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

AMENDMENT NO. 2

to

**FORM F-10
REGISTRATION STATEMENT**

*UNDER
THE SECURITIES ACT OF 1933*

ZYMEWORKS INC.

(Exact name of Registrant as specified in its charter)

British Columbia, Canada
(Province or other Jurisdiction
of Incorporation or Organization)

2834
(Primary Standard Industrial
Classification Code Number)

47-2569713
(I.R.S. Employer
Identification No.)

**Suite 540 – 1385 West 8th Avenue
Vancouver, British Columbia
Canada V6H 3V9
(604) 678-1388**

(Address and telephone number of Registrant's principal executive offices)

**The Corporation Trust Company
Corporation Trust Center
1209 Orange Street
Wilmington, DE 19801
(302) 658-7581**

(Name, address and telephone number of agent for service in the United States)

Copies to:

Riccardo A. Leofanti, Esq.
Skadden, Arps, Slate, Meagher & Flom LLP
222 Bay Street, Suite 1750, P.O. Box 258
Toronto, Ontario, Canada M5K 1J5
(416) 777-4700

Joseph A. Garcia
Jamie Kariya
Blake, Cassels & Graydon LLP
595 Burrard Street, Suite 2600
Vancouver, British Columbia, Canada V7X 1L3
(604) 631-3300

Approximate date of commencement of proposed sale of the securities to the public:
From time to time after this Registration Statement becomes effective.

Province of British Columbia, Canada
(Principal jurisdiction regulating this offering)

It is proposed that this filing shall become effective (check appropriate box):

- A. Upon filing with the Commission, pursuant to Rule 467(a) (if in connection with an offering being made contemporaneously in the United States and Canada).
- B. At some future date (check the appropriate box below):
- pursuant to Rule 467(b) on () at ().
 - pursuant to Rule 467(b) on () at () because the securities regulatory authority in the review jurisdiction has issued a receipt or notification of clearance on ().
 - pursuant to Rule 467(b) as soon as practicable after notification of the Commission by the Registrant or the Canadian securities regulatory authority of the review jurisdiction that a receipt or notification of clearance has been issued with respect hereto.
 - after the filing of the next amendment to this Form (if preliminary material is being filed).

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to the home jurisdiction's shelf prospectus offering procedures, check the following box.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registration Statement shall become effective as provided in Rule 467 under the Securities Act or on such date as the Commission, acting pursuant to Section 8(a) of the Securities Act, may determine.

PART I

INFORMATION REQUIRED TO BE DELIVERED TO OFFEREEES OR PURCHASERS

[Table of Contents](#)

This short form prospectus is a base shelf prospectus. This short form prospectus has been filed under legislation in all provinces and territories of Canada that permits certain information about these securities to be determined after this prospectus has become final and that permits the omission from this prospectus of that information. The legislation requires the delivery to purchasers of a prospectus supplement containing the omitted information within a specified period of time after agreeing to purchase any of these securities.

No securities regulatory authority has expressed an opinion about these securities and it is an offence to claim otherwise. This preliminary short form prospectus constitutes a public offering of these securities only in those jurisdictions where they may be lawfully offered for sale and therein only by persons permitted to sell such securities.

Information has been incorporated by reference in this short form prospectus from documents filed with securities commissions or similar authorities in Canada. Copies of the documents incorporated herein by reference may be obtained on request without charge from the Corporate Secretary of Zymeworks Inc. at 1385 West 8th Avenue, Suite 540, Vancouver, BC, Canada, V6H 3V9, telephone: (604) 678-1388, and are also available electronically at www.sedar.com and www.sec.gov.

SHORT FORM BASE SHELF PROSPECTUS

New Issue and Secondary Offering

May 24, 2018



ZYMEWORKS INC.

US\$250,000,000

Common Shares

Preferred Shares

Debt Securities

Warrants

Subscription Receipts

Units

This prospectus relates to the offering for sale from time to time, during the 25-month period that this prospectus, including any amendments hereto, remains effective, of the securities listed above in one or more series or issuances, with a total offering price of such securities, in the aggregate, of up to US\$250,000,000. The securities may be offered by us or by our securityholders. The securities may be offered separately or together, in amounts, at prices and on terms to be determined based on market conditions at the time of the sale and set forth in an accompanying prospectus supplement.

Our common shares are listed on the New York Stock Exchange (“NYSE”) and on the Toronto Stock Exchange (“TSX”) under the symbol “ZYME”. On May 23, 2018, the closing price per share of our common shares was US\$17.80 on the NYSE and C\$23.00 on the TSX. Unless otherwise specified in an applicable prospectus supplement, our preferred shares, debt securities, warrants, subscription receipts and units will not be listed on any securities or stock exchange or on any automated dealer quotation system. **There is currently no market through which our securities, other than our common shares, may be sold and purchasers may not be able to resell such securities purchased under this prospectus. This may affect the pricing of our securities, other than our common shares, in the secondary market, the transparency and availability of trading prices, the liquidity of these securities and the extent of issuer regulation.** See “Risk Factors”.

Our head office is located at 1385 West 8th Avenue, Suite 540, Vancouver, BC, Canada, V6H 3V9 and our registered office is located at Suite 2600, 595 Burrard Street, Three Bentall Centre, Vancouver, British Columbia, Canada, V7X 1L3.

(cover page continued on next page)

[Table of Contents](#)

All information permitted under securities legislation to be omitted from this prospectus will be contained in one or more prospectus supplements that will be delivered to purchasers together with this prospectus. Each prospectus supplement will be incorporated by reference into this prospectus for the purposes of securities legislation as of the date of the prospectus supplement and only for the purposes of the distribution of the securities to which the prospectus supplement pertains. You should read this prospectus and any applicable prospectus supplement carefully before you invest in any securities issued pursuant to this prospectus. Our securities may be sold pursuant to this prospectus through underwriters or dealers or directly or through agents designated from time to time at amounts and prices and other terms determined by us or any selling securityholders. In connection with any underwritten offering of securities, the underwriters may over-allot or effect transactions which stabilize or maintain the market price of the securities offered. Such transactions, if commenced, may discontinue at any time. See “Plan of Distribution”. A prospectus supplement will set out the names of any underwriters, dealers, agents or selling securityholders involved in the sale of our securities, the amounts, if any, to be purchased by underwriters, the plan of distribution for such securities, including the net proceeds we expect to receive from the sale of such securities, if any, the amounts and prices at which such securities are sold and the compensation of such underwriters, dealers or agents.

Investing in our securities involves a high degree of risk. You should carefully read the “[Risk Factors](#)” section beginning on page 16 of this prospectus.

We are permitted under a multijurisdictional disclosure system adopted by the securities regulatory authorities in Canada and the United States to prepare this prospectus in accordance with the disclosure requirements of Canada. Prospective investors in the United States should be aware that such requirements are different from those of the United States.

Effective January 1, 2014, we adopted United States generally accepted accounting principles (“U.S. GAAP”) as the reporting standard for our consolidated financial statements and changed our reporting currency from Canadian dollars to U.S. dollars. Accordingly, the presentation of financial statements may vary in a material way from financial statements prepared in accordance with International Financial Reporting Standards. Unless otherwise indicated, all dollar amounts and references to “\$” in our financial statements are to U.S. dollars.

Owning our securities may subject you to tax consequences both in Canada and the United States. Such tax consequences are not described in this prospectus and may not be fully described in any applicable prospectus supplement. You should read the tax discussion in any prospectus supplement with respect to a particular offering and consult your own tax advisor with respect to your own particular circumstances.

Your ability to enforce civil liabilities under U.S. federal securities laws may be affected adversely because we are incorporated under the laws of British Columbia, most of our officers, some of our directors and the experts named in this prospectus are Canadian residents, and a substantial portion of our assets and the assets of those officers, directors and experts are located outside of the United States.

Neither the U.S. Securities and Exchange Commission (the “SEC”), nor any state securities regulator has approved or disapproved the securities offered hereby or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offence.

No underwriter has been involved in the preparation of this prospectus or performed any review of the contents of this prospectus.

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS	1
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS	1
DOCUMENTS INCORPORATED BY REFERENCE	5
DOCUMENTS FILED AS PART OF THE REGISTRATION STATEMENT	7
EXCHANGE RATE INFORMATION	8
ZYMWORKS INC.	9
OUR BUSINESS	10
RISK FACTORS	16
USE OF PROCEEDS	61
PRIOR SALES	62
MARKET FOR SECURITIES	64
EARNINGS COVERAGE	65
CONSOLIDATED CAPITALIZATION	66
DESCRIPTION OF SHARE CAPITAL	67
DESCRIPTION OF DEBT SECURITIES	68
DESCRIPTION OF WARRANTS	80
DESCRIPTION OF SUBSCRIPTION RECEIPTS	82
DESCRIPTION OF UNITS	83
CERTAIN INCOME TAX CONSIDERATIONS	84
SELLING SECURITYHOLDERS	85
PLAN OF DISTRIBUTION	86
AUDITORS, TRANSFER AGENT AND REGISTRAR	89
AGENT FOR SERVICE OF PROCESS	90
LEGAL MATTERS	91
WHERE YOU CAN FIND MORE INFORMATION	91
ENFORCEABILITY OF CIVIL LIABILITIES	92

ABOUT THIS PROSPECTUS

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,” “Celgene,” “GSK,” “Daiichi Sankyo” and “Janssen” refer to Merck Sharp & Dohme Research Ltd., Eli Lilly and Company, Celgene Corporation and Celgene Alpine Investment Co. LLC, GlaxoSmithKline Intellectual Property Development Limited, Daiichi Sankyo Co., Ltd. and Janssen Biotech, Inc., respectively.

The names Azymetric, Zymeworks, ZymeCAD and the phrase “Building Better Biologics” are our registered trademarks. Additionally, AlbuCORE, EFECT and ZymeLink are subject to our pending trademark applications. 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.

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. Many of these statements appear, in particular, under the headings “Risk Factors” and “Our Business.” 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,

Table of Contents

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 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; and
- our ability to predict and manage government regulation.

All forward-looking statements, including, without limitation, 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;
- 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 set forth under “Risk Factors”), 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 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;
- 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;
- our ability to face significant competition;
- 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;

[Table of Contents](#)

- the competitive threat of 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;
- 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;
- 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 exposure to potential securities class action litigation;
- 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;
- unstable market and economic conditions;
- currency fluctuations and changes in foreign currency exchange rates;
- restrictions on our ability to seek financing, which may be imposed by future debt;
- our intention to rely on third-party manufacturers to produce our clinical product candidate supplies;
- our reliance on third parties to oversee clinical trials of our product candidates and, in some cases, maintain regulatory files for those product candidates;

[Table of Contents](#)

- our reliance on the performance of independent clinical investigators and contract research organizations (“CRO”);
- 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;
- we may be unable to protect the confidentiality of our proprietary information;
- the risk that the duration of our patents will not adequately protect our competitive position;
- our ability to obtain protection under the Hatch-Waxman Amendments and similar foreign legislation;
- 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 Food and Drug Association (“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;
- 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;
- our ability to retain key executives and attract and retain qualified personnel;
- our ability to manage organizational growth; and
- additional costs and expenses related to the anticipated change from foreign private issuer to U.S. domestic issuer status and our decision to voluntarily comply with certain U.S. domestic issuer reporting obligations before we are required to do so.

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.

DOCUMENTS INCORPORATED BY REFERENCE

Information has been incorporated by reference in this prospectus from documents filed with securities commissions or similar authorities in Canada which have also been filed with, or furnished to, the SEC. Copies of the documents incorporated by reference in this prospectus and not delivered with this prospectus may be obtained on request without charge from the Corporate Secretary of Zymeworks Inc. at 1385 West 8th Avenue, Suite 540, Vancouver, BC, Canada, V6H 3V9, telephone: (604) 678-1388 or by accessing the disclosure documents through the Internet on SEDAR, at www.sedar.com. Documents filed with, or furnished to, the SEC are available through EDGAR, at www.sec.gov.

The following documents, filed with the securities commissions or similar regulatory authorities in each of the provinces and territories of Canada and filed with, or furnished to, the SEC are specifically incorporated by reference into, and form an integral part of, this prospectus:

- our annual report on Form 10-K dated March 14, 2018 for the fiscal year ended December 31, 2017;
- our audited consolidated financial statements as at and for the year ended December 31, 2017, together with the notes thereto and the auditor's reports thereon;
- our management's discussion and analysis of our financial condition and results of operations for the year ended December 31, 2017;
- our quarterly report on Form 10-Q dated May 1, 2018 for the three month period ended March 31, 2018;
- our unaudited interim consolidated financial statements as at and for the three month periods ended March 31, 2018 and 2017;
- our management's discussion and analysis of our financial condition and results of operations for the three month period ended March 31, 2018;
- our management information circular dated May 2, 2018, distributed in connection with our annual general meeting of shareholders to be held on June 7, 2018, as filed on SEDAR on May 16, 2018;
- our Current Reports on Form 8-K dated March 14, April 17, April 23, April 25, April 30, May 1, May 10, May 16 and May 18, 2018, respectively; and
- each of the following material change reports:
 - (i) our report dated March 20, 2018 with respect to the Company's announcement that ZW49 is the first product candidate selected for clinical development utilizing the ZymeLink antibody drug conjugate platform;
 - (ii) our report dated April 17, 2018 with respect to preclinical data on ZW49;
 - (iii) our report dated April 24, 2018 with respect to Celgene Corporation having exercised its right to expand its collaboration agreement for the research, development, and commercialization of bispecific antibody therapeutics using Zymeworks' Azymetric platform;
 - (iv) our report dated April 25, 2018 regarding the abstract highlighting new data from the Company's adaptive Phase 1 clinical trial for ZW25 being selected for an oral presentation at the American Society of Clinical Oncology; and
 - (v) our report dated May 18, 2018 regarding a new license agreement with Daiichi Sankyo pursuant to which Daiichi Sankyo will acquire licenses to the Company's Azymetric and EFECT platforms to develop two additional bispecific antibody therapeutics.

Any documents of the type described in Section 11.1 of Form 44-101F1 *Short Form Prospectuses* filed by the Company with a securities commission or similar authority in any province or territory of Canada subsequent to the date of this short form prospectus and prior to the expiry of this prospectus, or the completion of the issuance of securities pursuant hereto, will be deemed to be incorporated by reference into this prospectus.

[Table of Contents](#)

In addition, to the extent that any document or information incorporated by reference into this prospectus is filed with the SEC pursuant to the *U.S. Securities Exchange Act of 1934*, as amended (the “Exchange Act”), after the date of this prospectus, such document or information will be deemed to be incorporated by reference as an exhibit to the registration statement of which this prospectus forms a part, except that we are not incorporating any information included in a Current Report on Form 8-K that has been or will be furnished (and not filed) with the SEC, unless such information is expressly incorporated herein.

A prospectus supplement containing the specific terms of any offering of our securities will be delivered to purchasers of our securities together with this prospectus and will be deemed to be incorporated by reference in this prospectus as of the date of the prospectus supplement and only for the purposes of the offering of our securities to which that prospectus supplement pertains.

Any statement contained in this prospectus or in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained herein or in any other subsequently filed document that also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. The modifying or superseding statement need not state that it has modified or superseded a prior statement or include any other information set forth in the document that it modifies or supersedes. The making of a modifying or superseding statement is not to be deemed an admission for any purposes that the modified or superseded statement, when made, constituted a misrepresentation, an untrue statement of material fact or an omission to state a material fact that is required to be stated or is necessary to make a statement not misleading in light of the circumstances in which it was made. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

Upon our filing of a new annual report on Form 10-K and the related annual financial statements and management’s discussion and analysis with applicable securities regulatory authorities during the currency of this prospectus, the previous annual report on Form 10-K, the previous annual financial statements and management’s discussion and analysis and all quarterly financial statements, supplemental information, material change reports and information circulars filed prior to the commencement of our financial year in which the new annual report on Form 10-K is filed will be deemed no longer to be incorporated into this prospectus for purposes of future offers and sales of our securities under this prospectus. Upon interim consolidated financial statements and the accompanying management’s discussion and analysis and material change reports being filed by us with the applicable securities regulatory authorities during the duration of this prospectus, all interim consolidated financial statements and the accompanying management’s discussion and analysis and material change reports filed prior to the new interim consolidated financial statements shall be deemed no longer to be incorporated into this prospectus for purposes of future offers and sales of securities under this prospectus.

References to our website in any documents that are incorporated by reference into this prospectus do not incorporate by reference the information on such website into this prospectus, and we disclaim any such incorporation by reference.

DOCUMENTS FILED AS PART OF THE REGISTRATION STATEMENT

The following documents have been or will be filed with the SEC as part of the registration statement of which this prospectus forms a part: (i) the documents listed under the heading "Documents Incorporated by Reference"; (ii) powers of attorney from our directors and officers; (iii) the consent of KPMG LLP; and (iv) the form of indenture relating to the debt securities that may be issued under this prospectus. A copy of the form of warrant agreement or subscription receipt agreement, as applicable, will be filed by post-effective amendments or by incorporation by reference to documents filed or furnished with the SEC under the Exchange Act.

EXCHANGE RATE INFORMATION

We express all amounts in this prospectus 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 noon exchange rate (for dates prior to March 1, 2017) or the Bank of Canada daily exchange rate (for dates on or after March 1, 2017). As of May 1, 2017, the Bank of Canada no longer publishes updated data for exchange rates published under previous methodologies, including daily noon and closing rates as well as high and low exchange rates.

