and for each of the years in the three-year period ended December 31, 2020 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2020, 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.

The audit report covering the consolidated financial statements as of December 31, 2020 and 2019 and for each of the years in the three-year period ended December 31, 2020, refers to a change in our accounting policies as of January 1, 2019 due to the adoption of ASC 842—*Leases*.

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 we filed with the Securities and Exchange Commission (the "SEC") under the Securities Act and 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 *http://www.sec.gov*. You may also obtain additional information by visiting our website at *http://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 shares and pre-funded warrants.

INCORPORATION OF CERTAIN INFORMATION 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. We have filed the documents listed below with the SEC under the Exchange Act, and these documents are incorporated herein by reference:

- Annual Report on Form 10-K for the fiscal year ended December 31, 2020, filed with the SEC on February 24, 2021;
- Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2021, June 30, 2021 and September 30, 2021, filed with the SEC on May 5, 2021, August 4, 2021 and November 3, 2021, respectively;
- Current Reports on Form 8-K filed with the SEC on April 19, 2021, May 6, 2021, May 18, 2021, September 16, 2021, October 1, 2021, January 5, 2022 and January 19, 2022;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2020 from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on March 23, 2021;
- the description of our common shares set forth in our registration statement on Form 8-A, filed with the SEC on April 24, 2017, including any amendments or reports filed for the purpose of updating such description.

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 after the date of this prospectus supplement and prior to the termination of the offering of common shares 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.

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.
1385 West 8th Avenue, Suite 540
Vancouver, British Columbia, Canada, V6H 3V9
Attn: Corporate Secretary
Phone: (604) 678-1388

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PROSPECTUS

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We may offer and issue from time to time common shares, preferred shares, debt securities in one or more series, warrants for the purchase of common shares or preferred shares or warrants for the purchase of debt securities, subscription receipts that are exchangeable for our equity securities and/or other securities or units comprised of one or more of the other securities described in this shelf prospectus in any combination, or any combination thereof, in one or more transactions under this prospectus. Securities may be offered separately or together, at times, in amounts, at prices and on terms to be determined based on market conditions at the time of sale and set forth in an accompanying prospectus supplement. From time to time, selling securityholders, who would be named in a prospectus supplement, may also offer and sell our securities at prices and on terms described in one or more prospectus supplements.

This prospectus provides you with a general description of the securities that we may offer. Each time we offer securities, we will provide you with a prospectus supplement that describes specific information about the particular securities being offered and may add, update or change information contained or incorporated by reference in this prospectus. You should read both this prospectus and the prospectus supplement, together with the additional information which is incorporated by reference into this prospectus and the prospectus supplement.

We or selling securityholders may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, broker-dealers, agents, directly to purchasers, or through any other means described in this prospectus under “Plan of Distribution” and in supplements to this prospectus in connection with a particular offering of securities. If any underwriters, dealers, or agents are involved in the sale of any of these securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement.

Our common shares are listed and posted for trading on the New York Stock Exchange (“NYSE”), under the symbol “ZYME.” On September 30, 2021, the last reported sale price of the common shares on the NYSE was $29.04 per common share. Unless otherwise specified in the applicable prospectus supplement, securities other than the common shares will not be listed on any securities exchange. **There is currently no market through which the securities, other than the common shares, may be sold and you may not be able to resell such securities purchased under this prospectus and any applicable prospectus supplement. This may affect the pricing of such securities in the secondary market, the transparency and availability of trading prices, the liquidity of the securities, and the extent of issuer regulation.**

Investing in our securities involves a high degree of risk. You should carefully read the “Risk Factors” section beginning on page 6 of this prospectus and carefully consider the discussion of risks and uncertainties under the heading “Risk Factors” contained in any applicable prospectus supplement and in the documents that are incorporated by reference.

These securities have not been approved or disapproved by the U.S. Securities and Exchange Commission (the “SEC”) or any state securities commission nor has the SEC or any state securities commission passed upon the accuracy or adequacy of this prospectus or any applicable prospectus supplement. Any representation to the contrary is a criminal offense.

The date of this prospectus is October 1, 2021.

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement on Form S-3 that we filed with the SEC as a "well-known seasoned issuer" as defined in Rule 405 of the Securities Act of 1933. Under the shelf registration process, we may from time to time, offer and sell to the public any combination of the securities described in the registration statement in one or more offerings. These securities may also be resold by selling securityholders.

You should rely only on the information contained or incorporated by reference in this prospectus or any applicable prospectus supplement and on the other information included in the registration statement of which this prospectus forms a part. We have not authorized anyone to provide you with different or additional information. If anyone provides you with different or additional information, you should not rely on it. We are not making an offer to sell or seeking an offer to buy the securities offered pursuant to this prospectus in any jurisdiction where the offer or sale is not permitted. You should assume that the information contained in this prospectus or any applicable prospectus supplement is accurate only as of the date on the front of those documents and that information contained in any document incorporated by reference is accurate only as of the date of that document, regardless of the time of delivery of this prospectus or any applicable prospectus supplement or of any sale of our securities pursuant thereto. 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 or any applicable prospectus supplement and the documents incorporated by reference in this prospectus or any applicable prospectus supplement 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.

In this prospectus and any prospectus supplement, unless otherwise indicated, 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 contain translations of some Canadian dollar amounts into U.S. dollars solely for your convenience. See "Exchange Rate Information."