	Year Ended December 31,			Three Months Ended March 31,	
	2015	2016	2017	2017	2018
Highest rate during the period	1.3990	1.4589	1.3743	1.3513	1.3088
Lowest rate during the period	1.1728	1.2544	1.2128	1.3016	1.2288
Average exchange rate for the period ⁽¹⁾	1.2907	1.3231	1.2986	1.3238	1.2647
Rate at the end of the period	1.3840	1.3427	1.2545	1.3310	1.2894

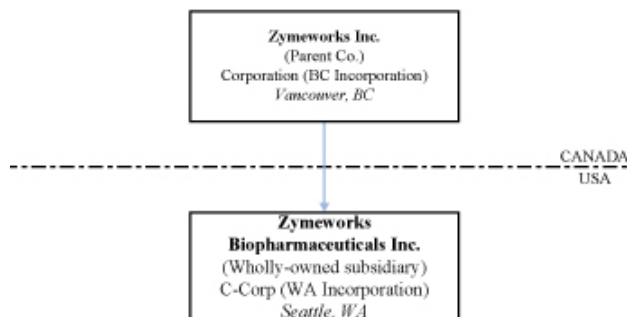
(1) Determined by averaging the rates on the last day of each month during the respective period.

On March 29, 2018, the Bank of Canada daily average rate of exchange was \$1.00 = C\$1.2894. On May 23, 2018, the Bank of Canada daily average rate of exchange was \$1.00 = C\$1.2876.

ZYMEWORKS INC.

We were incorporated on September 8, 2003 under the *Canada Business Corporations Act* (“CBCA”), 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) (“BCBCA”). Zymeworks continued to the BCBCA on May 2, 2017.

The following reflects our organizational structure. We have one wholly-owned subsidiary located in Seattle, Washington named Zymeworks Biopharmaceuticals Inc. Effective as of January 1, 2017, we completed a short-form amalgamation with our other previously wholly-owned subsidiary, Zymeworks Biochemistry Inc.



Our principal and registered office is located at 1385 West 8th Avenue, Suite 540, Vancouver, British Columbia, Canada V6H 3V9, and our telephone number is (604) 678-1388. Our website address is www.zymeworks.com. Information contained on, or accessible through, our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference.

OUR BUSINESS

Zymeworks is an innovative, clinical-stage biopharmaceutical company dedicated to the discovery, development and commercialization 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 wholly owned product candidates with the potential to drive superior outcomes in large underserved and unaddressed patient populations, as further described below.

Initial Public Offering

On May 3, 2017, we successfully closed our initial public offering (the “IPO”) pursuant to which we sold 4,894,467 common shares (including the sale of 394,467 common shares to the underwriters upon their partial exercise of their over-allotment option to purchase additional common shares on May 31, 2017). The public offering price of the common shares sold in the IPO was \$13.00 per share. We received net proceeds of approximately \$54.2 million, after underwriting discounts, commissions and estimated offering expenses. The common shares are listed for trading on the NYSE and the TSX under the symbol “ZYME”.

Description of Business and Products

Our lead product candidate, ZW25, is a novel bispecific antibody which targets two distinct domains of the human epidermal growth factor receptor 2, or HER2. In our adaptive Phase 1 clinical trial, ZW25 has been well tolerated with promising single agent anti-tumor activity in patients with heavily pretreated HER2-expressing cancers that have progressed after standard of care, including multiple HER2-targeted regimens. Its unique design may enable ZW25 to address patient populations with all levels of HER2 expression, including those with low to intermediate HER2-expressing tumors, who are otherwise limited to chemotherapy or hormone therapy. Our second product candidate, ZW49, capitalizes on the unique design and antibody framework of ZW25 and is a bispecific antibody-drug conjugate, or ADC, armed with our proprietary ZymeLink-cytotoxic payload. We designed ZW49 to be a best-in-class HER2-targeting ADC with a wide therapeutic window, for which we expect to file an Investigational New Drug, or IND, application in 2018. We are also advancing a deep pipeline of preclinical product candidates and discovery-stage programs in immuno-oncology and other therapeutic areas. In addition to our wholly owned pipeline, two of our therapeutic platforms have been further leveraged through multiple revenue-generating strategic partnerships with the following global pharmaceutical companies: Merck Sharp & Dohme Research Ltd., Eli Lilly and Company, Celgene Corporation and Celgene Alpine Investment Co. LLC, GlaxoSmithKline Intellectual Property Development Limited, Daiichi Sankyo Co., Ltd., and Janssen Biotech, Inc. or “Merck”, “Lilly”, “Celgene”, “GSK”, “Daiichi Sankyo” and “Janssen”, respectively.

Our proprietary capabilities and technologies include four modular, complementary therapeutic platforms that can be easily 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 superior patient outcomes. Our core platforms include Azymetric, ZymeLink, EFECT and AlbuCORE. 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 that is capable of rapidly delivering a steady pipeline of next-generation product candidates in oncology and other therapeutic areas.

We commenced active 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

[Table of Contents](#)

product sales 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. We have financed our operations primarily through private equity placements, an issuance of convertible debentures, payments received under license and collaboration agreements, government grants and Scientific Research and Experimental Development, or SR&ED, tax credits and a credit facility as well as our IPO in 2017. From inception through March 31, 2018, we received approximately \$200.2 million, net of share issue costs, from private equity placements, the issuance of convertible debt, which subsequently converted into equity securities, and our IPO. Payments received from our license and collaboration agreements include upfront fees and milestone payments as well as research support and reimbursement payments through our strategic partnerships and government grants. 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 March 31, 2018, combined with the collaboration payments we anticipate receiving, will enable us to fund the clinical and preclinical development of our lead product candidates for at least the next twelve months.

Through March 31, 2018, we had an accumulated deficit of \$130.0 million. We reported a net loss of \$21.2 million for the three months ended March 31, 2018. We expect that over the next several years we will increase our research and development expenditures in connection with the ongoing development of our product candidates and other clinical, preclinical and regulatory activities.

Strategic Partnerships and Collaborations

Our unique combination of proprietary protein engineering capabilities and resulting therapeutic platform technologies was initially recognized by Merck and Lilly, with whom we established strategic partnerships focused on our Azymetric and EFECT therapeutic platforms. We subsequently entered into broader strategic partnerships with Celgene and GSK and a collaboration and cross-licensing agreement with Daiichi Sankyo. Following the completion of the initial agreements with Merck, Lilly and GSK, the relationships were subsequently expanded to include either additional licenses or therapeutic platforms. Most recently, we executed a licensing and collaboration agreement with Janssen to develop and commercialize next generation bispecific antibody therapeutics. These relationships provide our strategic partners with access to components of our proprietary Azymetric and EFECT therapeutic platforms for their development of a defined number of protein therapeutics, for which we will not have ownership. These strategic partnerships have provided us with non-dilutive funding as well as access to proprietary therapeutic assets, which increase our ability to rapidly advance our product candidates while maintaining worldwide commercial rights to our wholly-owned therapeutic pipeline. Our strategic partnerships include the following:

Research and License Agreement with Merck

In August 2011, we entered into a research and license agreement with Merck, which was amended and restated in December 2014, to develop and commercialize three bispecific antibodies generated through the use of the Azymetric and EFECT platforms. Under the terms of the agreement, we granted Merck a worldwide, royalty-bearing antibody sequence pair exclusive license to research, develop and commercialize certain licensed products. We are eligible to receive up to \$190.75 million, including an upfront payment (\$1.25 million received in 2011), research milestone payments totaling \$3.5 million (\$2.0 million and \$1.5 million received in 2012 and 2013, respectively), payments for completion of IND-enabling studies of up to \$6.0 million, development milestone payments of up to \$66.0 million and commercial milestone payments of up to \$114.0 million. In addition, we are eligible to receive tiered royalties in the low to mid-single digits on product sales, with the royalty term being, on a product-by-product and country-by-country basis, either (i) for as long as there is Zymeworks patent coverage on products, or (ii) for five years, beginning from the first commercial sale, whichever period is longer. If there is no Zymeworks patent coverage on products, royalty rates will be reduced.

Under the agreement, we are sharing certain research and development responsibilities with Merck to generate bispecific antibodies with the Azymetric and EFECT platforms. Merck provides funding for a portion of our

internal and external research costs in support of the collaboration. After the conclusion of the research program, Merck will be solely responsible for the further research, development, manufacturing and commercialization of the products.

Licensing and Collaboration Agreement with Lilly

In December 2013, we entered into a licensing and collaboration agreement with Lilly to research, develop and commercialize one bispecific antibody, with an option for a second antibody, generated through the use of the Azymetric platform. Under the terms of the agreement, we granted Lilly a worldwide, royalty-bearing antibody target pair-specific exclusive license to research, develop and commercialize certain licensed products. We are eligible to receive up to \$103.0 million, including an upfront payment (\$1.0 million received in 2013) and per product potential milestone payments, comprised of research milestone payments totaling \$1.0 million (\$1.0 million received in 2015), IND submission milestone payments of \$2.0 million, development milestone payments of \$8.0 million and commercial milestone payments of \$40 million. In addition, we are eligible to receive tiered royalties in the low to mid-single digits on product sales, with the royalty term being, on a product-by-product and country-by-country basis, either (i) for as long as there is Zymeworks platform patent coverage on products, or (ii) for 10 years, beginning from the first commercial sale, whichever period is longer. If there is no Zymeworks patent coverage on products, royalty rates may be potentially reduced. In 2017, Lilly nominated a bispecific candidate from this agreement for preclinical development.

Under the agreement, we are sharing certain research and development responsibilities with Lilly to generate bispecific antibodies with the Azymetric platform. Lilly provides funding for a portion of our internal and external research costs in support of the collaboration. After the conclusion of the research program, Lilly will be solely responsible for the further research, development, manufacturing, and commercialization of the products.

Second Licensing and Collaboration Agreement with Lilly

In October 2014, we entered into a second licensing and collaboration agreement with Lilly to research, develop and commercialize three bispecific antibodies generated through the use of the Azymetric platform. This agreement did not alter or amend the initial agreement entered in 2013. Under the terms of the agreement, we granted Lilly a worldwide, royalty-bearing antibody target-pair exclusive (for two bispecific antibodies) and an antibody sequence pair-specific (for one bispecific antibody) license to research, develop and commercialize certain licensed products. In 2017, Lilly nominated a bispecific candidate from this agreement for preclinical development and discontinued the development of two other bispecific antibodies due to strategic portfolio realignment in those particular disease areas. We are currently eligible to receive up to \$125.0 million, comprised of research milestone payments of up to \$2.0 million (\$2.0 million earned in 2016), IND submission milestone payments of up to \$8.0 million, development milestone payments of up to \$20.0 million and commercial milestone payments of up to \$95.0 million. In addition, we are eligible to receive tiered royalties in the low to mid-single digits on product sales, with the royalty term being, on a product-by-product and country-by-country basis, either (i) for as long as there is Zymeworks platform patent coverage on products, or (ii) for 10 years, beginning from the first commercial sale, whichever period is longer. If there is no Zymeworks patent coverage on products, royalty rates may be potentially reduced. In conjunction with this collaboration agreement, Lilly purchased approximately \$24.0 million of our common shares.

Under the agreement, we are sharing certain research and development responsibilities with Lilly to generate bispecific antibodies with the Azymetric platform. We are responsible for our internal and external research costs in support of this collaboration. After the conclusion of the research program, Lilly will be solely responsible for the further research, development, manufacturing and commercialization of the products.

Licensing and Collaboration Agreement with Celgene

In December 2014, we entered into a collaboration agreement with Celgene to research, develop and commercialize up to eight bispecific antibodies generated through the use of the Azymetric platform. Under the

[Table of Contents](#)

terms of the agreement, we granted Celgene a right to exercise options to worldwide, royalty-bearing, antibody sequence pair-specific exclusive licenses to research, develop and commercialize certain licensed products. We received an upfront payment of \$8.0 million, which was accounted for as upfront collaboration consideration received in 2014. In April 2018, Celgene exercised its right to increase the number of programs under this collaboration from eight to ten and extended the research program term by 24 months until April 2020, for which are entitled to receive \$4.0 million in accordance with the terms of the collaboration agreement. As a result, Celgene has the right to exercise options on up to ten programs and if Celgene opts in on a program, we are eligible to receive up to \$164.0 million per product candidate (up to \$1.64 billion for all ten programs), comprised of a commercial license option payment of \$7.5 million, development milestone payments of up to \$101.5 million and commercial milestone payments of up to \$55.0 million. No development or commercial milestone payments or royalties have been received to date.

In addition, we are eligible to receive tiered royalties in the low to mid-single digits on product sales, with the royalty term being, on a product-by-product and country-by-country basis, either (i) for as long as there is Zymeworks platform patent coverage on products, or (ii) for 10 years, beginning from the first commercial sale, whichever period is longer. Celgene also has the right, prior to the first dosing of a patient in a Phase 3 clinical trial for a product, to buy down the royalty to a flat low-single digit rate with a payment of \$10.0 million per percentage point. In addition to this collaboration agreement, the parties also entered into an equity subscription agreement under which Celgene paid \$8.6 million for common shares.

Under the agreement, we are collaborating with Celgene to generate and develop a number of bispecific antibodies during the research program term. After the conclusion of the research program in April 2020, Celgene will be solely responsible for the further research, development, manufacturing and commercialization of the products.

Licensing and Collaboration Agreement with GSK

In December 2015, we entered into a collaboration and license agreement with GSK to research, develop and commercialize up to 10 new Fc-engineered monoclonal and bispecific antibodies generated through the use of the EFECT and Azymetric platforms. Under the terms of the agreement, we granted GSK a worldwide, royalty-bearing antibody target-exclusive license to new intellectual property generated to the EFECT platform under this collaboration and a non-exclusive license to the Azymetric platform to research, develop and commercialize future licensed products. We are eligible to receive up to \$1.1 billion, including research, development and commercial milestone payments of up to \$110.0 million for each product. In addition, we are eligible to receive tiered royalties in the low-single digits on net sales of products, with the royalty term being, on a product-by-product and country-by-country basis, either (i) for as long as there is Zymeworks patent coverage on products or certain joint patent coverage on products, or (ii) for 10 years beginning from the first commercial sale, whichever period is longer. If there is no Zymeworks patent coverage or certain joint patent coverage on products, royalty rates will be reduced. No development or commercial milestone payments or royalties have been received to date. We retained the right to develop up to four products, free of royalties, using the new intellectual property generated in this collaboration, and after a period of time, to grant licenses to such intellectual property for development of additional products by third parties.

Under the collaboration and license agreement, we are sharing certain research and development responsibilities with GSK to generate new Fc-engineered antibodies. Each party will bear its own costs for the responsibilities assigned to it during the research period. After the conclusion of the research period, each party will be solely responsible for the further research, development, manufacturing and commercialization of its own respective products. The research period will terminate when the “research collaboration plan” (as defined in the collaboration and license agreement) is complete or on December 1, 2018, whichever is earlier. During the term of the agreement and solely based on the outcome of the research collaboration, we have granted GSK exclusive rights to develop and commercialize monospecific antibodies against targets nominated by GSK. If GSK develops bispecific antibodies using its own platform approaches, we have granted GSK exclusive rights to develop and commercialize such antibodies comprising of specific antibody sequence pairs.

Second Licensing and Collaboration Agreement with GSK

In April 2016, we entered into a licensing agreement with GSK to research, develop and commercialize up to six bispecific antibodies generated through the use of the Azymetric platform. This may include bispecific antibodies incorporating new engineered Fc regions generated under the 2015 GSK agreement outlined in the preceding section. Under the terms of this agreement, we granted GSK a worldwide, royalty-bearing antibody sequence pair-specific exclusive license to research, develop and commercialize licensed products. We are eligible to receive up to \$908.0 million, including an upfront payment as a technology access fee (\$6.0 million received in 2016), research milestone payments of up to \$30.0 million, development milestone payments of up to \$152.0 million and commercial milestone payments of up to \$720.0 million. In addition, we are eligible to receive tiered royalties in the low to mid-single digits on product sales, with the royalty term being, on a product-by-product and country-by-country basis, either (i) for as long as there is Zymeworks patent coverage on products, or (ii) for 10 years beginning from the first commercial sale, whichever period is longer. If there is no Zymeworks patent coverage on products, royalty rates may be potentially reduced. No research, development or commercial milestone payments or royalties have been received to date. GSK has the right, prior to the first dosing of a patient in a Phase 3 clinical trial for a product, to buy down the royalty payable on such product by only 1% with a payment of \$10.0 million.

Under the agreement, GSK will bear all responsibility and all costs associated with research, development and commercialization of products generated using the Azymetric platform.

Licensing and Collaboration Agreement with Daiichi Sankyo

In September 2016, we entered into a collaboration and cross-license agreement with Daiichi Sankyo to research, develop and commercialize one bispecific antibody generated through the use of the Azymetric and EFECT platforms. Under the terms of the agreement, we granted Daiichi Sankyo a worldwide, royalty-bearing antibody sequence pair-specific exclusive license to research, develop and commercialize certain licensed products. We are eligible to receive up to \$149.9 million, including an upfront payment as a technology access fee of \$2.0 million (received in 2016), research (\$1.0 million received in 2017) and development milestone payments and a commercial option payment totaling up to \$67.9 million and commercial milestone payments of up to \$80.0 million. In addition, we are eligible to receive tiered royalties ranging from the low single digits up to 10% on product sales, with the royalty term being, on a product-by-product and country-by-country basis, either (i) for as long as there is Zymeworks platform patent coverage on products, or (ii) for 10 years beginning from the first commercial sale, whichever period is longer. No research, development or commercial milestone payments or royalties have been received to date. We also gained non-exclusive rights to develop and commercialize up to three products using Daiichi Sankyo's proprietary immune-oncology antibodies, with royalties in the low single digits to be paid to Daiichi Sankyo on sales of such products.