In this prospectus and in any prospectus supplement, 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 Inc., either alone or together with our wholly-owned subsidiary, Zymeworks Biopharmaceuticals Inc. Furthermore, except as otherwise indicated, references to "Merck," "Lilly," "BMS," "GSK," "Daiichi Sankyo," "Janssen," "LEO," "BeiGene," "Iconic" and "Pfizer" refer to Merck Sharp & Dohme Research Ltd., Eli Lilly and Company, 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. and Pfizer Inc., respectively.

The names Azymetric, Zymeworks, ZymeCAD, EFECT, ZymeLink and the phrase "Building Better Biologics" are our registered trademarks. Other trademarks, product names and company names appearing in this prospectus and any prospectus supplement and documents incorporated by reference in this prospectus and any prospectus supplement 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 under the section of this prospectus captioned "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. and its subsidiary.

Company Overview

Zymeworks is a clinical-stage biopharmaceutical company dedicated to the development of next-generation multifunctional biotherapeutics. Our suite of complementary therapeutic platforms and our fully integrated drug development engine provide the flexibility and compatibility to precisely engineer and develop highly differentiated product candidates. These capabilities have resulted in multiple product candidates with the potential to drive positive outcomes in large underserved and unaddressed patient populations.

Our lead product candidate, zanidatamab (formerly known as ZW25), is a novel bispecific antibody that targets two distinct domains of the human epidermal growth factor receptor 2 ("HER2"). The unique mechanism of action of zanidatamab may enable it to address unmet need in patient populations with HER2-expressing cancers, including those with lower levels of expression, for which there are no approved HER2-targeted agents. In clinical trials, monotherapy zanidatamab and zanidatamab in combination with chemotherapy have been well tolerated with promising antitumor activity in patients with heavily pretreated HER2-expressing cancers that have progressed after having received standard of care, including multiple HER2-targeted regimens. Based on these data, we initiated a number of global multicenter clinical trials to evaluate zanidatamab in specific indications and lines of therapy. These include (i) a pivotal trial in patients with previously treated HER2 gene amplified biliary tract cancer ("BTC"), (ii) the first-line treatment of HER2-positive metastatic gastroesophageal adenocarcinomas ("GEA"), BTC, or colorectal cancer in combination with standard of care chemotherapy, (iii) previously-treated locally advanced and/or metastatic HER2-positive, hormone receptor-positive breast cancer in combination with Pfizer's Ibrance (palbociclib) and fulvestrant, and (iv) previously-treated locally advanced and/or metastatic HER2-expressing breast cancer in combination with Seagen, Inc.'s Tukysa (tucatinib) and chemotherapy. Our partner, BeiGene, has initiated Phase 1b/2 clinical trials evaluating zanidatamab for (i) the first-line treatment of metastatic HER2-positive breast cancer in combination with docetaxel and for (ii) the first-line treatment of metastatic HER2-positive GEA in combination with tislelizumab and chemotherapy. In addition, zanidatamab continues to be evaluated in several indications including colorectal, endometrial and other HER2-expressing cancers.

Our second product candidate, ZW49, combines the unique design of zanidatamab with our ZymeLink antibody-drug conjugate ("ADC") platform, comprised of our proprietary cytotoxin (cancer cell-killing compound) and cleavable linker. We designed ZW49 to be a best-in-class HER2-targeting ADC to further address unmet need across a range of HER2-expressing cancers. A Phase 1 clinical trial to establish safety and antitumor activity of ZW49 began in 2019.

We are also advancing a deep pipeline of preclinical product candidates and discovery-stage programs in oncology (including immuno-oncology agents) and other therapeutic areas.

Our proprietary capabilities and technologies include several modular, complementary therapeutic platforms that can be used in combination with each other and with existing approaches. This ability to layer technologies

without compromising manufacturability enables us to engineer next-generation biotherapeutics with synergistic activity, which we believe will result in improved patient outcomes. Our core platforms include:

- *Azymetric*, our bispecific platform, which enables therapeutic antibodies to simultaneously bind multiple distinct locations on a target (known as an epitope) or to multiple targets. This is achieved by tailoring multiple configurations of the antibody's Fab regions (locations on the antibody to which epitopes bind);
- *ZymeLink*, our ADC platform, comprised of cytotoxins and the linker technology used to couple these cytotoxins to tumor-targeting antibodies or proteins. This platform can be used in conjunction with our other therapeutic platforms to increase safety and efficacy as compared to existing ADC technologies;
- *EFECT*, which enables finely tuned modulation (both up and down) of immune cell recruitment and function; and
- *ProTECT*, which enables tumor-specific activity that may reduce systemic toxicity, and simultaneously enhances localized immune co-stimulation or checkpoint modulation that may increase efficacy.

Our protein engineering expertise and proprietary structure-guided molecular modeling capabilities enable these therapeutic platforms. Together with our internal antibody discovery and generation technologies, we have established a fully integrated drug development engine and toolkit capable of rapidly delivering a steady pipeline of next-generation product candidates in oncology and other therapeutic areas.

Our Azymetric, EFECT and ZymeLink therapeutic platforms have been further leveraged through multiple revenue-generating strategic partnerships with the following global pharmaceutical companies: Merck, Lilly, BMS, GSK, Daiichi, Janssen, LEO, BeiGene, and Iconic.

Our goal is to leverage our next-generation therapeutic platforms and proprietary protein engineering capabilities to become a domain dominator in the discovery, development and commercialization of best-in-class multifunctional biotherapeutics for the treatment of cancer and other diseases with high unmet medical need.

We commenced operations in 2003 and have since devoted substantially all of our resources to research and development activities including developing our therapeutic platforms, identifying and developing potential product candidates and undertaking preclinical studies and clinical trials. Additionally, we have supported our research and development activities with general and administrative support, as well as by raising capital, conducting business planning and protecting our intellectual property. We have not generated any revenue from the sale of approved products to date and do not expect to do so until such time as we obtain regulatory approval and commercialize one or more of our product candidates. We cannot be certain of the timing or success of approval of our product candidates.

Since our initial public offering ("IPO") in 2017, we have funded our operations primarily through follow-on public offerings, including the issuance of pre-funded warrants, and payments received under our license and collaboration agreements. Payments received from our license and collaboration agreements include upfront fees, milestone payments, as well as research support and reimbursement payments. Prior to our IPO, we also received financing from private equity placements and the issuance of convertible debt, which was subsequently converted into equity securities, and a credit facility. From inception to June 30, 2021, we received $796.5 million, net of equity issue costs, from these sources of financing including proceeds from exercises of stock options and employee stock purchase plans. As of June 30, 2021, we had $359.8 million of cash resources consisting of cash, cash equivalents and short-term investments.

Although it is difficult to predict our funding requirements, based upon our current operating plan, we anticipate that our existing cash and cash equivalents and short-term investments as of June 30, 2021, combined with the

collaboration payments we anticipate receiving, will enable us to fund our planned operations into the second half of 2022 and potentially beyond.

We reported a net loss of $112.1 million for the six months ended June 30, 2021 and through June 30, 2021, we had an accumulated deficit of $583.4 million. Over the next several years, we expect to continue to incur losses as we increase our research and development expenditures in connection with the ongoing development of our product candidates and other clinical, preclinical and regulatory activities.

Corporate Information

We were incorporated on September 8, 2003 under the *Canada Business Corporations Act*, under the name "Zymeworks Inc." On October 22, 2003, we were registered as an extra-provincial company under the *Company Act* (British Columbia), the predecessor to the *Business Corporations Act* (British Columbia), or the BCBCA. Zymeworks continued to the BCBCA on May 2, 2017. Our principal office is located at 1385 West 8th Avenue, Suite 540, Vancouver, British Columbia, Canada V6H 3V9, and our telephone number is (604) 678-1388. We have one wholly owned subsidiary located in Seattle, Washington named Zymeworks Biopharmaceuticals Inc. Our corporate website address is *www.zymeworks.com.* The references to *www.zymeworks.com* in this 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 or the documents incorporated by reference herein or therein. Investors should not rely on any such information in deciding whether to invest in our securities.

The Securities That May Be Offered

We may offer or sell common shares, preferred shares, debt securities, warrants, subscription rights and units in one or more offerings and in any combination, and the selling securityholders to be named in a supplement to this prospectus may from time to time offer and sell our securities. 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. We will not receive any proceeds from the sale of our securities by the selling securityholders.

The securities may be sold to or through underwriters, dealers or agents or directly to purchasers or as otherwise set forth in the section of this prospectus captioned "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 Shares

We or the selling securityholders may offer common shares, no par value, either alone or underlying other registered securities convertible into our common shares. The shareholders of the Company are entitled to one vote for each common share on all matters to be voted on by the shareholders. Our articles provide for a classified (or staggered) board of directors consisting of three classes of directors, with directors serving staggered three-year terms. Shareholders of the Company are not entitled to cumulative voting in the election of directors. Each common share is equal to every other common share and all common shares participate equally on liquidation, dissolution or winding up of our Company, whether voluntary or involuntary, or any other distribution of our assets among our shareholders for the purpose of winding up our affairs after the Company has paid out its liabilities.

Preferred Shares

We may issue our preferred shares from time to time in one or more series. The terms of each series of preferred shares, including the number of shares, the designation, rights, preferences, privileges, priorities, restrictions, conditions and limitations, will be determined at the time of creation of each such series by our board of directors, without shareholder approval, provided that all preferred shares will rank equally within their class as to dividends and distributions in the event of our dissolution, liquidation or winding-up.

Debt Securities

We may offer secured or unsecured obligations in the form of one or more series of senior or subordinated debt securities. 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 issue debt securities that are convertible into shares of our common shares.

The debt securities will be issued under an indenture between us and a trustee to be specified 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 shares, preferred shares or debt securities. We may offer warrants independently or together with other securities.

Subscription Receipts

We may issue subscription receipts that are exchangeable for our equity securities and/or other securities. Our equity securities and/or other securities issued or delivered upon the exchange of subscription receipts will be issued for no additional consideration.