Under the agreement, we are sharing certain research and development responsibilities with Daiichi Sankyo to generate bispecific antibodies with the Azymetric platform. Daiichi Sankyo is responsible for our internal and external research costs in support of this collaboration during the research program term. After the research program term, Daiichi Sankyo will be solely responsible for the further research, development, manufacturing and commercialization of the products. Under the non-exclusive immuno-oncology antibody license to Zymeworks, we are solely responsible for all research, development and commercialization of the resulting products.

Second Licensing Agreement with Daiichi Sankyo

In May 2018, we entered into a new license agreement with Daiichi Sankyo to research, develop and commercialize two bispecific antibodies generated through the use of the Azymetric and EFECT platforms.

Under the terms of the agreement, we granted Daiichi Sankyo a worldwide, royalty-bearing, antibody sequence pair-specific, exclusive license to research, develop and commercialize certain products. We are eligible to receive up to \$484.7 million including an upfront payment as a technology access fee (\$18.0 million earned on

[Table of Contents](#)

execution of the agreement), development milestone payments totaling up to \$126.7 million and commercial milestone payments of up to \$340.0 million. In addition, we are eligible to receive tiered royalties ranging from the low single digits up to 10% on product sales, with the royalty term being, on a product-by-product and country-by-country basis, either (i) for as long as there is Zymeworks platform patent coverage on products, or (ii) for 10 years beginning from the first commercial sale, whichever period is longer. If there is no Zymeworks patent coverage on products, royalty rates may be reduced. No development or commercial milestone payments or royalties have been received to date. Under the agreement, Daiichi Sankyo will be solely responsible for the research, development, manufacturing and commercialization of the products.

Licensing and Collaboration Agreement with Janssen

In November 2017, we entered into a collaboration agreement with Janssen to research, develop and commercialize up to six bispecific antibodies generated through the use of the Azymetric and EFECT platforms. Under the terms of the agreement, we granted Janssen a worldwide, royalty-bearing, antibody sequence pair-specific exclusive license to research, develop and commercialize certain products. We are eligible to receive up to \$1.45 billion, including an upfront payment of \$50.0 million (received in 2017), development milestone payments of up to \$282.0 million and commercial milestone payments of up to \$1.12 billion. In addition, we are eligible to receive tiered royalties in the mid-single digits on product sales, with the royalty term being, on a product-by-product and country-by-country basis, either (i) for as long as there is Zymeworks platform patent coverage on products, or (ii) for 10 years, beginning from the first commercial sale, whichever period is longer. If there is no Zymeworks patent coverage on products, royalty rates may be potentially reduced. No development or commercial milestone payments or royalties have been received to date. Janssen has the right, prior to the first dosing of a patient in a Phase 3 clinical trial for a product, to buy down the royalty relating to such product by only 1% with a payment of \$10.0 million. Janssen also has the option to develop two additional bispecific antibodies under this agreement subject to a future option payment.

Under the agreement, Janssen will be solely responsible for the research, development, manufacturing and commercialization of the products.

Our Strategy

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.

Our key strategies to achieve this goal are to:

- aggressively advance our lead product candidate, ZW25, through the clinic in multiple HER2-expressing tumor types;
- pursue a rapid and multi-faceted development strategy for our novel and highly differentiated pipeline into clinical trials across many oncology indications with a critically high unmet medical need;
- leverage our therapeutic platforms and proprietary protein engineering capabilities to continue to discover and develop additional novel product candidates;
- leverage our strategic partnerships, while pursuing additional collaborations that can augment the power of our platforms and value of our pipeline; and
- continue to develop innovative therapeutic platforms and expand our therapeutic focus into logical areas such as autoimmunity and inflammatory diseases.

RISK FACTORS

Investing in our securities is speculative and involves a high degree of risk. You should consider carefully the following risk factors, as well as the other information in this prospectus, including our consolidated financial statements and notes thereto, before you decide to purchase our securities. You should also refer to the other information set forth or incorporated by reference in this prospectus or any applicable prospectus supplement. If any of the following risks actually occur, our business, financial condition, results of operations and prospects could be materially adversely affected, the value of our securities could decline and you may lose all or part of your investment. This prospectus also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of a number of factors, including the risks described below. See "Cautionary Note Regarding Forward-Looking Statements."

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

We have a limited number of product candidates, all which are still in preclinical or early 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 regulatory authorities outside the United States. Our product candidates are in early stages of development and we have not submitted an application, or received marketing approval, for any of our product candidates. Furthermore, the fact that our core competencies have been recognized through strategic partnerships does not improve our product candidates' outlook for regulatory approval. We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA. Obtaining regulatory approval of our product candidates will depend on many factors, including, but not limited to, the following:

- successfully completing formulation and process development activities;
- completing clinical trials that demonstrate the efficacy and safety of our product candidates;
- receiving marketing approval from applicable regulatory authorities;
- establishing commercial manufacturing capabilities; 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 very expensive, time consuming and 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 non-U.S. regulatory authorities.

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 foreign regulatory authorities. 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 planned clinical trials may produce negative or inconclusive results, and we or any of our

Table of Contents

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 non-U.S. regulatory authorities, despite having progressed through preclinical studies and initial clinical trials. Product candidates that have shown promising results in early clinical trials may still suffer significant setbacks in subsequent clinical trials or registration clinical trials. For example, a number of companies in the pharmaceutical industry, including those with greater resources and experience than us, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials. Similarly, preclinical interim results of a clinical trial do not necessarily predict final results.

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 enrolling an adaptive Phase 1 clinical trial of ZW25 in patients with recurrent or metastatic HER2-expressing solid tumors, and expect to file an IND application for ZW49 in 2018. 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. 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 clinical research organizations (“CROs”) the terms of which can be subject to extensive negotiation and may vary significantly among different sites or CROs; and
- delay or failure to obtain institutional review board (“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;

[Table of Contents](#)

- inability to monitor patients adequately during or after treatment by us or our CROs;
- our CROs or clinical study sites failing to comply with 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 produce or obtain sufficient quantities of a product candidate to complete clinical studies;
- the inability to address any noncompliance with regulatory requirements or safety concerns that arise during the course of a clinical trial;
- the need to repeat or terminate clinical trials as a result of inconclusive or negative results or unforeseen complications in testing; and
- 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.

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.

If we are unable to enroll patients in clinical trials, we will be unable to complete these trials on a timely basis.

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 products for the treatment of rare diseases, which have limited pools of patients from which to draw for clinical testing. If we 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.

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 future 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.

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 subjects or in subsequent human clinical trials of that product candidate or any other 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. For example, in February 2018, we elected to discontinue the development of one of our product candidates, ZW33, in favor of pursuing a new product candidate, ZW49.

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 such 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 early clinical development. Additionally, all of our product candidates are required to undergo ongoing safety testing in humans as part of clinical trials. Consequently, not all adverse effects of drugs can be predicted or anticipated. 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. While we believe our lead product candidates have demonstrated a favorable safety profile in animals, ZW25 has recently commenced dosing in an adaptive Phase 1 clinical trial and ZW49 has never been tested in humans. Therefore, the results from clinical trials may not demonstrate a favorable safety profile in humans. The results of future clinical trials may show that ZW25 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 Phase 1 clinical trial 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.

Table of Contents

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;
- 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. In addition, several companies are also developing bispecific antibodies. Other companies are developing new treatments for cancer that enhance the Fc regions of antibodies to create more potent antibodies, including MacroGenics, Inc., XenCor, Inc. and F. Hoffmann-La Roche AG.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe effects, are more convenient or are 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.

[Table of Contents](#)

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.

Our product candidates, for which we intend to seek approval, may face competition sooner than anticipated.

Our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of biosimilar products. Biosimilar products are expected to become available over the coming years. Even if our product candidates achieve marketing approval, they may be priced at a significant premium over competitive biosimilar products, if any have been approved by then. The Biologics Price Competition and Innovation Act of 2009, which is included in the Patient Protection and Affordable Care Act (“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 biological 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 a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full Biologics License Application (“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. From time to time, there are proposals to repeal or modify the PPACA and it is uncertain how any such proposals, if approved, would affect these provisions.

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;
- lack of significant adverse side effects;
- 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;
- the degree of cost-effectiveness of our product candidates;
- availability of alternative therapies at similar or lower cost, including generic and over-the-counter products;

Table of Contents

- 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 ZW25 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.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. The FDA has granted Orphan Drug Designation to ZW25 for the treatment of gastric and ovarian cancer 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 European Medicines Agency (“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 10 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.

Even if we obtain orphan drug exclusivity for ZW25, 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. If we fail to maintain our current Orphan Drug Designations for our product candidate, ZW25, or for any other product candidates that receive an Orphan Drug Designation in the future, or if the FDA approves Orphan Drug Designation for similar product candidates of other pharmaceutical companies, our competitive position would be harmed.

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 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.

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.

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 (the "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.

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 presently 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

[Table of Contents](#)

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 any of the foregoing estimates 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 expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

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 forego or delay pursuit of opportunities with other therapeutic platforms or product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs, therapeutic platforms and product candidates for specific indications may not yield any commercially viable products. 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.

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

A key element of our strategy is to use and expand 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 a steady stream of 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.

Table of Contents

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 practices (“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.

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.

[Table of Contents](#)

If any of our product candidates are approved for commercial sale, we will be highly dependent upon consumer perceptions of us and the safety and quality of our products. We could be adversely affected if we are subject to negative publicity. We could also be adversely affected if any of our products or any similar products distributed by other companies prove to be, or are asserted to be, harmful to patients. Because of our dependence upon consumer perceptions, any adverse publicity associated with illness or other adverse effects resulting from patients' use or misuse of our products or any similar products distributed by other companies could have a material adverse impact on our financial condition or results of operations.

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.

Changes 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.

Acquisitions or joint ventures could disrupt our business, cause dilution to our shareholders and otherwise harm our business.

We actively evaluate various strategic transactions on an ongoing basis. We may acquire other businesses, products or technologies as well as pursue strategic alliances, joint ventures or investments in complementary businesses. 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;
- 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.

Foreign acquisitions involve unique risks in addition to those mentioned above, including those related to integration of operations across different cultures and languages, currency risks and the particular economic, political and regulatory risks associated with specific countries.

Also, the anticipated benefit of any strategic alliance, joint venture or acquisition may not materialize or such strategic alliance, joint venture or acquisition 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 future joint ventures or acquisitions, 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, 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, or 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, 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 collect and store petabytes of sensitive data, including legally protected health information, personally identifiable 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, including 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.

The secure processing, storage, maintenance and transmission of this critical information are vital to our operations and business strategy, and we devote significant resources to protecting such information. Although we take measures to protect sensitive information from unauthorized access or disclosure, our information technology and infrastructure and that of any third-party billing and collections provider we may utilize, may be vulnerable to attacks by hackers or viruses or breached due to employee error, malfeasance or other disruptions. Any such breach or interruption could compromise our networks and the information stored there could be accessed by unauthorized parties, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, such as HIPAA, and regulatory penalties. Although we have implemented security measures and a formal enterprise security program to prevent unauthorized access to patient data, there is no guarantee that we can continue to protect our systems from breach. Unauthorized access, loss or dissemination could also disrupt our operations (including our ability to conduct our analyses, provide test results, bill payors or providers,

Table of Contents

process claims and appeals, 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.

The U.S. Office of Civil Rights may impose penalties on us or our CROs if we, or our CROs, do not fully comply with requirements of HIPAA. Penalties will vary significantly depending on factors such as whether we, or our CROs, knew or should have known of the failure to comply, or whether our failure, or that of our CROs, to comply was due to willful neglect. These penalties include civil monetary penalties of \$100 to \$50,000 per violation, up to an annual cap of \$1,500,000 for identical violations. A person who knowingly obtains or discloses individually identifiable health information in violation of HIPAA may face a criminal penalty of up to \$50,000 per violation and up to one-year imprisonment. The criminal penalties increase to \$100,000 per violation and up to five-years imprisonment if the wrongful conduct involves false pretenses, and to \$250,000 per violation and up to 10-years imprisonment if the wrongful conduct involves the intent to sell, transfer, or use identifiable health information for commercial advantage, personal gain, or malicious harm. The U.S. Department of Justice is responsible for criminal prosecutions under HIPAA. Furthermore, in the event of a breach as defined by HIPAA, we have specific reporting requirements to the Office of Civil Rights under the HIPAA regulations as well as to affected individuals, and we may also have additional reporting requirements to other state and federal regulators, including the Federal Trade Commission, and to 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, the interpretation and application of consumer, health-related and data protection laws in the United States, the European Union (“EU”) and elsewhere are often uncertain, contradictory and in flux. 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.

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.

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 was enacted, which includes measures that have significantly changed, or will significantly change, the way healthcare is financed by both governmental and private insurers. Among the provisions of the PPACA of importance to the pharmaceutical industry are the following:

- an annual, non-deductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;

Table of Contents

- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% of the average manufacturer price (“AMP”) for branded drugs or the difference between AMP and best price, whichever is greater. For generic drugs the rebate is 13%;
- Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period;
- extension of manufacturers’ Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories;
- requirement that applicable manufacturers and group purchasing organizations report annually to the U.S. Department of Health and Human Services (“HHS”) information regarding certain payments and other transfers of value given to physicians and teaching hospitals, and any ownership or investment interest physicians, or their immediate family members, have in their company;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- a licensure framework for follow-on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare & Medicaid Innovation at the Centers for Medicare & Medicaid Services to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the PPACA, including recent tax legislation that removed the financial penalties for people who do not carry health insurance. There is still uncertainty as to whether the PPACA will undergo additional revisions, and we cannot predict the impact of any future modifications, and it is uncertain how any such proposals, if approved, would affect these provisions.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and will remain in effect through 2025 unless additional Congressional action is taken. 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 customers for our product candidates, if approved, and, accordingly, our financial operations. Also, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which have resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products.

In the EU similar political, economic and regulatory developments may affect our ability to profitably commercialize our current or any future products. In addition to continuing pressure on prices and cost

Table of Contents

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 abroad. 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 weakness, including inflation, or political 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;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;
- 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;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing foreign operations, including differing labor relations;

Table of Contents

- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

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, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, that may constrain the business or financial arrangements and relationships through which we conduct clinical research on product candidates and market, sell and distribute any products for which we obtain marketing approval. In addition, we may be subject to transparency laws and patient privacy regulation by the federal government and by the U.S. states and foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include, but are not limited to, the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which impose criminal and civil penalties, including civil whistleblower or qui tam actions, 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;
- the U.S. Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) 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 the Health Information Technology for Economic and Clinical Health Act of 2009 (“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;
- the federal Open Payments program under the Physician Payments Sunshine Act, created under Section 6002 of the PPACA and its implementing regulations, requires certain manufacturers of drugs,

Table of Contents

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 to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to HHS ownership and investment interests held by physicians (as defined above) and their immediate family members; and

- analogous state and foreign laws and regulations, including: state anti-kickback and false claims laws which may apply to our business practices, including, but not limited to, 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 pre-empted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under the U.S. federal Anti-Kickback Statute and analogous state laws, 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. 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, without limitation, 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 non-compliance 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 which 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 may engage third parties for clinical trials outside of the United States, to sell our products abroad 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, 2017 and 2016 and for the three months ended March 31, 2018 was \$10.4 million, \$33.8 million and \$21.3 million, respectively. As of March 31, 2018 our accumulated deficit was approximately \$130.0 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 and personnel to support our product development efforts and operations as a public company. 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. For example, our expenses could increase if we are required by the FDA to perform trials in addition to those that we currently expect to perform, or if there are any delays in completing our currently planned clinical trials or in the development of any of our product candidates.

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 a clinical trial. We and our partners are still in the early stages of 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 for the foreseeable future.

[Table of Contents](#)

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 preclinical and clinical development as well as other potential product candidates through discovery. Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. In order to obtain such 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. Furthermore, in August 2016 we entered into a license agreement with Innovative Targeting Solutions Inc. (“ITS”) which requires licensing payments to ITS totaling \$12.0 million over the following five-year period.

Although it is difficult to predict our liquidity requirements, based upon our current operating plan, we believe that our existing cash and cash equivalents and short term investments will enable us to fund our operating expenses and capital expenditure requirement into 2019. We may also be eligible to receive certain research, development and commercial milestone payments in the future, as described under “Our Business – Strategic Partnerships and Collaborations.” However, because successful development of our product candidates and the achievement of milestones by our strategic partners is uncertain, we are unable to estimate the actual funds we will require to complete research and development and to commercialize our product candidates.

Our future funding requirements will depend on many factors, including but not limited to:

- 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 need and ability to hire 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.

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.

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 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.

Unstable market and economic conditions may have serious adverse consequences on our business and financial condition.

Global credit and financial markets experienced extreme disruptions at various points over the last decade, characterized by diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If another such disruption in credit and financial markets and deterioration of confidence in economic conditions occurs, our business may be adversely affected. If the equity and credit markets were to deteriorate significantly in the future, it may make any necessary debt or equity financing more difficult to complete, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and share price and could require us to delay or abandon development or commercialization plans. In addition, there is a risk that one or more of our current strategic partners, service providers, manufacturers and other partners would not survive or be able to meet their commitments to us under such circumstances, which could directly affect our ability to attain our operating goals on schedule and on budget.