Units

We may issue units comprised of one or more of the other 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

Investing in our securities is speculative and involves a high degree of risk. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the any applicable prospectus supplement and any free writing prospectus, together with all the information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus, including the risks, uncertainties and assumptions discussed under the heading "Item 1A. Risk Factors" in our annual report on Form 10-K for the year ended December 31, 2020, as revised or supplemented by our subsequent quarterly reports on Form 10-Q or our current reports on Form 8-K, which are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. These risks, as well as risks currently unknown to us, could materially adversely affect our future business, operations and financial condition and could cause purchasers of securities to lose all or part of their investments. The risks and uncertainties we have described are not the only risks we face; risks and uncertainties not currently known to us or that we currently deem to be immaterial may also materially and adversely affect our business, financial condition, results of operations and prospects.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents incorporated by reference herein, includes and incorporates by reference "forward-looking statements" within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and "forward-looking information" within the meaning of Canadian securities laws, or collectively, forward-looking statements. 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 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; and
- the impact of the COVID-19 pandemic on our business and operations.

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 maintain good business relationships with our 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 acquisitions;
- 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 (including those referred to under “Risk Factors,” above), could affect future performance and cause actual results to differ materially from those matters expressed in or implied by forward-looking statements:

- our ability to obtain regulatory approval for our 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;
- the extent to which our business may be adversely affected by the COVID-19 pandemic;
- 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 (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;
- 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 shareholders 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;
- 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 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;
- 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.

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.

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.

EXCHANGE RATE INFORMATION

We express all amounts in this prospectus and the documents incorporated by reference herein in U.S. dollars, except where otherwise indicated. References to "$" and "US$" are to U.S. dollars and references to "C$" are to Canadian dollars. The following table sets forth, for the periods indicated, the high, low, average and end of period rates of exchange for one U.S. dollar, expressed in Canadian dollars, published by the Bank of Canada during the respective periods.

The following table sets forth certain exchange rates based on the Bank of Canada daily exchange rate.

	Year Ended December 31,			Six Months Ended June 30,	
	2018	2019	2020	2020	2021
Highest rate during the period	1.3642	1.3600	1.4496	1.4496	1.2828
Lowest rate during the period	1.2288	1.2988	1.2718	1.2970	1.2040
Average exchange rate for the period(1)	1.3004	1.3236	1.3415	1.3696	1.2465
Rate at the end of the period	1.3642	1.2988	1.2732	1.3628	1.2394

(1) Determined by averaging the rates on the last day of each month during the respective period.

On September 29, 2021 the Bank of Canada daily average rate of exchange was $1.00 = C$1.2741.

EARNINGS COVERAGE

If we offer debt securities having a term to maturity in excess of one year or preferred shares under this prospectus and any applicable prospectus supplement, the applicable prospectus supplement will include earnings coverage ratios giving effect to the issuance of such securities, as required by Canadian securities laws.

USE OF PROCEEDS

Specific information about the use of proceeds from the specific issuance of any securities will be set forth in the applicable prospectus supplement.

Unless otherwise set forth in the applicable prospectus supplement, we will not receive any proceeds in the event that securities are sold by a selling securityholder.

As we currently have no revenues from product sales, we experienced a negative operating cash flow for the year ended December 31, 2020 and expect to experience a negative operating cash flow for the 2021 fiscal year. In order to raise additional funds to finance future growth opportunities, we may, from time to time, issue securities (including debt securities). See “Risk Factors.”

CONSOLIDATED CAPITALIZATION

There have been no material changes in our share and loan capital, on a consolidated basis, since June 30, 2021, the date of our most recently filed financial statements.

PRIOR SALES

As required by Canadian securities laws, information in respect of our common shares that were issued within the previous twelve-month period, including common shares that were issued upon the exercise of options granted under our incentive stock option plan, the common shares that we issued pursuant to the employee stock purchase plan, and the common shares that we issued pursuant to the exercise of warrants will be provided as required in any applicable prospectus supplement.

MARKET FOR SECURITIES

Our common shares are listed and posted for trading on the NYSE under the symbol “ZYME.” Trading price and volume will be provided as required for our common shares in each prospectus supplement to this prospectus.

DESCRIPTION OF SHARE CAPITAL

General

The following description of the common shares and preferred shares summarizes material rights of our common shares and preferred shares, as contained in our notice of articles and articles and any amendments thereto. This summary is not a complete description of the share rights associated with our common shares and preferred shares. For more detailed information, please see the forms of our BCBCA notice of articles and articles, which are filed as exhibits to the registration statement of which this prospectus forms a part.

Share Capital

The Company's authorized share capital consists of an unlimited number of common shares and an unlimited number of preferred shares. As of September 30, 2021, 46,553,960 common shares and no preferred shares were issued and outstanding. Our common shares are listed on the NYSE under the symbol "ZYME."

Common Shares

The shareholders of the Company are entitled to one vote for each common share on all matters to be voted on by the shareholders. Our articles provide for a classified (or staggered) board of directors consisting of three classes of directors, with directors serving staggered three-year terms. Shareholders of the Company are not entitled to cumulative voting in the election of directors. Each common share is equal to every other common share and all common shares participate equally on liquidation, dissolution or winding up of our Company, whether voluntary or involuntary, or any other distribution of our assets among our shareholders for the purpose of winding up our affairs after the Company has paid out its liabilities. There are no limitations on the right of nonresident or foreign owners of the common shares to hold or vote the common shares. The shareholders are entitled to receive pro rata such dividends as may be declared by our board of directors out of funds legally available for such purpose and to receive pro rata the remaining property of the Company upon dissolution. No shares have been issued subject to call or assessment. There are no pre-emptive or conversion rights, and no provisions for redemption, retraction, purchase or cancellation, surrender, sinking fund or purchase fund. Provisions as to the creation, modification, amendment or variation of such rights or such provisions are contained in the BCBCA and the articles of the Company. Generally speaking, substantive changes to our share capital require the approval of the shareholders by special resolution (at least two-thirds of the votes cast).

Dividend Policy

The Company has neither declared nor paid dividends on its common shares. The Company has no present intention of paying dividends on its common shares, as it anticipates that all available funds will be invested to finance the growth of its business.

Preferred Shares

We may issue our preferred shares from time to time in one or more series. The terms of each series of preferred shares, including the number of shares, the designation, rights, preferences, privileges, priorities, restrictions, conditions and limitations, will be determined at the time of creation of each such series by our board of directors, without shareholder approval, provided that all preferred shares will rank equally within their class as to dividends and distributions in the event of our dissolution, liquidation or winding-up.

Advance Notice Policy

Our articles include an advance notice policy (the "Advance Notice Policy"). The Advance Notice Policy provides that any shareholder seeking to nominate a candidate for election as a director (a "Nominating Shareholder") at any annual meeting of the shareholders, or at any special meeting of shareholders if one of the purposes for which the special meeting was called was the election of directors, must give timely notice thereof in proper written form to our Corporate Secretary.

To be timely, a Nominating Shareholder's notice must be made: (i) in the case of an annual meeting of shareholders (including an annual and special meeting), not less than 30 days prior to the date of the annual meeting of shareholders, provided, however, that in the event that the annual meeting of shareholders is to be held on a date that is less than 50 days after the date on which the first public announcement of the meeting was made, notice by the Nominating Shareholder may be made not later than the close of business on the 10th day following the date of such first public announcement; and (ii) in the case of a special meeting of shareholders

(which is not also an annual meeting) called for the purpose of electing directors (whether or not called for other purposes as well), not later than the close of business on the 15th day following the day on which the first public announcement of the date of the special meeting of shareholders was made. The articles also prescribe the proper written form for a Nominating Shareholder's notice.

The chair of the meeting shall have the power and duty to determine whether a nomination was made in accordance with the notice procedures set forth in the articles and, if any proposed nomination is not in compliance with such provisions, the discretion to declare that such defective nomination will be disregarded.

Notwithstanding the foregoing, the Board of Directors may, in their sole discretion, waive any requirement in the Advance Notice Policy.

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 issue 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 specified in an accompanying prospectus supplement. We have summarized select portions of the indenture below. 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. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

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;
- 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 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;
- any obligation we have to redeem or purchase 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 redeemed or purchased, in whole or in part, pursuant to such obligation;
- the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- 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;
- 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 currency of denomination of the debt securities, which may be United States dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;
- 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;
- if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units 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 of, premium, if any, or interest 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 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 addition to, deletion of or change in the covenants 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;

- 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 issue 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 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 under the heading "Global Debt Securities and Book-Entry System" below, 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 depositary, and registered in the name of the depositary or a nominee of the depositary.

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue 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 afford 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 the applicable 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;
- 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, 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 provides 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 provides 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 above under the heading “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 of 1939, as amended (the “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 provides 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 provides 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 under the heading “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 Shareholders

None of our past, present or future directors, officers, employees or shareholders, 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 WARRANTS

General

This section describes the general terms that will apply to any warrants we may issue. We will not offer warrants for sale separately to any member of the public in Canada unless the offering is in connection with and forms part of the consideration for an acquisition or merger transaction or unless the applicable prospectus supplement containing the specific terms of the warrants to be offered separately is first approved for filing by the securities commissions or similar regulatory authorities in each of the provinces and territories of Canada where the warrants will be offered for sale.

Subject to the foregoing, we may issue warrants independently or together with other securities, and warrants sold with other securities may be attached to or separate from the other securities. Warrants will be issued under one or more warrant indentures or warrant agency agreements to be entered into by us and one or more banks or trust companies acting as warrant agent.

This summary of some of the provisions of the warrants is not complete. The statements made in this prospectus relating to any warrant agreement and warrants to be issued under this prospectus are summaries of certain anticipated provisions thereof and do not purport to be complete and are subject to, and are qualified in their entirety by reference to, all provisions of the applicable warrant agreement. You should refer to the warrant indenture or warrant agency agreement relating to the specific warrants being offered for the complete terms of the warrants. A copy of any warrant indenture or warrant agency agreement relating to an offering or warrants will be filed by us with the securities regulatory authorities in Canada and the United States after we have entered into it.

The applicable prospectus supplement relating to any warrants that we offer will describe the particular terms of those warrants and include specific terms relating to the offering.

Original purchasers of warrants (if offered separately) will have a contractual right of rescission against us in respect of the exercise of such warrant. The contractual right of rescission will entitle such original purchasers to receive, upon surrender of the underlying securities acquired upon exercise of the warrant, the total of the amount paid on original purchase of the warrant and the amount paid upon exercise, in the event that this prospectus (as supplemented or amended) contains a misrepresentation, provided that: (i) the exercise takes place within 180 days of the date of the purchase of the warrant under the applicable prospectus supplement; and (ii) the right of rescission is exercised within 180 days of the date of purchase of the warrant under the applicable prospectus supplement. This contractual right of rescission will be consistent with the statutory right of rescission described under section 131 of the *Securities Act* (British Columbia), and is in addition to any other right or remedy available to original purchasers under section 131 of the *Securities Act* (British Columbia) or otherwise at law.