We are subject to risks associated with currency fluctuations, and changes in foreign currency exchange rates could impact our results of operations.

Management assesses its functional currency to be the U.S. dollar based on management's analysis of the primary economic environment in which we operate.

As of March 31, 2018, approximately 7.4% of our cash and cash equivalents was denominated in Canadian dollars. Fluctuations in U.S. dollar and Canadian dollar exchange rates could result in a material increase in reported expenses relative to revenue, and therefore could cause our operating income (expense) to appear to decline materially. Fluctuations in foreign currency exchange rates also impact the reporting of our receivables and payables in non-Canadian currencies. As a result of such foreign currency fluctuations, it could be more difficult to detect underlying trends in our business and results of operations. In addition, to the extent that fluctuations in currency exchange rates cause our results of operations to differ from our expectations or the expectations of our investors, the trading price of our common shares could be adversely affected.

From time to time, we may engage in exchange rate hedging activities in an effort to mitigate the impact of exchange rate fluctuations. For example, we maintain a natural currency hedge against fluctuations in the U.S./Canadian foreign exchange rate by matching the amount of U.S. dollar and Canadian dollar investments to the expected amount of future U.S. dollar and Canadian dollar obligations, respectively. Any hedging technique we implement may fail to be effective. If our hedging activities are not effective, changes in currency exchange rates may have a more significant impact on the trading price of our common shares.

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 do not yet have any capability for sales, marketing or distribution. 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, Celgene, GSK, Daiichi Sankyo and Janssen. 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; and
- 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, Celgene, GSK, Daiichi Sankyo and Janssen may be terminated for convenience upon the completion of a specified notice period.

We may not realize the anticipated benefits of our strategic partnerships.

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. Moreover, our estimates of the potential revenue we are eligible to receive under our strategic partnerships may include potential payments in respect of therapeutic programs for which our partners have discontinued development or may discontinue development in the future. Furthermore, our strategic partners may not keep us informed as to the status of their in-house research activities and they may fail to exercise options embedded within certain agreements. Any discontinuation of product development by our strategic partners could reduce the amounts receivable under our strategic partnerships below the stated amounts we are eligible to receive under those agreements. If we do not receive the funding we expect under these 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. All of the risks relating to product development, regulatory approval and commercialization described in our most recent Quarterly Report on Form 10-Q also apply to the activities of our program strategic partners. For example, in 2017 Lilly nominated a bispecific candidate from their 2014 agreement with us for preclinical development and discontinued the development of two other bispecific antibodies due to strategic portfolio realignment in those particular disease areas. As a result, we have updated our projections and are currently eligible to receive up to \$125.0 million under this agreement, comprised of research milestone payments of up to \$2.0 million (\$2.0 million earned in 2016), IND submission milestone payments of up to \$8.0 million, development milestone payments of up to \$20.0 million and commercial milestone payments of up to \$95.0 million.

Additionally, subject to its contractual obligations to us, if one of our strategic partners is involved in a business combination, the partner might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our strategic partners terminates its agreement with us, we may find it more difficult to attract new partners.

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 its 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

[Table of Contents](#)

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 clinical product candidates. Any failure by a third-party manufacturer to produce acceptable product candidate for us may 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 nor do we have any in-house manufacturing experience or personnel. 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.

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 synthesize and 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 current cGMPs 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.

The manufacture of our product candidates is complex. We and our third-party manufacturers may encounter difficulties in production. If we encounter any such difficulties, our ability to supply our product candidates for clinical trials or, if approved, for commercial sale could be delayed or halted entirely.

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 extremely 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 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 starting cells that are stored in a cell bank. We have one master

[Table of Contents](#)

cell bank for each antibody manufactured in accordance with cGMP and multiple working cell banks. While we believe we would have adequate back up should any cell bank be lost in a catastrophic event, it is possible that we could lose multiple cell banks and have our manufacturing severely impacted by the need to replace the cell banks. 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.

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.

[Table of Contents](#)

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. These services include external tax advice and 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 the “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 we are unable to invalidate those patents, or if licenses for them are not available on commercially reasonable terms or at all, 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

[Table of Contents](#)

anti-cancer agents, as well as compositions and methods for making and using anti-HER2 antibody conjugates comprising certain toxins, 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 to be found to infringe any such patents, and we were unable to invalidate those patents, or if licenses for them are not available on commercially reasonable terms, or at all, 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 or 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 technology that we require may materially harm our business, financial condition and results of operations. Moreover, our failure to maintain a license to 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 have become commonplace. The types of situations in which we may become a party to such litigation or proceedings include:

- we or our strategic partners may initiate litigation or other proceedings against third parties seeking to invalidate the patents held by those third parties, to obtain a judgment that our products or processes do not infringe those third parties' patents or to obtain a judgement that those parties' patents are unenforceable;
- if our competitors file patent applications that claim technology also claimed by us or our licensors, we or our licensors may be required to participate in interference, derivation or opposition proceedings to determine the priority of invention, which could jeopardize our patent rights and potentially provide a third party with a dominant patent position;
- if third parties initiate litigation claiming that our processes or products infringe their patent or other intellectual property rights or initiating other proceedings, including post-grant proceedings and *inter partes* reviews, we and our strategic partners will need to defend against such proceedings; and
- if a license to necessary technology is terminated, the licensor may initiate litigation claiming that our processes or products infringe or misappropriate their patent or other intellectual property rights and/or that we breached our obligations under the license agreement, and we and our strategic partners would need to defend against such proceedings.

These lawsuits would 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 the third party's patents and would order us or our strategic partners to stop the activities 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 will 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 foreign countries.

Moreover, the patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years 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 foreign 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 foreign 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 foreign 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 United States 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, particularly in a foreign jurisdiction, 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, particularly in a foreign jurisdiction, and could require us to pay substantial damages, cease the 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 foreign 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

[Table of Contents](#)

- 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 and 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 owned by or licensed 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 or not infringed or trade secrets not

[Table of Contents](#)

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, 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 natural 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 foreign legislation 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 proprietary computational technologies, including unpatented know-how and other proprietary information, as trade secrets. To maintain the confidentiality of trade secrets and proprietary information, we enter into confidentiality agreements with our employees, consultants, strategic partners and others upon the commencement of their relationships with us. These agreements require 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. Thus, despite such agreement, such inventions may become assigned to third parties. 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 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.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming and the outcome is unpredictable. 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 which 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. The United States has enacted and is currently implementing wide-ranging patent reform legislation. Further, 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 combination of events 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 does file 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 going forward 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 United States 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 foreign countries do not protect

[Table of Contents](#)

intellectual property rights to the same extent as federal and state 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 United States 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 foreign jurisdictions. The legal systems of certain countries, particularly certain developing 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, particularly developing countries. For example, unlike other countries, 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 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 and insider trading.

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 (“Code of Conduct”) 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.

If we market products in a manner that violates healthcare fraud and abuse laws, or if we violate government price reporting 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 once 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, but are not limited to, anti-kickback, false claims, data privacy and security and transparency statutes and regulations.

Federal false claims laws prohibit 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. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are several statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. 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.

Over the past few years, a number of pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of promotional and marketing activities, such as:

- providing free trips, free goods, sham consulting fees and grants and other monetary benefits to prescribers;

[Table of Contents](#)

- reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates;
- engaging in off-label promotion; and
- submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates.

The 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 pre-empted by HIPAA, thus complicating compliance efforts.

Additionally, the PPACA also included the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologicals 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 or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members. Failure to comply with required reporting requirements could subject applicable manufacturers and others to substantial civil money 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

[Table of Contents](#)

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 the 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.

We expect to change from foreign private issuer to U.S. domestic issuer status in the future, which may result in additional costs and expenses to us.

We are currently a "foreign private issuer," as such term is defined in Rule 405 under the U.S. Securities Act of 1933, as amended (the "Securities Act"), and are not subject to the same requirements that are imposed upon U.S. domestic issuers by the SEC. While we have voluntarily chosen to file periodic reports on U.S. domestic issuer forms, such as our most recent Quarterly Report on Form 10-Q, we will maintain our status as a foreign private issuer and are not subject to certain other requirements imposed on U.S. domestic issuers. However, we will no longer be a foreign private issuer if a majority of our common shares are held in the United States and (i) a majority of our directors or executive officers are U.S. citizens or residents; (ii) a majority of our assets are located in the United States; or (iii) our business is administered principally in the United States. As of December 31, 2017, the majority of our common shares are held in the United States. Moreover, the majority of our directors are U.S. citizens. Accordingly, with the expectation that we may no longer be considered a foreign private issuer as of the next determination date, we have voluntarily chosen to file periodic reports on U.S. domestic issuer forms, beginning with our 2017 Annual Report on Form 10-K. The next determination date with respect to our foreign private issuer status is June 30, 2018. If, as we expect, we no longer qualify as a foreign private issuer on that determination date, as of January 1, 2019 we will no longer be eligible to use the rules and forms designated for foreign private issuers and we will be considered a U.S. domestic issuer. The regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer may be significantly more than the costs incurred as a foreign private issuer. If we are not a foreign private issuer, we will be required to file periodic and current reports and registration statements on U.S. domestic issuer forms with the SEC, which are generally more detailed and extensive than the forms available to a foreign private issuer. In addition, we will no longer be eligible to rely upon exemptions from corporate governance requirements that are available to foreign private issuers or to benefit from other accommodations for foreign private issuers under the rules of the SEC or NYSE.

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on the research and development, clinical and business expertise of Dr. Ali Tehrani, Ph.D., our President and Chief Executive Officer, Mr. Neil Klompas, our Chief Financial Officer, and other members of our senior management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We currently maintain “key person” insurance coverage for Dr. Tehrani (C\$5.0 million) and Mr. Neil Klompas (C\$2.0 million). The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. In addition, we will need to expand and 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 executive officers and key 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. 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 growth strategy will be limited.

We will need to grow our organization, and we may experience difficulty in managing this growth, which could disrupt our operations.

As of March 31, 2018 we had 154 full-time employees. As our development and commercialization plans and strategies develop, we expect to expand our employee base for managerial, operational, financial and other resources. Additionally, as our product candidates enter and advance through preclinical studies and any clinical trials, we will 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 these growth activities. We may not be able to effectively manage the 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. Our expected 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 our expected 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

Our share price is likely to be volatile and the market price of our common shares may drop below the price paid by shareholders.

Investors should consider an investment in our common shares as risky and invest only if they can withstand a significant loss and wide fluctuations in the market value of their investment. In addition, the stock market has recently experienced significant volatility, particularly with respect to pharmaceutical, biotechnology and other life sciences company stocks. The volatility of pharmaceutical, biotechnology and other life sciences company stocks often does not relate to the operating performance of the companies represented by the stock. 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 shares;
- additions or departures of key personnel;
- changes in the structure of health care payment systems in the United States or overseas;
- failure of any of our product candidates, if approved, to achieve commercial success;
- economic and other external factors or other disasters or crises;
- 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;
- overall fluctuations in U.S. equity markets; and
- other factors that may be unanticipated or out of our control.

In addition, in the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our shareholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit and divert the time and attention of our management, which could seriously harm our business.

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

An active trading market for our 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 shares or sell their shares at or above the prices at which they acquired their shares or sell their 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 shares and may impair our ability to acquire other companies or technologies by using our 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.

We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to corporate governance standards.

As a public company, we incur significant legal, accounting and other expenses. In addition, our administrative staff are required to perform additional tasks not required for a private company. For example, as a public company, we have adopted additional internal controls and disclosure controls and procedures, retained a transfer agent and adopted an insider trading policy. As a public company, we bear all of the internal and external costs of preparing and distributing periodic public reports in compliance with our obligations under the securities laws. We expect these costs to increase in 2018 as we transition from filing periodic and current reports and registration statements, as applicable, with the SEC on forms available to foreign private issuers to those required to be filed by domestic issuers and to otherwise prepare for the anticipated change from a foreign private issuer to a U.S. domestic issuer.

In addition, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act and the related rules and regulations implemented by the SEC, the applicable Canadian securities regulators, the NYSE and the TSX, have legal and financial compliance costs and make some compliance activities time consuming. We intend to invest resources to comply with evolving laws, regulations and standards, and such investment will result in increased general and administrative expenses and may divert management's time and attention from our other business activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us and our business may be harmed. Additionally, as a public company, we maintain our directors' and officers' liability insurance coverage, which results in higher insurance costs. In the future, it may be more expensive or more difficult for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These factors could also make it more difficult for us to attract and retain qualified members of our board of directors, particularly to serve on our audit committee and compensation committee, and qualified executive officers.

Under the corporate governance standards of the NYSE, a majority of our board of directors and each member of our audit committee must be an independent director no later than the first anniversary of the completion of our IPO. The policies of the TSX require our board of directors to consist of at least two independent directors and Canadian securities laws require each member of the audit committee to be independent within the meaning of Canadian securities laws. As of the date of our most recent Quarterly Report on Form 10-Q, we meet these requirements but we may in the future encounter difficulty in attracting and retaining qualified persons to serve

on our board of directors and the audit committee, and our board of directors and management may be required to divert significant time and attention and resources away from our business to identify qualified directors. If we fail to attract and retain the required number of independent directors, we may be subject to the delisting of our common shares from the NYSE and TSX.

As a foreign private issuer, we are subject to different U.S. securities laws and rules than a U.S. domestic issuer, in particular, certain disclosure requirements, which could limit the information publicly available to our shareholders.

As a foreign private issuer, we are currently not required to comply with all of the periodic disclosure and current reporting requirements of the Securities Exchange Act of 1934, as amended (the “Exchange Act”) that apply to U.S. domestic issuers and, as such, there may be less publicly available information about us than if we were a U.S. domestic issuer. Furthermore, our officers, directors and principal shareholders are currently exempt from the insider reporting and short-swing profit recovery requirements in Section 16 of the Exchange Act. Accordingly, our shareholders may not know on as timely a basis when our officers, directors and principal shareholders purchase or sell their common shares, as the reporting deadlines under the corresponding Canadian insider reporting requirements are longer. As a foreign private issuer, we are also exempt from the requirements of Regulation FD (Fair Disclosure) which, generally, are meant to ensure that select groups of investors are not privy to specific information about an issuer before other investors. As a result of such varied reporting obligations, shareholders should not expect to receive the same information at the same time as information provided by U.S. domestic issuers.

In addition, as a foreign private issuer, we have the option to follow certain Canadian corporate governance practices rather than those of the United States, except to the extent that such laws would be contrary to U.S. securities laws, provided that we disclose the requirements we are not following and describe the Canadian practices we follow instead. As a result, our shareholders may not have the same protections afforded to shareholders of companies that are subject to all domestic U.S. corporate governance requirements. As described in our most recent Quarterly Report on Form 10-Q, we expect to no longer qualify as a foreign private issuer as of our next determination date of June 30, 2018, such that as of January 1, 2019, we will be considered a U.S. domestic issuer.

We are an emerging growth company, and any decision on our part to comply only with certain reduced reporting and disclosure requirements applicable to emerging growth companies could make our common shares less attractive to investors.

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act (“JOBS Act”). For as long as we continue to be an emerging growth company, we may choose to take advantage of exemptions from various reporting requirements applicable to other public companies that are not emerging growth companies, including, but not limited to, not being required to have our independent registered public accounting firm audit our internal control over financial reporting under Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years following the completion of our IPO on May 3, 2017, although, if we have more than \$1.07 billion in annual revenue, if the market value of our common shares held by non-affiliates exceeds \$700 million as of June 30 of any year, or we issue more than \$1.0 billion of non-convertible debt over a three-year period before the end of that five-year period, we would cease to be an emerging growth company as of the following December 31. Investors could find our common shares less attractive if we choose to rely on these exemptions. If some investors find our common shares less attractive as a result of any choices to reduce future disclosure, there may be a less active trading market for our common shares and our share price may be more volatile.

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

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. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations.

Pursuant to Section 404 of the Sarbanes-Oxley Act (“Section 404”) and related rules adopted by the SEC and the U.S. Public Company Accounting Oversight Board, (“PCAOB”) and National Instrument 52-109 – Certification of Disclosure in Issuers’ Annual and Interim Filings (“NI 52-109”) our management is required to disclose changes made in our internal control over financial reporting on a quarterly basis and assess the effectiveness of our disclosure controls and procedures annually. We have elected to take advantage of certain exceptions from reporting requirements that are available to emerging growth companies under the JOBS Act and therefore we are not required to deliver an auditor’s attestation report on the effectiveness of our internal control over financial reporting pursuant to Section 404 until after the date we are no longer an emerging growth company. We could be an emerging growth company for up to five years from our IPO, although circumstances could cause us to lose that status earlier, including if the market value of our shares held by non-affiliates exceeds \$700 million as of any June 30 before that time, in which case we would no longer be an emerging growth company as of the following December 31. An independent assessment of the effectiveness of our internal control could detect problems that our management’s assessment might not. 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.

Our management and independent registered public accounting firm did not perform an evaluation of the design and operating effectiveness of our internal control over financial reporting in accordance with the provisions of Section 404 and NI 52-109 as of December 31, 2015 and December 31, 2016. Had we and our independent registered public accounting firm performed such an evaluation, control deficiencies may have been identified by management or our independent registered public accounting firm, and those control deficiencies could have also represented one or more material weaknesses. Undetected material weaknesses in our internal controls could lead to financial statement restatements and require us to incur the expense of remediation.

As of December 31, 2017, our management did perform an evaluation of the design and operating effectiveness of our internal control over financial reporting based on the Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (“2013 COSO Framework”) in accordance with the provisions of NI 52-109. However, no independent assessment of the design and operating effectiveness of our internal controls was performed by our independent registered public accounting firm as of December 31, 2017 pursuant to certain exceptions under the JOBS Act, as described above. Had our independent registered public accounting firm performed such an evaluation, control deficiencies may have been identified by our independent registered public accounting firm and those control deficiencies could have also represented one or more material weaknesses. Undetected material weaknesses in our internal controls could lead to financial statement restatements and require us to incur the expense of remediation.

We are at risk of securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology companies have experienced significant stock price volatility in recent years and our stock price declined following our IPO. 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.

We do not anticipate paying cash dividends, 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. 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.

The NYSE or TSX may delist our securities from its exchange, which could limit investors' ability to make transactions in our securities and subject us to additional trading restrictions.

Our securities may fail to meet the continued listing requirements to be listed on the NYSE or TSX. If the NYSE or TSX delists our common shares from trading on its exchange, we could face significant material adverse consequences, including:

- a limited availability of market quotations for our securities;
- a determination that our common shares is a "penny stock" which will require brokers trading in our common shares to adhere to more stringent rules and possibly result in a reduced level of trading activity in the secondary trading market for our common shares;
- a limited amount of news and analyst coverage for our company; and
- a decreased ability to issue additional securities or obtain additional financing in the future.

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 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. We cannot predict whether investors will 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.

We are governed by the BCBCA and our principal place of business is in Canada. Many of our directors and officers, as well as certain experts named herein, 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

[Table of Contents](#)

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.

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.

U.S. holders of our company's common shares may suffer adverse tax consequences if we are characterized as a passive foreign investment company.

We believe that we were not classified as a passive foreign investment company ("PFIC") for the taxable year ending December 31, 2017. However, the determination as to whether we are a PFIC for any taxable year is based on the application of complex U.S. federal income tax rules that are subject to differing interpretations. If we are a PFIC for any taxable year during which a U.S. Holder (as defined under Item 5 in our Annual Report on Form 10-K, "Market for Registrant's Common Equity, Related Shareholder Matters and Issuer Purchases of Equity Securities – Certain United States Income Tax Considerations For United States Holders") holds the common shares, it would likely result in adverse U.S. federal income tax consequences for such U.S. Holder. U.S. Holders should carefully read Item 5 in our Annual Report on Form 10-K, "Market for Registrant's Common Equity, Related Shareholder Matters and Issuer Purchases of Equity Securities – Certain United States Income Tax Considerations For United States Holders" for more information and consult their own tax advisors regarding the likelihood and consequences if we are treated as a PFIC for U.S. federal income tax purposes, including the advisability of making a "qualified electing fund" election (including a protective election), which may mitigate certain possible adverse U.S. federal income tax consequences but may result in an inclusion in gross income without receipt of such income.

Insiders have 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 directors, named executive officers and principal shareholders, together with their affiliates and related persons, beneficially own, in the aggregate, approximately 51.3% of our outstanding common shares as of April 20, 2018. As a result, these shareholders, if acting together, may have the ability to determine 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, these persons, acting together, may have the ability to control the management and affairs of our company. Accordingly, this concentration of ownership may 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

[Table of Contents](#)

- 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.

USE OF PROCEEDS

Unless we otherwise indicate in a prospectus supplement, we currently intend to use the net proceeds from any sale of our securities to advance business objectives outlined above under “Our Business – Our Strategy” and in the documents incorporated by reference herein, for working capital requirements and for our clinical development expenses, clinical trials and additional product candidate manufacturing.

As we currently have no revenues from product sales, we experienced a negative operating cash flow for the year ended December 31, 2017 and expect to experience a negative operating cash flow for the 2018 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”.

More detailed information regarding the use of proceeds from the sale of securities will be described in any applicable prospectus supplement. We may also, from time to time, issue securities otherwise than pursuant to a prospectus supplement to this prospectus.

PRIOR SALES

The following table summarizes issuances of our common shares and securities convertible or exchangeable into common shares during the 12-month period preceding the date of this prospectus.

<u>Date of Issuance</u>	<u>Type of Security</u>	<u>Number of Securities Issued</u>	<u>Issuance/ Exercise Price per Security (C\$)</u>	<u>Issuance/ Exercise Price per Security (US\$)(1)</u>
May 22, 2018	Common Shares Issued on Exercise of Stock Options	400	12.10	9.38
May 22, 2018	Common Shares Issued on Exercise of Stock Options	1,625	20.74	16.09
May 22, 2018	Common Shares Issued on Exercise of Stock Options	4,255	14.44	11.20
May 18, 2018	Common Shares Issued on Exercise of Stock Options	355	12.10	9.38
May 18, 2018	Common Shares Issued on Exercise of Stock Options	4,190	4.75	3.68
May 17, 2018	Common Shares Issued on Exercise of Stock Options	3,142	4.75	3.68
May 16, 2018	Stock Options	36,400	21.04	16.32
May 16, 2018	Stock Options	41,000	—	16.42
May 15, 2018	Common Shares Issued on Exercise of Stock Options	1,000	4.75	3.68
May 10, 2018	Common Shares Issued on Exercise of Warrants	79,481	—	8.67
May 8, 2018	Common Shares Issued on Exercise of Stock Options	1,222	12.10	9.38
May 3, 2018	Stock Options	26,858	—	15.90
May 1, 2018	Common Shares Issued on Exercise of Stock Options	1,047	4.75	3.68
March 23, 2018	Common Shares Issued on Exercise of Stock Options	1,000	7.26	5.63
March 22, 2018	Common Shares Issued on Exercise of Stock Options	1,000	4.75	3.68
March 21, 2018	Common Shares Issued on Exercise of Stock Options	1,000	4.75	3.68
March 19, 2018	Stock Options	234,025	15.59	12.09
March 19, 2018	Stock Options	565,500	—	11.84
February 27, 2018	Common Shares Issued on Exercise of Stock Options	917	12.10	9.38
February 27, 2018	Common Shares Issued on Exercise of Stock Options	795	4.75	3.68
February 7, 2018	Common Shares Issued on Exercise of Stock Options	800	4.75	3.68
January 25, 2018	Common Shares Issued on Exercise of Stock Options	695	4.75	3.68
January 10, 2018	Common Shares Issued on Exercise of Stock Options	1,000	4.75	3.68
January 8, 2018	Common Shares Issued Pursuant to Company's Employee Stock Purchase Plan	7,610	—	6.57
January 3, 2018	Common Shares Issued Pursuant to Company's Employee Stock Purchase Plan	5,637	—	6.57
December 31, 2017	Common Shares Issued on Exercise of Stock Options	7,647	4.75	3.68

[Table of Contents](#)

<u>Date of Issuance</u>	<u>Type of Security</u>	<u>Number of Securities Issued</u>	<u>Issuance/ Exercise Price per Security (C\$)</u>	<u>Issuance/ Exercise Price per Security (US\$)(1)</u>
December 29, 2017	Common Shares Issued on Exercise of Stock Options	2,131	4.75	3.68
December 28, 2017	Common Shares Issued on Exercise of Stock Options	21,562	4.75	3.68
December 21, 2017	Common Shares Issued on Exercise of Stock Options	15,302	4.75	3.68
December 21, 2017	Stock Options	59,000	9.94	7.71
December 21, 2017	Stock Options	9,000	—	7.75
December 14, 2017	Common Shares Issued on Exercise of Stock Options	1,657	4.75	3.68
December 7, 2017	Common Shares Issued on Exercise of Stock Options	1,195	4.75	3.68
December 6, 2017	Common Shares Issued on Exercise of Stock Options	400	4.75	3.68
November 29, 2017	Common Shares Issued on Exercise of Stock Options	9,176	4.75	3.68
November 22, 2017	Common Shares Issued on Exercise of Stock Options	900	4.75	3.68
November 20, 2017	Common Shares Issued on Exercise of Stock Options	2,095	4.75	3.68
November 17, 2017	Common Shares Issued on Exercise of Stock Options	2,095	5.37	4.16
November 17, 2017	Common Shares Issued on Exercise of Stock Options	2,100	4.75	3.68
November 15, 2017	Common Shares Issued on Exercise of Stock Options	500	4.75	3.68
October 25, 2017	Common Shares Issued on Exercise of Stock Options	8,171	5.37	4.16
October 16, 2017	Common Shares Issued on Exercise of Stock Options	8,170	5.37	4.16
October 16, 2017	Common Shares Issued on Exercise of Stock Options	20,950	7.26	5.63
August 14, 2017	Stock Options	18,855	—	6.80
July 12, 2017	Common Shares Issued on Exercise of Stock Options	5,236	4.75	3.68
June 12, 2017	Stock Options	208,225	13.21	10.25
June 12, 2017	Stock Options	622,625	—	9.82
May 31, 2017	Common Shares Issued on Underwriters' Partial Exercise of Over-Allotment Option	394,467	—	13.00

Canadian dollar amounts have been converted to U.S. dollars based on the historical Canadian to U.S. daily average rate of exchange as at March 29, 2018. For further information, see "Exchange Rate Information."

MARKET FOR SECURITIES

Our common shares are listed for trading on the TSX and on the NYSE under the trading symbol “ZYME”. The following tables set forth the high and low sale prices and the trading volume for our common shares on the TSX and the NYSE for each of the months indicated.

Toronto Stock Exchange

<u>Month</u>	<u>High</u>	<u>Low</u>	<u>Volume</u> (No. of Common Shares)
June, 2017	15.80	10.50	52,106
July, 2017	11.05	8.81	46,962
August, 2017	11.48	8.05	31,962
September, 2017	11.20	8.60	13,171
October, 2017	11.60	10.41	77,167
November, 2017	11.60	9.00	553,565
December, 2017	11.38	9.37	51,700
January, 2018	17.20	9.64	105,228
February, 2018	16.40	12.12	28,626
March, 2018	16.47	12.60	58,315
April, 2018	23.15	14.00	100,648
May, 2018 ⁽¹⁾	24.30	18.28	424,216

(1) From May 1, 2018 to May 23, 2018, the last trading day prior to the date of this prospectus.

On May 23, 2018, the closing price of our common shares on the TSX was C\$23.00 per share.

NYSE

<u>Month</u>	<u>High</u>	<u>Low</u>	<u>Volume</u> (No. of Common Shares)
June, 2017	11.72	7.53	164,555
July, 2017	8.51	7.03	54,128
August, 2017	8.80	6.31	41,854
September, 2017	8.75	7.04	45,961
October, 2017	9.25	8.09	34,799
November, 2017	9.24	6.87	124,548
December, 2017	8.91	7.27	63,357
January, 2018	14.00	7.69	107,781
February, 2018	13.41	9.57	100,508
March, 2018	12.50	9.73	68,589
April, 2018	17.95	10.55	161,026
May, 2018 ⁽¹⁾	18.97	14.27	265,788

(1) From May 1, 2018 to May 23, 2018, the last trading day prior to the date of this prospectus.

On May 23, 2018, the closing price of our common shares on the NYSE was \$17.80 per share.

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.

CONSOLIDATED CAPITALIZATION

There have been no material changes in the share and loan capital of the Company, on a consolidated basis, since March 31, 2018, the date of the most recently filed financial statements of the Company.

DESCRIPTION OF SHARE CAPITAL

General

The following is a summary of the 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 at the date of this prospectus, 25,561,177 common shares and no preferred shares are issued and outstanding.

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. 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. 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.

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.

DESCRIPTION OF DEBT SECURITIES

In this description of debt securities section, “we”, “us”, “our”, or “Zymeworks” refer to Zymeworks Inc. but not to its subsidiaries.

This section describes the general terms that will apply to any debt securities issued pursuant to this prospectus. We may issue debt securities in one or more series under an indenture, or the indenture, to be entered into between us and one or more trustees. The indenture will be subject to and governed by the *United States Trust Indenture Act of 1939*, as amended (the “Trust Indenture Act”), and the BCBCA. A copy of the form of the indenture will be filed with the SEC as an exhibit to the registration statement of which this prospectus forms a part. The following description sets forth certain general terms and provisions of the debt securities and is not intended to be complete. For a more complete description, prospective investors should refer to the indenture and the terms of the debt securities. If debt securities are issued, we will describe in the applicable prospectus supplement the particular terms and provisions of any series of the debt securities and a description of how the general terms and provisions described below may apply to that series of the debt securities. Prospective investors should rely on information in the applicable prospectus supplement and not on the following information to the extent that the information in such prospectus supplement is different from the following information.

We may issue debt securities and incur additional indebtedness other than through the offering of debt securities pursuant to this prospectus.

General

The indenture will not limit the aggregate principal amount of debt securities that we may issue under the indenture and will not limit the amount of other indebtedness that we may incur. The indenture will provide that we may issue debt securities from time to time in one or more series and may be denominated and payable in U.S. dollars, Canadian dollars or any foreign currency. Unless otherwise indicated in the applicable prospectus supplement, the debt securities will be our unsecured obligations. The indenture will also permit us to increase the principal amount of any series of the debt securities previously issued and to issue that increased principal amount.

The applicable prospectus supplement for any series of debt securities that we offer will describe the specific terms of the debt securities and may include, but is not limited to, any of the following:

- the title of the debt securities;
- the aggregate principal amount of the debt securities;
- the percentage of principal amount at which the debt securities will be issued;
- whether payment on the debt securities will be senior or subordinated to our other liabilities or obligations;
- whether the payment of the debt securities will be guaranteed by any other person;
- the date or dates, or the methods by which such dates will be determined or extended, on which we may issue the debt securities and the date or dates, or the methods by which such dates will be determined or extended, on which we will pay the principal and any premium on the debt securities and the portion (if less than the principal amount) of debt securities to be payable upon a declaration of acceleration of maturity;
- whether the debt securities will bear interest, the interest rate (whether fixed or variable) or the method of determining the interest rate, the date from which interest will accrue, the dates on which we will pay interest and the record dates for interest payments, or the methods by which such dates will be determined or extended;

Table of Contents

- the place or places we will pay principal, premium, if any, and interest and the place or places where debt securities can be presented for registration of transfer or exchange;
- whether and under what circumstances we will be required to pay any additional amounts for withholding or deduction for Canadian taxes with respect to the debt securities, and whether and on what terms we will have the option to redeem the debt securities rather than pay the additional amounts;
- whether we will be obligated to redeem or repurchase the debt securities pursuant to any sinking or purchase fund or other provisions, or at the option of a holder and the terms and conditions of such redemption;
- whether we may redeem the debt securities at our option and the terms and conditions of any such redemption;
- the denominations in which we will issue any registered debt securities, if other than denominations of \$1,000 and any multiple of \$1,000 and, if other than denominations of \$5,000, the denominations in which any unregistered debt security shall be issuable;
- whether we will make payments on the debt securities in a currency or currency unit other than U.S. dollars or by delivery of our common shares or other property;
- whether payments on the debt securities will be payable with reference to any index or formula;
- whether we will issue the debt securities as global securities and, if so, the identity of the depositary for the global securities;
- whether we will issue the debt securities as unregistered securities (with or without coupons), registered securities or both;
- the periods within which and the terms and conditions, if any, upon which we may redeem the debt securities prior to maturity and the price or prices of which and the currency or currency units in which the debt securities are payable;
- any changes or additions to events of default or covenants;
- the applicability of, and any changes or additions to, the provisions for defeasance described under “Defeasance” below;
- whether the holders of any series of debt securities have special rights if specified events occur;
- any mandatory or optional redemption or sinking fund or analogous provisions;
- the terms, if any, for any conversion or exchange of the debt securities for any other securities;
- rights, if any, on a change of control;
- provisions as to modification, amendment or variation of any rights or terms attaching to the debt securities; and
- any other terms, conditions, rights and preferences (or limitations on such rights and preferences) including covenants and events of default which apply solely to a particular series of the debt securities being offered which do not apply generally to other debt securities, or any covenants or events of default generally applicable to the debt securities which do not apply to a particular series of the debt securities.

Unless stated otherwise in the applicable prospectus supplement, no holder of debt securities will have the right to require us to repurchase the debt securities and there will be no increase in the interest rate if we become involved in a highly leveraged transaction or we have a change of control.

Table of Contents

We may issue debt securities bearing no interest or interest at a rate below the prevailing market rate at the time of issuance, and offer and sell these securities at a discount below their stated principal amount. We may also sell any of the debt securities for a foreign currency or currency unit, and payments on the debt securities may be payable in a foreign currency or currency unit. In any of these cases, we will describe certain Canadian federal and U.S. federal income tax consequences and other special considerations in the applicable prospectus supplement.

We may issue debt securities with terms different from those of debt securities previously issued and, without the consent of the holders thereof, we may reopen a previous issue of a series of debt securities and issue additional debt securities of such series (unless the reopening was restricted when such series was created).

Ranking and Other Indebtedness

Unless otherwise indicated in an applicable prospectus supplement, our debt securities will be unsecured obligations and will rank equally with all of our other unsecured and unsubordinated debt from time to time outstanding and equally with other securities issued under the indenture. The debt securities will be structurally subordinated to all existing and future liabilities, including trade payables, of our subsidiaries.

Our board of directors may establish the extent and manner, if any, to which payment on or in respect of a series of debt securities will be senior or will be subordinated to the prior payment of our other liabilities and obligations and whether the payment of principal, premium, if any, and interest, if any, will be guaranteed by any other person and the nature and priority of any security.