Equity Warrants

The particular terms of each issue of equity warrants will be described in the applicable prospectus supplement. This description will include, where applicable:

- the designation and aggregate number of equity warrants;
- the price at which the equity warrants will be offered;
- the currency or currencies in which the equity warrants will be offered;
- the date on which the right to exercise the equity warrants will commence and the date on which the right will expire;
- the number of common shares or preferred shares that may be purchased upon exercise of each equity warrant and the price at which and currency or currencies in which the common shares or preferred shares may be purchased upon exercise of each equity warrant;

- the terms of any provisions allowing or providing for adjustments in (i) the number and/or class of shares that may be purchased, (ii) the exercise price per share or (iii) the expiry of the equity warrants;
- whether we will issue fractional shares;
- whether we have applied to list the equity warrants or the underlying shares on a stock exchange;
- the designation and terms of any securities with which the equity warrants will be offered, if any, and the number of the equity warrants that will be offered with each security;
- the date or dates, if any, on or after which the equity warrants and the related securities will be transferable separately;
- whether the equity warrants will be subject to redemption and, if so, the terms of such redemption provisions;
- material U.S. and Canadian federal income tax consequences of owning the equity warrants; and
- any other material terms or conditions of the equity warrants.

Debt Warrants

The particular terms of each issue of debt warrants will be described in the related prospectus supplement. This description will include, where applicable:

- the designation and aggregate number of debt warrants;
- the price at which the debt warrants will be offered;
- the currency or currencies in which the debt warrants will be offered;
- the designation and terms of any securities with which the debt warrants are being offered, if any, and the number of the debt warrants that will be offered with each security;
- the date or dates, if any, on or after which the debt warrants and the related securities will be transferable separately;
- the principal amount of debt securities that may be purchased upon exercise of each debt warrant and the price at which and currency or currencies in which that principal amount of debt securities may be purchased upon exercise of each debt warrant;
- the date on which the right to exercise the debt warrants will commence and the date on which the right will expire;
- the minimum or maximum amount of debt warrants that may be exercised at any one time;
- whether the debt warrants will be subject to redemption, and, if so, the terms of such redemption provisions;
- material U.S. and Canadian federal income tax consequences of owning the debt warrants; and
- any other material terms or conditions of the debt warrants.

Prior to the exercise of their warrants, holders of warrants will not have any of the rights of holders of the securities subject to the warrants.

DESCRIPTION OF SUBSCRIPTION RECEIPTS

We may issue subscription receipts that are exchangeable for our equity securities and/or other securities. The particular terms and provisions of subscription receipts offered by any prospectus supplement, and the extent to which the general terms and provisions described below may apply to them, will be described in the applicable prospectus supplement. This description will include, without limitation, where applicable:

- the number of subscription receipts;
- the price at which the subscription receipts will be offered;
- the terms, conditions and procedures for the exchange of the subscription receipts into or for our equity securities and/or other securities;
- the number of our equity securities and/or other securities that may be issued or delivered upon exchange of each subscription receipt; and
- whether the subscription receipts will be issued in fully registered or global form.

Our equity securities and/or other securities issued or delivered upon the exchange of subscription receipts will be issued for no additional consideration.

Original purchasers of subscription receipts will have a contractual right of rescission against us in respect of the conversion of the subscription receipt. The contractual right of rescission will entitle such original purchasers to receive the amount paid on original purchase of the subscription receipt upon surrender of the underlying securities gained thereby, in the event that this prospectus (as supplemented or amended) contains a misrepresentation, provided that: (i) the conversion takes place within 180 days of the date of the purchase of the subscription receipt under this prospectus; and (ii) the right of rescission is exercised within 180 days of the date of purchase of the subscription receipt under this prospectus. This contractual right of rescission will be consistent with the statutory right of rescission described under section 131 of the Securities Act (British Columbia), and is in addition to any other right or remedy available to original purchasers under section 131 of the Securities Act (British Columbia) or otherwise at law.

DESCRIPTION OF UNITS

The following description sets forth certain general terms and provisions of units to which any prospectus supplement may relate.

We may issue units comprised of one or more of the other 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. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued, if any, 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, if any, 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 of this prospectus captioned “Where You Can Find More Information.”

The applicable prospectus supplement may describe:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions 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.

The applicable prospectus supplement will describe the terms of any units. The preceding description and any description of units in the applicable prospectus supplement does not purport to be complete and is subject to and is qualified in its entirety by reference to the unit agreement and, if applicable, collateral arrangements and depositary arrangements relating to such units.

SELLING SECURITYHOLDERS

Information about selling securityholders, where applicable, will be set forth in a prospectus supplement, in a post-effective amendment or in filings we make with the SEC under the Exchange Act which are incorporated by reference into this prospectus.

PLAN OF DISTRIBUTION

We or any selling securityholders may sell the securities offered by this prospectus for cash or other consideration (i) to or through underwriters, dealers, placement agents or other intermediaries, (ii) directly to one or more purchasers or (iii) in connection with acquisitions of assets or shares or another entity or company.