Debt Securities in Global Form

The Depositary and Book-Entry

Unless otherwise specified in the applicable prospectus supplement, a series of the debt securities may be issued in whole or in part in global form as a “global security” and will be registered in the name of and be deposited with a depository, or its nominee, each of which will be identified in the applicable prospectus supplement relating to that series. Unless and until exchanged, in whole or in part, for the debt securities in definitive registered form, a global security may not be transferred except as a whole by the depository for such global security to a nominee of the depository, by a nominee of the depository to the depository or another nominee of the depository or by the depository or any such nominee to a successor of the depository or a nominee of the successor.

The specific terms of the depository arrangement with respect to any portion of a particular series of the debt securities to be represented by a global security will be described in the applicable prospectus supplement relating to such series. We anticipate that the provisions described in this section will apply to all depository arrangements.

Upon the issuance of a global security, the depository therefor or its nominee will credit, on its book entry and registration system, the respective principal amounts of the debt securities represented by the global security to the accounts of such persons, designated as “participants”, having accounts with such depository or its nominee. Such accounts shall be designated by the underwriters, dealers or agents participating in the distribution of the debt securities or by us if such debt securities are offered and sold directly by us. Ownership of beneficial interests in a global security will be limited to participants or persons that may hold beneficial interests through participants. Ownership of beneficial interests in a global security will be shown on, and the transfer of that ownership will be effected only through, records maintained by the depository therefor or its nominee (with respect to interests of participants) or by participants or persons that hold through participants (with respect to interests of persons other than participants). The laws of some states in the United States may require that certain purchasers of securities take physical delivery of such securities in definitive form.

Table of Contents

So long as the depository for a global security or its nominee is the registered owner of the global security, such depository or such nominee, as the case may be, will be considered the sole owner or holder of the debt securities represented by the global security for all purposes under the indenture. Except as provided below, owners of beneficial interests in a global security will not be entitled to have a series of the debt securities represented by the global security registered in their names, will not receive or be entitled to receive physical delivery of such series of the debt securities in definitive form and will not be considered the owners or holders thereof under the indenture.

Any payments of principal, premium, if any, and interest, if any, on global securities registered in the name of a depository or its nominee will be made to the depository or its nominee, as the case may be, as the registered owner of the global security representing such debt securities. None of us, the trustee or any paying agent for the debt securities represented by the global securities will have any responsibility or liability for any aspect of the records relating to or payments made on account of beneficial ownership interests of the global security or for maintaining, supervising or reviewing any records relating to such beneficial ownership interests.

We expect that the depository for a global security or its nominee, upon receipt of any payment of principal, premium, if any, or interest, if any, will credit participants' accounts with payments in amounts proportionate to their respective beneficial interests in the principal amount of the global security as shown on the records of such depository or its nominee. We also expect that payments by participants to owners of beneficial interests in a global security held through such participants will be governed by standing instructions and customary practices, as is now the case with securities held for the accounts of customers registered in "street name", and will be the responsibility of such participants.

Discontinuance of Depository's Services

If a depository for a global security representing a particular series of the debt securities is at any time unwilling or unable to continue as depository and a successor depository is not appointed by us within 90 days, we will issue such series of the debt securities in definitive form in exchange for a global security representing such series of the debt securities. If an event of default under the indenture has occurred and is continuing, debt securities in definitive form will be printed and delivered upon written request by the holder to the trustee. In addition, we may at any time and in our sole discretion determine not to have a series of the debt securities represented by a global security and, in such event, will issue a series of the debt securities in definitive form in exchange for all of the global securities representing that series of debt securities.

Debt Securities in Definitive Form

A series of the debt securities may be issued in definitive form, solely as registered securities, solely as unregistered securities or as both registered securities and unregistered securities. Registered securities will be issuable in denominations of \$1,000 and integral multiples of \$1,000 and unregistered securities will be issuable in denominations of \$5,000 and integral multiples of \$5,000 or, in each case, in such other denominations as may be set out in the terms of the debt securities of any particular series. Unless otherwise indicated in the applicable prospectus supplement, unregistered securities will have interest coupons attached.

Unless otherwise indicated in the applicable prospectus supplement, payment of principal, premium, if any, and interest, if any, on the debt securities (other than global securities) will be made at the office or agency of the trustee, or at our option we can pay principal, interest, if any, and premium, if any, by check mailed or delivered to the address of the person entitled at the address appearing in the security register of the trustee or electronic funds wire or other transmission to an account of the person entitled to receive payments. Unless otherwise indicated in the applicable prospectus supplement, payment of interest, if any, will be made to the persons in whose name the debt securities are registered at the close of business on the day or days specified by us.

At the option of the holder of debt securities, registered securities of any series will be exchangeable for other registered securities of the same series, of any authorized denomination and of a like aggregate principal amount

Table of Contents

and tenor. If, but only if, provided in an applicable prospectus supplement, unregistered securities (with all unmatured coupons, except as provided below, and all matured coupons in default) of any series may be exchanged for registered securities of the same series, of any authorized denominations and of a like aggregate principal amount and tenor. In such event, unregistered securities surrendered in a permitted exchange for registered securities between a regular record date or a special record date and the relevant date for payment of interest shall be surrendered without the coupon relating to such date for payment of interest, and interest will not be payable on such date for payment of interest in respect of the registered security issued in exchange for such unregistered security, but will be payable only to the holder of such coupon when due in accordance with the terms of the indenture. Unless otherwise specified in an applicable prospectus supplement, unregistered securities will not be issued in exchange for registered securities.

The applicable prospectus supplement may indicate the places to register a transfer of the debt securities in definitive form. Except for certain restrictions set forth in the indenture, no service charge will be payable by the holder for any registration of transfer or exchange of the debt securities in definitive form, but we may, in certain instances, require a sum sufficient to cover any tax or other governmental charges payable in connection with these transactions.

We shall not be required to:

- issue, register the transfer of or exchange any series of the debt securities in definitive form during a period beginning at the opening of business 15 days before any selection of securities of that series of the debt securities to be redeemed and ending on the relevant redemption date if the debt securities for which such issuance, registration or exchange is requested may be among those selected for redemption;
- register the transfer of or exchange any registered security in definitive form, or portion thereof, called for redemption, except the unredeemed portion of any registered security being redeemed in part;
- exchange any unregistered security called for redemption except to the extent that such unregistered security may be exchanged for a registered security of that series and like tenor; provided that such registered security will be simultaneously surrendered for redemption with written instructions for payment consistent with the provisions of the indenture; or
- issue, register the transfer of or exchange any of the debt securities in definitive form which have been surrendered for repayment at the option of the holder, except the portion, if any, thereof not to be so repaid.

Merger, Amalgamation or Consolidation

The indenture will provide that we may not consolidate with or amalgamate or merge with or into any other person, enter into any statutory arrangement with any person or convey, transfer or lease our properties and assets substantially as an entirety to another person, unless among other items:

- we are the surviving person, or the resulting, surviving or transferee person, if other than us, is organized and existing under the laws of the United States, any state thereof or the District of Columbia, Canada, or any province or territory thereof, or, if the amalgamation, merger, consolidation, statutory arrangement or other transaction would not impair the rights of holders, any other country;
- the successor person (if not us) assumes all of our obligations under the debt securities and the indenture; and
- we or such successor person will not be in default under the indenture immediately after the transaction.

When such a person assumes our obligations in such circumstances, subject to certain exceptions, we shall be discharged from all obligations under the debt securities and the indenture.

Additional Amounts

Unless otherwise specified in the applicable prospectus supplement, all payments made by or on behalf of us under or with respect to the debt securities will be made free and clear of and without withholding or deduction for or on account of any present or future tax, duty, levy, impost, assessment or other government charge (including penalties, interest and other liabilities related thereto) imposed or levied by or on behalf of the Government of Canada or of any province or territory thereof or by any authority or agency therein or thereof having power to tax, or Canadian Taxes, unless we are required to withhold or deduct Canadian Taxes by law or by the interpretation or administration thereof by the relevant government authority or agency.

If we are so required to withhold or deduct any amount for or on account of Canadian Taxes from any payment made under or with respect to the debt securities, we will pay as additional interest such additional amounts, or the additional amounts, as may be necessary so that the net amount received by a holder of the debt securities after such withholding or deduction will not be less than the amount such holder of the debt securities would have received if such Canadian Taxes had not been withheld or deducted (a similar payment will also be made to holders of the debt securities, other than excluded holders (as defined herein), that are exempt from withholding but required to pay tax under Part XIII of the *Income Tax Act* (Canada) (the "ITA"), directly on amounts otherwise subject to withholding); provided, however, that no additional amounts will be payable with respect to a payment made to a holder of the debt securities, or an excluded holder, in respect of the beneficial owner thereof:

- with which we do not deal at arm's length (for purposes of the ITA) at the time of the making of such payment;
- which is subject to such Canadian Taxes by reason of the debt securities holder's failure to comply with any certification, identification, information, documentation or other reporting requirement if compliance is required by law, regulation, administrative practice or an applicable treaty as a precondition to exemption from, or a reduction in the rate of deduction or withholding of, such Canadian Taxes;
- which is subject to such Canadian Taxes by reason of the debt securities holder being a resident, domicile or national of, or engaged in business or maintaining a permanent establishment or other physical presence in or otherwise having some connection with Canada or any province or territory thereof otherwise than by the mere holding of the debt securities or the receipt of payments thereunder; or
- which is subject to such Canadian Taxes because it is not entitled to the benefit of an otherwise applicable tax treaty by reason of the legal nature of such holder of the debt securities.

We will make such withholding or deduction and remit the full amount deducted or withheld to the relevant authority as and when required in accordance with applicable law. We will pay all taxes, interest and other liabilities which arise by virtue of any failure of us to withhold, deduct and remit to the relevant authority on a timely basis the full amounts required in accordance with applicable law. We will furnish to the holder of the debt securities, within 60 days after the date the payment of any Canadian Taxes is due pursuant to applicable law, certified copies of tax receipts evidencing such payment by us.

Whenever in the indenture there is mentioned, in any context, the payment of principal, premium, if any, interest or any other payment under or with respect to a debt security, such mention shall be deemed to include mention of the payment of additional amounts to the extent that, in such context, additional amounts are, were or could be payable in respect thereof.

The foregoing obligations shall survive any termination, defeasance or discharge of the indenture.

Tax Redemption

If and to the extent specified in the applicable prospectus supplement, the debt securities of a series will be subject to redemption at any time, in whole but not in part, at a redemption price equal to the principal amount thereof together with accrued and unpaid interest to the date fixed for redemption, upon the giving of a notice as described below, if (1) we determine that (a) as a result of any change in or amendment to the laws (or any regulations or rulings promulgated thereunder) of Canada or of any political subdivision or taxing authority thereof or therein affecting taxation, or any change in position regarding application or interpretation of such laws, regulations or rulings (including a holding by a court of competent jurisdiction), which change or amendment is announced or becomes effective on or after a date specified in the applicable prospectus supplement if any date is so specified, we have or will become obligated to pay, on the next succeeding date on which interest is due, additional amounts with respect to any debt security of such series as described under “Additional Amounts” or (b) on or after a date specified in the applicable prospectus supplement, any action has been taken by any taxing authority of, or any decision has been rendered by a court of competent jurisdiction in, Canada or any political subdivision or taxing authority thereof or therein, including any of those actions specified in (a) above, whether or not such action was taken or decision was rendered with respect to us, or any change, amendment, application or interpretation shall be proposed, which, in any such case, in the written opinion to us of legal counsel of recognized standing, will result in our becoming obligated to pay, on the next succeeding date on which interest is due, additional amounts with respect to any debt security of such series and (2) in any such case, we, in our business judgment, determine that such obligation cannot be avoided by the use of reasonable measures available to us; provided however, that (i) no such notice of redemption may be given earlier than 90 days prior to the earliest date on which we would be obligated to pay such additional amounts were a payment in respect of the debt securities then due, and (ii) at the time such notice of redemption is given, such obligation to pay such additional amounts remains in effect.

In the event that we elect to redeem the debt securities of such series pursuant to the provisions set forth in the preceding paragraph, we shall deliver to the trustee a certificate, signed by an authorized officer, stating that we are entitled to redeem the debt securities of such series pursuant to their terms.

Provision of Financial Information

We will file with the trustee, within 20 days after we file or furnish them with the SEC, copies of our annual reports and of the information, documents and other reports (or copies of such portions of any of the foregoing as the SEC may by rules and regulations prescribe) which we are required to file or furnish with the SEC pursuant to Section 13 or 15(d) of the Exchange Act.

Notwithstanding that we may not remain subject to the reporting requirements of Section 13 or 15(d) of the Exchange Act or otherwise report on an annual and quarterly basis on forms provided for such annual and quarterly reporting pursuant to rules and regulations promulgated by the SEC, we will continue to provide the trustee:

- within 20 days after the time periods required for the filing or furnishing of such forms by the SEC, annual reports on Form 40-F, Form 20-F or Form 10-K, as applicable, or any successor form; and
- within 20 days after the time periods required for the filing of such forms by the SEC, reports on Form 8-K or Form 6-K (or any successor form), as applicable, which, regardless of applicable requirements shall, at a minimum, contain such information required to be provided in quarterly reports under the laws of Canada or any province thereof to security holders of a corporation with securities listed on the TSX, whether or not we have any of the debt securities listed on such exchange. Each of such reports, to the extent permitted by the rules and regulations of the SEC, will be prepared in accordance with Canadian disclosure requirements and generally accepted accounting principles provided, however, that we shall not be obligated to file or furnish such reports with the SEC if the SEC does not permit such filings.

Events of Default

Unless otherwise specified in the applicable prospectus supplement relating to a particular series of debt securities, the following is a summary of events which will, with respect to any series of the debt securities, constitute an event of default under the indenture with respect to the debt securities of that series:

- we fail to pay principal of, or any premium on, any debt security of that series when it is due and payable;
- we fail to pay interest or any additional amounts payable on any debt security of that series when it becomes due and payable, and such default continues for 30 days;
- we fail to make any required sinking fund or analogous payment for that series of debt securities;
- we fail to observe or perform any of the covenants described in the section “— Merger, Amalgamation or Consolidation” for a period of 30 days;
- we fail to comply with any of our other agreements in the indenture that affect or are applicable to the debt securities for 60 days after written notice by the trustee or to us and the trustee by holders of at least 25% in aggregate principal amount of the outstanding debt securities of any series affected thereby;
- a default (as defined in any indenture or instrument under which we or one of our subsidiaries has at the time of the indenture relating to this prospectus or will thereafter have outstanding any indebtedness) has occurred and is continuing, or we or any of our subsidiaries has failed to pay principal amounts with respect to such indebtedness at maturity and such event of default or failure to pay has resulted in such indebtedness under such indentures or instruments being declared due, payable or otherwise being accelerated, in either event so that an amount in excess of the greater of \$10,000,000 and 2% of our shareholders’ equity will be or become due, payable and accelerated upon such declaration or prior to the date on which the same would otherwise have become due, payable and accelerated, or the accelerated indebtedness, and such acceleration will not be rescinded or annulled, or such event of default or failure to pay under such indenture or instrument will not be remedied or cured, whether by payment or otherwise, or waived by the holders of such accelerated indebtedness, then (i) if the accelerated indebtedness will be as a result of an event of default which is not related to the failure to pay principal or interest on the terms, at the times, and on the conditions set out in any such indenture or instrument, it will not be considered an event of default for the purposes of the indenture governing the debt securities relating to this prospectus until 30 days after such indebtedness has been accelerated, or (ii) if the accelerated indebtedness will occur as a result of such failure to pay principal or interest or as a result of an event of default which is related to the failure to pay principal or interest on the terms, at the times, and on the conditions set out in any such indenture or instrument, then (A) if such accelerated indebtedness is, by its terms, non-recourse to us or our subsidiaries, it will be considered an event of default for purposes of the indenture governing the debt securities relating to this prospectus; or (B) if such accelerated indebtedness is recourse to us or our subsidiaries, any requirement in connection with such failure to pay or event of default for the giving of notice or the lapse of time or the happening of any further condition, event or act under such indenture or instrument in connection with such failure to pay or event of default will be applicable together with an additional seven days before being considered an event of default for the purposes of the indenture relating to this prospectus;
- certain events involving our bankruptcy, insolvency or reorganization; and
- any other event of default provided for in that series of debt securities.

A default under one series of debt securities will not necessarily be a default under another series. The trustee may withhold notice to the holders of the debt securities of any default, except in the payment of principal or premium, if any, or interest, if any, if in good faith it considers it in the interests of the holders to do so.

Table of Contents

If an event of default for any series of debt securities occurs and continues, the trustee or the holders of at least 25% in aggregate principal amount of the debt securities of that series, subject to any subordination provisions, may require us to repay immediately:

- the entire principal and interest and premium, if any, of the debt securities of the series; or
- if the debt securities are discounted securities, that portion of the principal as is described in the applicable prospectus supplement.

If an event of default relates to events involving our bankruptcy, insolvency or reorganization, the principal of all debt securities will become immediately due and payable without any action by the trustee or any holder. Subject to certain conditions, the holders of a majority of the aggregate principal amount of the debt securities of the affected series can rescind this accelerated payment requirement. If debt securities are discounted securities, the applicable prospectus supplement will contain provisions relating to the acceleration of maturity of a portion of the principal amount of the discounted securities upon the occurrence or continuance of an event of default.

Other than its duties in case of a default, the trustee is not obligated to exercise any of the rights or powers that it will have under the indenture at the request, order or direction of any holders, unless the holders offer the trustee reasonable indemnity. If they provide this reasonable indemnity, the holders of a majority in aggregate principal amount of any series of debt securities may, subject to certain limitations, direct the time, method and place of conducting any proceeding or any remedy available to the trustee, or exercising any power conferred upon the trustee, for any series of debt securities.

We will be required to furnish to the trustee a statement annually as to our compliance with all conditions and covenants under the indenture and, if we are not in compliance, we must specify any defaults. We will also be required to notify the trustee as soon as practicable upon becoming aware of any event of default.

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

- the holder has previously given to the trustee written notice of a continuing event of default with respect to the debt securities of the affected series;
- the holders of at least 25% in principal amount of the outstanding debt securities of the series affected by an event of default have made a written request, and the holders have offered reasonable indemnity, to the trustee to institute a proceeding as trustee; and
- the trustee has failed to institute a proceeding, and has not received from the holders of a majority in aggregate principal amount of the outstanding debt securities of the series affected by an event of default a direction inconsistent with the request, within 60 days after their notice, request and offer of indemnity.

However, such above-mentioned limitations do not apply to a suit instituted by the holder of a debt security for the enforcement of payment of the principal of or any premium, if any, or interest on such debt security on or after the applicable due date specified in such debt security.

Defeasance

When we use the term “defeasance”, we mean discharge from some or all of our obligations under the indenture. Unless otherwise specified in the applicable prospectus supplement, if we deposit with the trustee sufficient cash or government securities to pay the principal, interest, if any, premium, if any, and any other sums due to the stated maturity date or a redemption date of the debt securities of a series, then at our option:

- we will be discharged from the obligations with respect to the debt securities of that series; or

Table of Contents

- we will no longer be under any obligation to comply with certain restrictive covenants under the indenture, and certain events of default will no longer apply to us.

If this happens, the holders of the debt securities of the affected series will not be entitled to the benefits of the indenture except for registration of transfer and exchange of debt securities and the replacement of lost, stolen or mutilated debt securities. These holders may look only to the deposited fund for payment on their debt securities.

To exercise our defeasance option, we must deliver to the trustee:

- an opinion of counsel in the United States to the effect that the holders of the outstanding debt securities of the affected series will not recognize a gain or loss for U.S. federal income tax purposes as a result of a defeasance and will be subject to U.S. federal income tax on the same amounts, in the same manner and at the same times as would have been the case if the defeasance had not occurred;
- an opinion of counsel in Canada or a ruling from the Canada Revenue Agency to the effect that the holders of the outstanding debt securities of the affected series will not recognize income, or a gain or loss for Canadian federal, provincial or territorial income or other tax purposes as a result of a defeasance and will be subject to Canadian federal, provincial or territorial income tax and other tax on the same amounts, in the same manner and at the same times as would have been the case had the defeasance not occurred; and
- a certificate of one of our officers and an opinion of counsel, each stating that all conditions precedent provided for relating to defeasance have been complied with.

If we are to be discharged from our obligations with respect to the debt securities, and not just from our covenants, the U.S. opinion must be based upon a ruling from or published by the United States Internal Revenue Service or a change in law to that effect.

In addition to the delivery of the opinions described above, the following conditions must be met before we may exercise our defeasance option:

- no event of default or event that, with the passing of time or the giving of notice, or both, shall constitute an event of default shall have occurred and be continuing for the debt securities of the affected series;
- we are not an “insolvent person” within the meaning of applicable bankruptcy and insolvency legislation; and
- other customary conditions precedent are satisfied.

Modification and Waiver

Modifications and amendments of the indenture may be made by us and the trustee with the consent of the holders of a majority in aggregate principal amount of the outstanding debt securities of each series affected by the modification. However, without the consent of each holder affected, no modification may:

- change the stated maturity of the principal of, premium, if any, or any installment of interest, if any, on any debt security;
- reduce the principal, premium, if any, or rate of interest, if any, or any obligation to pay any additional amounts;
- reduce the amount of principal of a debt security payable upon acceleration of its maturity;
- change the place or currency of any payment;
- affect the holder’s right to require us to repurchase the debt securities at the holder’s option;

Table of Contents

- impair the right of the holders to institute a suit to enforce their rights to payment;
- adversely affect any conversion or exchange right related to a series of debt securities;
- change the percentage of debt securities required to modify the indenture or to waive compliance with certain provisions of the indenture; or
- reduce the percentage in principal amount of outstanding debt securities necessary to take certain actions.

The holders of a majority in principal amount of outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive, insofar as only that series is concerned, past defaults under the indenture and compliance by us with certain restrictive provisions of the indenture. However, these holders may not waive a default in any payment on any debt security or compliance with a provision that cannot be modified without the consent of each holder affected.

We may modify the indenture without the consent of the holders to:

- evidence our successor under the indenture;
- add covenants or surrender any right or power for the benefit of holders;
- add events of default;
- provide for unregistered securities to become registered securities under the indenture and make other such changes to unregistered securities that in each case do not materially and adversely affect the interests of holders of outstanding securities;
- establish the forms of the debt securities;
- appoint a successor trustee under the indenture;
- add provisions to permit or facilitate the defeasance or discharge of the debt securities as long as there is no material adverse effect on the holders;
- cure any ambiguity, correct or supplement any defective or inconsistent provision, make any other provisions in each case that would not materially and adversely affect the interests of holders of outstanding securities and related coupons, if any;
- comply with any applicable laws of the United States and Canada in order to effect and maintain the qualification of the indenture under the Trust Indenture Act; or
- change or eliminate any provisions where such change takes effect when there are no securities outstanding under the indenture.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the laws of the State of New York.

The Trustee

The trustee under the indenture or its affiliates may provide banking and other services to us in the ordinary course of their business.

The indenture will contain certain limitations on the rights of the trustee, as long as it or any of its affiliates remains our creditor, to obtain payment of claims in certain cases or to realize on certain property received on any claim as security or otherwise. The trustee and its affiliates will be permitted to engage in other transactions with us. If the trustee or any affiliate acquires any conflicting interest and a default occurs with respect to the debt securities, the trustee must eliminate the conflict or resign.

Resignation of Trustee

The trustee may resign or be removed with respect to one or more series of the debt securities and a successor trustee may be appointed to act with respect to such series. In the event that two or more persons are acting as trustee with respect to different series of debt securities, each such trustee shall be a trustee of a trust under the indenture separate and apart from the trust administered by any other such trustee, and any action described herein to be taken by the “trustee” may then be taken by each such trustee with respect to, and only with respect to, the one or more series of debt securities for which it is trustee.

Consent to Service

In connection with the indenture, we will designate and appoint the Corporation Trust Company, Corporation Trust Center, 1209 Orange Street, Wilmington, Delaware, 19801, as our authorized agent upon which process may be served in any suit or proceeding arising out of or relating to the indenture or the debt securities that may be instituted in any U.S. federal or New York state court located in the Borough of Manhattan, in the City of New York, or brought by the trustee (whether in its individual capacity or in its capacity as trustee under the indenture), and will irrevocably submit to the non-exclusive jurisdiction of such courts.

Enforceability of Judgments

Since all or substantially all of our assets, as well as the assets of most of our directors and officers, are outside the United States, any judgment obtained in the United States against us or certain of our directors or officers, including judgments with respect to the payment of principal on the debt securities, may not be collectible within the United States.

We have been advised that the laws of the Province of British Columbia and the federal laws of Canada applicable therein permit an action to be brought against us in a court of competent jurisdiction in the Province of British Columbia on any final and conclusive judgment in personam of any federal or state court located in the State of New York, or a New York Court, which is subsisting and unsatisfied for a sum certain with respect to the enforcement of the indenture and the debt securities that is not impeachable as void or voidable under the internal laws of the State of New York if: (1) the New York Court rendering such judgment had jurisdiction over the judgment debtor, as recognized by the courts of the Province of British Columbia (and submission by us in the indenture to the jurisdiction of the New York Court will be sufficient for that purpose); (2) proper service of process in respect of the proceedings in which such judgment was obtained was made in accordance with New York 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, the federal laws of Canada or contrary to any order made by the Attorney General of Canada and under the *Foreign Extraterritorial Measures Act* (Canada) or 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; (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 been advised that there is doubt as to the enforceability in Canada by a court in original actions, or in actions to enforce judgments of U.S. courts, of civil liabilities predicated solely upon the U.S. federal securities laws.

DESCRIPTION OF WARRANTS

General

This section describes the general terms that will apply to any warrants for the purchase of common shares, or equity warrants, or for the purchase of debt securities, or debt warrants. 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 of 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.

Original purchasers are further advised that in certain Canadian provinces and territories the statutory right of action for damages in connection with a prospectus misrepresentation is limited to the amount paid for the security that was purchased under a prospectus, and therefore a further payment at the time of exercise may not be recoverable in a statutory action for damages. A Canadian purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for the particulars of these rights, or consult with a legal advisor.

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;

Table of Contents

- 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 that may be purchased upon exercise of each equity warrant and the price at which and currency or currencies in which the common 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.

Original purchasers are further advised that in certain Canadian provinces and territories the statutory right of action for damages in connection with a prospectus misrepresentation is limited to the amount paid for the security that was purchased under a prospectus, and therefore a further payment at the time of exercise may not be recoverable in a statutory action for damages. A Canadian purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for the particulars of these rights, or consult with a legal advisor.

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.

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.

CERTAIN INCOME TAX CONSIDERATIONS

The applicable prospectus supplement may describe certain Canadian federal income tax consequences to an investor who is a non-resident of Canada or to an investor who is a resident of Canada of acquiring, owning and disposing of any of our securities offered thereunder.

The applicable prospectus supplement may also describe certain U.S. federal income tax consequences of the acquisition, ownership and disposition of any of our securities offered thereunder by an initial investor who is a U.S. person (within the meaning of the U.S. Internal Revenue Code), including, to the extent applicable, such consequences relating to debt securities payable in a currency other than the U.S. dollar, issued at an original issue discount for U.S. federal income tax purposes or containing early redemption provisions or other special items.

SELLING SECURITYHOLDERS

Our common shares may be sold under this prospectus by way of a secondary offering by or for the account of certain of our securityholders. The prospectus supplement that we will file in connection with any offering of our common shares by selling securityholders will include the following information:

- the names of the selling securityholders;
- the number or amount of our common shares owned, controlled or directed by each selling securityholder;
- the number or amount of our common shares being distributed for the account of each selling securityholder;
- the number or amount of securities to be owned by the selling securityholders after the distribution and the percentage that number or amount represents of the total number of our outstanding securities; and
- whether our common shares are owned by the selling securityholders both of record and beneficially, of record only or beneficially only.

PLAN OF DISTRIBUTION

New Issue

We may issue our 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 an acquisitions of assets or shares or another entity or company.

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

- the name or names of any underwriters, dealers or other placement agents;
- the number and the purchase price of, and form of consideration for, our securities;
- any proceeds to us; and
- any commissions, fees, discounts and other items constituting underwriters', dealers' or agents' compensation.

Our 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 price or at negotiated prices, including sales in transactions that are deemed to be "at the market distributions" as defined in *National Instrument 44-102 Shelf Distributions*, including sales made directly on the TSX, 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 public 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 the Company.

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

Under agreements which may be entered into by us, underwriters, dealers and agents who participate in the distribution of our securities may be entitled to indemnification by us against certain liabilities, including liabilities under the Securities Act, and applicable Canadian provincial securities legislation, or to contribution with respect to payments which such underwriters, dealers or agents may be required to make in respect thereof. The underwriters, dealers and agents with whom we enter into agreements 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" as defined under applicable Canadian securities legislation, 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 our securities or effect any other transactions that are intended to stabilize the market price of our securities.

In connection with any offering of our securities, other than an "at the market distribution", the underwriters may over-allot or effect transactions which stabilize or maintain the market price of our 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.

Secondary Offering

This prospectus may also, from time to time, relate to the offering of our common shares by certain selling securityholders.

Table of Contents

The selling securityholders may sell all or a portion of our common shares beneficially owned by them and offered hereby from time to time directly or through one or more underwriters, broker-dealers or agents. If our common shares are sold through underwriters or broker-dealers, the selling securityholders will be responsible for underwriting discounts or commissions or agent's commissions. Our common shares may be sold by the selling securityholders in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions, as follows:

- on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale;
- in the over-the-counter market;
- in transactions otherwise than on these exchanges or systems or in the over-the-counter market;
- through the writing of options, whether such options are listed on an options exchange or otherwise;
- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales;
- sales pursuant to Rule 144 under the U.S. Securities Act;
- broker-dealers may agree with the selling securityholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

If the selling securityholders effect such transactions by selling our common shares to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling securityholders or commissions from purchasers of our common shares for whom they may act as agent or to whom they may sell as principal (which discounts, concessions or commissions as to particular underwriters, broker-dealers or agents may be in excess of those customary in the types of transactions involved). In connection with sales of our common shares or otherwise, the selling securityholders may enter into hedging transactions with broker-dealers, which may in turn engage in short sales of our common shares in the course of hedging in positions they assume. The selling securityholders may also sell our common shares short and deliver our common shares covered by this prospectus to close out short positions and to return borrowed shares in connection with such short sales. The selling securityholders may also loan or pledge our common shares to broker-dealers that in turn may sell such shares.

The selling securityholders may pledge or grant a security interest in some or all of the common shares owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell our common shares from time to time pursuant to this prospectus or any supplement to this prospectus filed under General Instruction I.L. of Form F-10 under the U.S. Securities Act, amending, if necessary, the list of selling securityholders to include, pursuant to a prospectus amendment or prospectus supplement, the pledgee, transferee or other successors in interest as selling securityholders under this prospectus. The selling securityholders also may transfer and donate our common shares in other circumstances in which case the transferees, donees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

Table of Contents

The selling securityholders and any broker-dealer participating in the distribution of our common shares may be deemed to be “underwriters” within the meaning of the U.S. Securities Act, and any commission paid, or any discounts or concessions allowed to, any such broker-dealer may be deemed to be underwriting commissions or discounts under the U.S. Securities Act. At the time a particular offering of our common shares is made, a prospectus supplement, if required, will be distributed which will identify the selling securityholders and provide the other information set forth under “Selling Securityholders”, set forth the aggregate amount of our common shares being offered and the terms of the offering, including the name or names of any broker-dealers or agents, any discounts, commissions and other terms constituting compensation from the selling securityholders and any discounts, commissions or concessions allowed or reallocated or paid to broker-dealers.

Under the securities laws of some states, our common shares may be sold in such states only through registered or licensed brokers or dealers. In addition, in some states our common shares may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with.

There can be no assurance that any securityholder will sell any or all of our common shares registered pursuant to the registration statement, of which this prospectus forms a part.

The selling securityholders and any other person participating in such distribution will be subject to applicable provisions of Canadian securities legislation and the Exchange Act and the rules and regulations thereunder, including, without limitation, Regulation M under the Exchange Act, which may limit the timing of purchases and sales of any of our common shares by the selling securityholders and any other participating person. Regulation M may also restrict the ability of any person engaged in the distribution of our common shares to engage in market-making activities with respect to our common shares. All of the foregoing may affect the marketability of our common shares and the ability of any person or entity to engage in market-making activities with respect to our common shares.

Once sold under the shelf registration statement, of which this prospectus forms a part, our common shares will be freely tradable in the hands of person other than our affiliates.

AUDITORS, TRANSFER AGENT AND REGISTRAR

KPMG LLP was appointed as our auditor at our annual meeting of shareholders held on June 24, 2015. 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 fiscal 2016 and 2017 audited consolidated financial statements, which have been filed with the securities regulatory authorities and incorporated by reference herein. KPMG LLP is independent with respect to the Company within the meaning of the Rules of Professional Conduct of the Chartered Professional Accountants of British Columbia.

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.

AGENT FOR SERVICE OF PROCESS

Each of Lota Zoth, Kenneth J. Hillan, Hollings C. Renton and Natalie Sacks (collectively, the “Non-Canadian Directors”), reside outside of Canada and has appointed the following agent for service of process in Canada:

<u>Name of Person</u>	<u>Name and Address of Agent</u>
Non-Canadian Directors	Blake, Cassels & Graydon LLP Suite 2600, 595 Burrard Street, Vancouver, British Columbia, Canada

Purchasers are advised that it may not be possible for investors to enforce judgments obtained in Canada against any person or company that is incorporated, continued or otherwise organized under the laws of a foreign jurisdiction or resides outside of Canada, even if the party has appointed an agent for service of process.

LEGAL MATTERS

Certain legal matters related to our securities offered by this prospectus will be passed upon on our behalf by Blake, Cassels & Graydon LLP, with respect to matters of Canadian law, and Skadden, Arps, Slate, Meagher & Flom LLP, with respect to matters of U.S. law. As of the date of this prospectus, the partners and associates of Blake, Cassels & Graydon LLP beneficially own, directly or indirectly, less than 1% of our outstanding common shares.

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. In addition, we are subject to the informational requirements of the Exchange Act, and, in accordance with the Exchange Act, we also file reports with, and furnish other information to, the SEC. Under a multijurisdictional disclosure system adopted by the United States and Canada, these reports and other information (including financial information) may be prepared in accordance with the disclosure requirements of Canada, which differ in certain respects from those in the United States. As a foreign private issuer, we are exempt from the rules under the Exchange Act prescribing the furnishing and content of proxy statements, and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required to publish financial statements as promptly as U.S. companies.

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 and any document we file with, or furnish to, the SEC at the SEC's public reference room at Station Place, 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms. Certain of our filings are also electronically available on EDGAR, and may be accessed at www.sec.gov.