Each prospectus supplement with respect to our securities being offered will set forth the terms of the offering, including:

- the name or names of any underwriters, dealers or other placement agents;
- if applicable, the names of any selling securityholders;
- the number and the purchase price of, and form of consideration for, the securities;
- the proceeds to the Company from such sale;
- any commissions, fees, discounts and other items constituting underwriters', dealers' or agents' compensation;
- all other items constituting underwriting compensation; and
- any exchanges on which the securities will be listed.

The securities may be sold, from time to time, in one or more transactions at a fixed price or prices which may be changed or at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices, including sales in transactions that are deemed to be "at-the-market distributions" in accordance with Rule 415(a)(4) under the Securities Act, including sales made directly on the NYSE or other existing trading markets for the securities. The prices at which the securities may be offered may vary as between purchasers and during the period of distribution. If, in connection with the offering of securities at a fixed price or prices, the underwriters have made a bona fide effort to sell all of the securities at the initial offering price fixed in the applicable prospectus supplement, the public offering price may be decreased and thereafter further changed, from time to time, to an amount not greater than the initial offering price fixed in such prospectus supplement, in which case the compensation realized by the underwriters will be decreased by the amount that the aggregate price paid by purchasers for the securities is less than the gross proceeds paid by the underwriters to us.

Only underwriters named in the prospectus supplement are deemed to be underwriters in connection with our securities offered by that prospectus supplement.

We may agree to pay the underwriters or agents a commission for various services relating to the issue and sale of any securities offered hereby. Where we pay such commission, it will be paid out of the general corporate funds of the Company.

Underwriters, dealers and agents who participate in the distribution of the securities may be entitled to, under agreements to be entered into with us, indemnification by us against certain liabilities, including liabilities under the Securities Act, and Canadian securities legislation, or to contribution with respect to payments which such underwriters, dealers or agents may be required to make in respect thereof. Such underwriters, dealers and agents may be customers of, engage in transactions with, or perform services for, us in the ordinary course of business.

No underwriter or dealer involved in an "at-the-market distribution," no affiliate of such underwriter or dealer and no person acting jointly or in concert with such underwriter or dealer has over-allotted, or will over-allot, our securities in connection with an offering of the securities or effect any other transactions that are intended to stabilize the market price of our securities.

In connection with any offering of securities, other than an "at-the-market distribution," the underwriters may over-allot or effect transactions which stabilize or maintain the market price of the securities offered at a level above that which might otherwise prevail in the open market. Such transactions, if commenced, may be discontinued 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.

CANADIAN AND U.S. FEDERAL INCOME TAX CONSIDERATIONS

Information regarding material Canadian and U.S. federal income tax consequences to persons investing in the securities offered by this prospectus will be set forth in an applicable prospectus supplement. You should consult your own tax advisors prior to any acquisition of our securities.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon on behalf of the Company by Blake, Cassels & Graydon LLP with respect to Canadian legal matters, and by Wilson Sonsini Goodrich & Rosati, P.C. with respect to U.S. legal matters. Additional legal matters may be passed on for us, or any underwriters, dealers or agents by counsel we will name in the applicable prospectus supplement.

AUDITORS, TRANSFER AGENT AND REGISTRAR

KPMG LLP was reappointed as our auditor at our annual meeting of shareholders held on May 5, 2021. KPMG LLP is located at 900 – 777 Dunsmuir Street, P.O. Box 10426 Pacific Centre, Vancouver, British Columbia, Canada, V7Y 1K3. KPMG LLP has reported on our 2020, 2019 and 2018 audited consolidated financial statements, which have been filed with the securities regulatory authorities and incorporated by reference herein. KPMG LLP are the auditors of the Company and have confirmed with respect to the Company that they are independent within the meaning of the relevant rules and related interpretations prescribed by the relevant professional bodies in Canada and any applicable legislation or regulations.

Our transfer agent and the registrar for our common shares in Canada is Computershare Investor Services Inc. located at 100 University Avenue, 8th Floor, Toronto, Ontario, Canada, M5J 2Y1 and, in the United States is Computershare Trust Company, N.A. located at 1011-250 Royall Street, Canton, Massachusetts, USA 02021.

INTEREST OF EXPERTS

The consolidated financial statements of Zymeworks as of December 31, 2020 and 2019, and for each of the years in the three-year period ended December 31, 2020, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2020 have been incorporated by reference herein in reliance upon the report 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.

The audit report covering the consolidated financial statements as of December 31, 2020 and 2019 and for each of the years in the three-year period ended December 31, 2020, refers to a change in our accounting policies as of January 1, 2019 due to the adoption of ASC 842 — *Leases*.

DOCUMENTS INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" information we file with the SEC. This means that we can disclose important information to you by referring you to those documents. Any information we reference in this manner is considered part of this prospectus, except for any information superseded by information contained directly in this prospectus, any accompanying prospectus supplement or any subsequently filed document deemed to be incorporated by reference. Copies of the documents incorporated by reference in this prospectus may be obtained on written or oral request without charge from the Secretary of the Company at 1385 West 8th Avenue, Suite 540, Vancouver, British Columbia, Canada V6H 3V9. Copies of documents incorporated by reference in this prospectus may also be requested by telephone at 604-678-1388. We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains an internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, where our SEC filings are also available. The address of the SEC's website is http://www.sec.gov. We maintain a website at http://www.zymeworks.com. The references to our website in this prospectus or the documents incorporated by reference herein are inactive textual references only and information contained in or accessible through our website does not constitute a part of this prospectus.

We incorporate by reference the documents listed below and future filings we make with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (excluding, unless otherwise provided therein or herein, documents not deemed "filed" with the SEC and information furnished pursuant to Item 2.02 and Item 7.01 on any Current Report on Form 8-K or certain exhibits furnished pursuant to Item 9.01 of Form 8-K) after the date of the initial filing of this registration statement on Form S-3 to which this prospectus relates until the termination of any offering under this prospectus or such time as all securities offered by this prospectus have been sold and all conditions to the consumption of such sales have been satisfied.

(a) annual report on Form 10-K for the fiscal year ended December 31, 2020, filed with the SEC on February 24, 2021;

(b) quarterly reports on Form 10-Q for the quarterly periods ended March 31, 2021 and June 30, 2021, filed with the SEC on May 5, 2021 and August 4, 2021, respectively;

(c) current reports on Form 8-K, filed with the SEC on April 19, 2021, May 6, 2021, May 18, 2021 and September 16, 2021;

(d) the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on March 23, 2021;

(e) The description of our common shares contained in our registration statement on Form 8-A, filed on April 24, 2017, including any amendments or reports filed for the purpose of updating such description; and

(f) 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, 2020, but before the end of the offering of the securities made by this prospectus.

WHERE YOU CAN FIND MORE INFORMATION

We are required to file with the securities commission or authority in each of the provinces and territories of Canada annual and quarterly reports, material change reports and other information. You may read any document we file with or furnish to the securities commissions and authorities of the provinces and territories of Canada through SEDAR at https://www.sedar.com.

We file annual, quarterly and other 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 http://www.sec.gov. Our annual report on Form 10-K, quarterly reports on Form 10-Q, and current reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge through the Internet. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

We maintain a website at http://www.zymeworks.com. The references to our website in this prospectus or the documents incorporated by reference herein are inactive textual references only and information contained in or accessible through our website does not constitute 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.

ENFORCEABILITY OF CIVIL LIABILITIES

We are a corporation existing under the BCBCA. Some of our directors, officers and the experts named in this prospectus are residents of Canada or otherwise reside outside the United States, and all or a substantial portion of their assets may be, and a substantial portion our assets are, located outside the United States. We have appointed an agent for service of process in the United States, but it may be difficult for holders of common shares who reside in the United States to effect service within the United States upon those directors, officers and experts who are not residents of the United States. It may also be difficult for holders of common shares who reside in the United States to realize in the United States upon judgments of courts of the United States predicated upon our civil liability and the civil liability of our directors, officers and experts under the U.S. federal securities laws. We have been advised by our Canadian counsel, Blake, Cassels & Graydon LLP, that a judgment of a U.S. court for a sum certain predicated solely upon civil liability under U.S. federal securities laws or the securities or ‘‘blue sky’’ laws of any state within the United States, would probably be enforceable in Canada if the U.S. court in which the judgment was obtained has a basis for jurisdiction in the matter that would be recognized by a Canadian court and: (1) the U.S. court rendering such judgment had jurisdiction over the judgment debtor, as recognized by the courts of the Province of British Columbia; (2) proper service of process in respect of the proceedings in which such judgment was obtained was made in accordance with applicable U.S. federal or state law; (3) such judgment was not obtained by fraud or in a manner contrary to natural justice and the enforcement thereof would not be inconsistent with public policy, as such terms are understood under the laws of the Province of British Columbia and the federal laws of Canada or contrary to any order or regulation under the Foreign Extraterritorial Measures Act (Canada), the United Nations Act (Canada) or the Special Economic Measures Act (Canada), or any order made by the Competition Tribunal under the Competition Act(Canada); (4) the enforcement of such judgment would not be contrary to the laws of general application limiting the enforcement of creditors’ rights, including bankruptcy, reorganization, winding-up, moratorium and similar laws, and does not constitute, directly or indirectly, the enforcement of foreign laws which a court in the Province of British Columbia would characterize as revenue, expropriatory or penal laws; (5) in an action to enforce a default judgment, the judgment does not contain a manifest error on its face; (6) the action to enforce such judgment is commenced within the appropriate limitation period under the laws of the Province of British Columbia and is commenced and maintained in accordance with the procedural requirements of British Columbia law; (7) interest payable on the debt securities is not characterized by a court in the Province of British Columbia as interest payable at a criminal rate within the meaning of Section 347 of the Criminal Code (Canada); and (8) the judgment does not conflict with another final and conclusive judgment in the same cause of action; except that a court in the Province of British Columbia may stay an action to enforce a foreign judgment if an appeal of a judgment is pending or time for appeal has not expired; and except that any court in the Province of British Columbia may give judgment only in Canadian dollars. We have also been advised by Blake, Cassels & Graydon LLP, however, that there is substantial doubt whether an action could be brought in Canada in the first instance on the basis of liability predicated solely upon U.S. federal securities laws. See “Risk Factors.”

9,160,000 Common Shares
Pre-funded Warrants to Purchase 3,340,000 Common Shares

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

Jefferies **Evercore ISI** **Stifel** **Wells Fargo Securities**

Lead Co-Manager

Raymond James

January 26, 2022