ENFORCEABILITY OF CIVIL LIABILITIES

We are a corporation existing under the BCBCA. Most of our officers, some of our directors 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 of the Company's assets are, located outside the United States. We have appointed an agent for service of process in the United States (as set forth below), but it may be difficult for holders of securities 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 securities 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 United States federal securities laws. We have been advised that a judgment of a U.S. court 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 likely be enforceable in Canada if the United States court in which the judgment was obtained has a basis for jurisdiction in the matter that would be recognized by a Canadian court for the same purposes. We have also been advised, however, that there is substantial doubt whether an action could be brought in Canada in the first instance on the basis of the liability predicated solely upon U.S. federal securities laws.

We filed with the SEC, concurrently with our registration statement on Form F-10 of which this prospectus is a part, an appointment of agent for service of process on Form F-X. Under the Form F-X, we appointed The Corporation Trust Company, Corporation Trust Center, 1209 Orange Street, Wilmington, Delaware, 19801 as our agent for service of process in the United States in connection with any investigation or administrative proceeding conducted by the SEC, and any civil suit or action brought against or involving us in a U.S. court arising out of or related to or concerning the offering of securities under this prospectus.

PART II

INFORMATION NOT REQUIRED TO BE DELIVERED TO OFFEREES OR PURCHASERS

Indemnification.

Under the BCBCA, we may indemnify an individual who:

- a) is or was our director or officer;
- b) is or was a director or officer (1) at our request, or (2) of another corporation at the time when such corporation is or was an affiliate of ours; or
- c) at our request, is or was, or holds or held a position equivalent to that of a director or officer of a partnership, trust, joint venture or other unincorporated entity, against a judgment, penalty or fine awarded or imposed in, or an amount paid in settlement of, any legal proceeding or investigative action, whether current, threatened, pending or completed, in which such eligible party is involved because of that association with us or other entity.

However, indemnification is prohibited under the BCBCA if:

- a) such eligible party did not act honestly and in good faith with a view to our best interests (or the other entity, as the case may be);
- b) in the case of a proceeding other than a civil proceeding, such eligible party did not have reasonable grounds for believing that such person's conduct was lawful;
- c) the indemnity or payment is made under an earlier agreement to indemnify or pay expenses and, at the time that the agreement to indemnify or pay expenses was made, we were prohibited from giving the indemnity or paying the expenses by our articles; or
- d) the indemnity or payment is made otherwise than under an earlier agreement to indemnify or pay expenses and, at the time that the indemnity or payment is made, we were prohibited from giving the indemnity or paying the expenses by our articles.

We may not indemnify or pay the expenses of an eligible party in respect of an action brought against an eligible party by or on behalf of us.

The BCBCA allows us to pay, as they are incurred in advance of a final disposition of a proceeding, the expenses actually and reasonably incurred by the eligible party, provided that we receive from such eligible party an undertaking to repay the amounts advanced if it is ultimately determined that such payment is prohibited. Following the final disposition of an eligible proceeding, the BCBCA requires us to pay the expenses actually and reasonably incurred by the eligible party in respect of that proceeding if the eligible party has not been reimbursed for those expenses and is wholly successful, on the merits or otherwise, in the outcome of the proceeding, or is substantially successful on the merits in the outcome of the proceeding.

Despite the foregoing, on application by us or an eligible party, a court may:

- a) order us to indemnify an eligible party in respect of an eligible proceeding;
- b) order us to pay some or all of the expenses incurred by an eligible party in an eligible proceeding;
- c) order enforcement of or any payment under an indemnification agreement;
- d) order us to pay some or all of the expenses actually and reasonably incurred by a person in obtaining the order of the court; and
- e) make any other order the court considers appropriate.

[Table of Contents](#)

The BCBCA provides that we may purchase and maintain insurance for the benefit of an eligible party (or their heirs and personal or other legal representatives of the eligible party) against any liability that may be incurred by reason of the eligible party being or having been a director or officer, or in an equivalent position of ours or that of an associated corporation.

Our articles provide that we will indemnify any of our directors, former directors, officers, and former officers and other parties specified by the articles against all costs, charges, and expenses, including an amount paid to settle an action or satisfy a judgment, reasonably incurred by them for any civil, criminal or administrative action or proceeding to which they are or may be made a party by reason of having been a director or officer.

We have entered into indemnity agreements with certain of our officers and directors, pursuant to which we are obligated to indemnify and hold harmless such persons against all costs, charges, and expenses, including any amounts paid to settle actions or satisfy judgments, reasonably incurred by them in respect of any civil, criminal, administrative, investigative, or other proceeding to which they are made a party by reason of being or having been an officer or director. However, such indemnification obligations arise only to the extent that the party seeking indemnification was acting honestly and in good faith with a view to our best interests, and, in the case of criminal or administrative actions or proceedings enforced by monetary penalties, that such person had reasonable grounds for believing that his or her conduct was lawful. Under the indemnity agreements, we may advance to the indemnified parties the expenses incurred in defending any such actions or proceedings, but if the director or officer does not meet the conditions to qualify for indemnification, such amounts shall be repaid.

As permitted by the BCBCA, the Registrant has purchased directors' and officers' liability insurance that, under certain circumstances, insures its directors and officers against the costs of defense, settlement, or payment of a judgment.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers or persons controlling the Registrant pursuant to the foregoing provisions, the Registrant has been informed that in the opinion of the U.S. Securities and Exchange Commission (the "SEC") such indemnification is against public policy as expressed in the Securities Act of 1933 and is therefore unenforceable.

Table of Contents

Exhibits

The following exhibits have been filed as part of the Registration Statement:

<u>Exhibit No.</u>	<u>Description</u>
4.1	Annual Report on Form 10-K for the fiscal year ended December 31, 2017 filed with the SEC on March 14, 2018 (File No. 001-38068).
4.2	Audited consolidated financial statements as at and for the fiscal year ended December 31, 2017, together with the notes thereto and the auditor's report thereon (incorporated by reference to Item 8 of our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 filed with the SEC on March 14, 2018 (File No. 001-38068)).
4.3	Management's discussion and analysis of the financial condition and results of operations for the fiscal year ended December 31, 2017 (incorporated by reference to Item 7 of our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 filed with the SEC on March 14, 2018 (File No. 001-38068)).
4.4	Quarterly Report on Form 10-Q for the three month period ended March 31, 2018 filed with the SEC on May 1, 2018 (File No. 001-38068).
4.5	Unaudited interim consolidated financial statements as at and for the three months ended March 31, 2018, together with the notes thereto (incorporated by reference to Item 1 of our Quarterly Report on Form 10-Q filed with the SEC on May 1, 2018 (File No. 001-38068)).
4.6	Management's discussion and analysis of the financial condition and results of operations for the three months ended March 31, 2018 (incorporated by reference to Item 2 of our Quarterly Report on Form 10-Q filed with the SEC on May 1, 2018 (File No. 001-38068)).
4.7*	Material change report dated March 20, 2018 with respect to our announcement that ZW49 is the first product candidate selected for clinical development using the ZymeLink antibody-drug conjugate platform.
4.8*	Material change report, dated April 17, 2018, with respect to our presentation of preclinical data on ZW49.
4.9*	Material change report, dated April 24, 2018 with respect to Celgene Corporation having exercised its right to expand its collaboration agreement for the research, development, and commercialization of bispecific antibody therapeutics using Zymeworks' Azymetric platform.
4.10*	Material change report, dated April 25, 2018, with respect to our announcement that the abstract highlighting new data from our adaptive Phase 1 clinical trial for ZW25 has been selected for an oral presentation at the American Society of Clinical Oncology.
4.11	Current Report on Form 8-K, dated March 14, 2018 filed with the SEC on March 14, 2018 (File No. 001-38068) (including Exhibit 99.1 thereto, which is deemed filed under the U.S. Securities Exchange Act of 1934 and is incorporated by reference into this Registration Statement).
4.12	Current Report on Form 8-K, dated April 17, 2018 filed with the SEC on April 18, 2018 (File No. 001-38068).
4.13	Current Report on Form 8-K, dated April 23, 2018 filed with the SEC on April 23, 2018 (File No. 001-38068).
4.14	Current Report on Form 8-K, dated April 25, 2018 filed with the SEC on April 25, 2018 (File No. 001-38068).

Table of Contents

<u>Exhibit No.</u>	<u>Description</u>
4.15	Current Report on Form 8-K, dated April 30, 2018 filed with the SEC on April 30, 2018 (File No. 001-38068).
4.16	Current Report on Form 8-K, dated May 1, 2018 filed with the SEC on May 1, 2018 (File No. 001-38068) (including Exhibit 99.1 thereto, which is deemed filed under the U.S. Securities Exchange Act of 1934 and is incorporated by reference into this Registration Statement).
4.17	Current Report on Form 8-K, dated May 10, 2018 filed with the SEC on May 10, 2018 (File No. 001-38068).
4.18	Current Report on Form 8-K, dated May 16, 2018 filed with the SEC on May 16, 2018 (File No. 001-38068) (including Exhibit 99.1 thereto, which is deemed filed under the U.S. Securities Exchange Act of 1934 and is incorporated by reference into this Registration Statement).
4.19†	Current Report on Form 8-K, dated May 14, 2018 filed with the SEC on May 18, 2018 (File No. 001-38068).
5.1**	Consent of KPMG LLP.
6.1*	Powers of Attorney.
7.1*	Form of Indenture.

* Previously filed.

** Filed herewith.

† Registrant has omitted portions of Exhibit 99.1 to this Current Report on Form 8-K pursuant to a confidential treatment request, in accordance with Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

PART III

UNDERTAKING AND CONSENT TO SERVICE OF PROCESS

Item 1. Undertaking.

The Registrant undertakes to make available, in person or by telephone, representatives to respond to inquiries made by the Commission staff, and to furnish promptly, when requested to do so by the Commission staff, information relating to the securities registered pursuant to Form F-10 or to transactions in such securities.

Item 2. Consent to Service of Process.

- (a) The Registrant has previously filed with the Commission a written irrevocable consent and power of attorney on Form F-X.
- (b) Pursuant to Section 305(b)(2) of the Trust Indenture Act of 1939, as amended, the Registrant will designate at a later date a Canadian trustee (the “Canadian Trustee”) under the indenture included as Exhibit 7.1 hereto, and will cause the Canadian Trustee to file with the Commission at such later date a written irrevocable consent and power of attorney on Form F-X.
- (c) Pursuant to Section 305(b)(2) of the Trust Indenture Act of 1939, as amended, the Registrant will designate at a later date a U.S. trustee (the “U.S. Trustee”) under the indenture included as Exhibit 7.1 hereto, and will file at such later date an application for determining the U.S. Trustee’s eligibility under the Trust Indenture Act of 1939, as amended.
- (d) Any change to the name or address of the Registrant’s and the Canadian Trustee’s agent for service of process shall be communicated promptly to the Commission by amendment to Form F-X referencing the file number of this Registration Statement.

EXHIBIT INDEX

<u>Exhibit No.</u>	<u>Description</u>
4.1	Annual Report on Form 10-K for the fiscal year ended December 31, 2017 filed with the SEC on March 14, 2018 (File No. 001-38068).
4.2	Audited consolidated financial statements as at and for the fiscal year ended December 31, 2017, together with the notes thereto and the auditor's report thereon (incorporated by reference to Item 8 of our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 filed with the SEC on March 14, 2018 (File No. 001-38068)).
4.3	Management's discussion and analysis of the financial condition and results of operations for the fiscal year ended December 31, 2017 (incorporated by reference to Item 7 of our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 filed with the SEC on March 14, 2018 (File No. 001-38068)).
4.4	Quarterly Report on Form 10-Q for the three month period ended March 31, 2018 filed with the SEC on May 1, 2018 (File No. 001-38068).
4.5	Unaudited interim consolidated financial statements as at and for the three months ended March 31, 2018, together with the notes thereto (incorporated by reference to Item 1 of our Quarterly Report on Form 10-Q filed with the SEC on May 1, 2018 (File No. 001-38068)).
4.6	Management's discussion and analysis of the financial condition and results of operations for the three months ended March 31, 2018 (incorporated by reference to Item 2 of our Quarterly Report on Form 10-Q filed with the SEC on May 1, 2018 (File No. 001-38068)).
4.7*	Material change report dated March 20, 2018 with respect to our announcement that ZW49 is the first product candidate selected for clinical development using the ZymeLink antibody-drug conjugate platform.
4.8*	Material change report, dated April 17, 2018, with respect to our presentation of preclinical data on ZW49.
4.9*	Material change report, dated April 24, 2018 with respect to Celgene Corporation having exercised its right to expand its collaboration agreement for the research, development, and commercialization of bispecific antibody therapeutics using Zymeworks' Azymetric platform.
4.10*	Material change report, dated April 25, 2018, with respect to our announcement that the abstract highlighting new data from our adaptive Phase 1 clinical trial for ZW25 has been selected for an oral presentation at the American Society of Clinical Oncology.
4.11	Current Report on Form 8-K, dated March 14, 2018 filed with the SEC on March 14, 2018 (File No. 001-38068) (including Exhibit 99.1 thereto, which is deemed filed under the U.S. Securities Exchange Act of 1934 and is incorporated by reference into this Registration Statement).
4.12	Current Report on Form 8-K, dated April 17, 2018 filed with the SEC on April 18, 2018 (File No. 001-38068).
4.13	Current Report on Form 8-K, dated April 23, 2018 filed with the SEC on April 23, 2018 (File No. 001-38068).
4.14	Current Report on Form 8-K, dated April 25, 2018 filed with the SEC on April 25, 2018 (File No. 001-38068).
4.15	Current Report on Form 8-K, dated April 30, 2018 filed with the SEC on April 30, 2018 (File No. 001-38068).

Table of Contents

<u>Exhibit No.</u>	<u>Description</u>
4.16	<u>Current Report on Form 8-K, dated May 1, 2018 filed with the SEC on May 1, 2018 (File No. 001-38068) (including Exhibit 99.1 thereto, which is deemed filed under the U.S. Securities Exchange Act of 1934 and is incorporated by reference into this Registration Statement).</u>
4.17	<u>Current Report on Form 8-K, dated May 10, 2018 filed with the SEC on May 10, 2018 (File No. 001-38068).</u>
4.18	<u>Current Report on Form 8-K, dated May 16, 2018 filed with the SEC on May 16, 2018 (File No. 001-38068) (including Exhibit 99.1 thereto, which is deemed filed under the U.S. Securities Exchange Act of 1934 and is incorporated by reference into this Registration Statement).</u>
4.19†	<u>Current Report on Form 8-K, dated May 14, 2018 filed with the SEC on May 18, 2018 (File No. 001-38068).</u>
5.1**	<u>Consent of KPMG LLP.</u>
6.1*	<u>Powers of Attorney.</u>
7.1*	<u>Form of Indenture.</u>

* Previously-filed.
** Filed herewith.
† Registrant has omitted portions of Exhibit 99.1 to this Current Report on Form 8-K pursuant to a confidential treatment request, in accordance with Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form F-10 and has duly caused this Amendment No. 2 to the Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Vancouver, British Columbia on May 24, 2018.

ZYMEWORKS INC.

By: /s/ Ali Tehrani

Name: Ali Tehrani

Title: President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, this Amendment No. 2 to the Registration Statement has been signed below by or on behalf of the following persons in the capacities indicated on May 24, 2018.

<u>Signature</u>	<u>Title</u>
<u>/s/ Ali Tehrani</u>	Ali Tehrani Director, President and Chief Executive Officer (Principal Executive Officer)
<u>/s/ Neil Klompas</u>	Neil Klompas Chief Financial Officer (Principal Financial and Accounting Officer)
<u>*</u>	Nick Bedford Director, Chair of the Board of Directors
<u>*</u>	Kenneth Hillan Director
<u>*</u>	Hollings Renton Director
<u>*</u>	Natalie Sacks Director
<u>*</u>	Lota Zoth Director

* By: /s/ Neil Klompas
Neil Klompas
Attorney-in-fact

AUTHORIZED REPRESENTATIVE

Pursuant to the requirements of Section 6(a) of the Securities Act of 1933, as amended, the Authorized Representative has duly caused this Amendment No. 2 to the Registration Statement to be signed on its behalf by the undersigned, solely in its capacity as the duly authorized representative of the Registrant in the United States, on May 24, 2018.

ZYMEWORKS BIOPHARMACEUTICALS INC.
(Authorized Representative in the United States)

By: /s/ Ali Tehrani

Name: Ali Tehrani

Title: President



*KPMG LLP
PO Box 10426 777 Dunsmuir Street
Vancouver BC V7Y 1K3
Canada
Telephone (604) 691-3000
Fax (604) 691-3031*

Consent of Independent Registered Public Accounting Firm

The Board of Directors
Zymeworks Inc.

We consent to the incorporation by reference in this Registration Statement on Form F-10 of Zymeworks Inc. (No. 333-224623) of our report dated March 14, 2018, with respect to the consolidated balance sheets of Zymeworks Inc. at December 31, 2017 and December 31, 2016 and the related consolidated statements of loss and comprehensive loss, changes in redeemable convertible preferred shares and shareholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2017, which are also incorporated by reference herein.

A handwritten signature in black ink that reads 'KPMG LLP' with a horizontal line underneath.

Chartered Professional Accountants
May 24, 2018
Vancouver, Canada

KPMG LLP is a Canadian limited liability partnership and a member firm of the KPMG network of independent member firms affiliated with KPMG International Cooperative ("KPMG International"), a Swiss entity. KPMG Canada provides services to KPMG LLP.