CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered	Proposed maximum offering price per common share(1)	Proposed maximum aggregate offering price	Amount of registration fee(2)
Common Shares, no par value	6,950,433	\$51.84	\$360,310,447	\$39,309.87

- (1) Estimated solely for purposes of calculating the registration fee pursuant to Rule 457(c) of the Securities Act of 1933, as amended, or the Securities Act, based on the market value of common shares of Zymeworks Inc., or the Company, being registered, as established by the average of the high and low prices of the Company's common shares as reported on the New York Stock Exchange on November 30, 2020, which was \$51.84.
- (2) The filing fee is calculated and being paid pursuant to Rule 457(r) under the Securities Act and relates to the Registration Statement on Form S-3ASR (File No. 333-234517) filed by the Registrant on November 5, 2019.

Prospectus Supplement (To prospectus dated November 5, 2019)



Zymeworks Inc.

6,950,433 Common shares

This prospectus supplement registers for resale, from time to time, up to 6,950,433 of our common shares by the selling shareholders named herein. The prices at which such selling shareholders may dispose of their shares will be determined by the selling shareholders or their transferees. We will not receive proceeds from any sale of common shares by the selling shareholders, but we have agreed to pay certain registration expenses relating to such common shares and this prospectus supplement. The selling shareholders from time to time may offer and sell the shares held directly to purchasers or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, commissions or concessions. For further information regarding the possible methods by which the shares may be distributed, see "Plan of Distribution."

Our common shares are listed for trading on the New York Stock Exchange, or the NYSE, under the symbol "ZYME." On December 3, 2020, the closing price per share of our common shares on the NYSE was \$54.40.

The selling shareholders are entities affiliated with one of our directors, Dr. Kelvin Neu.

The common shares offered hereby have not been qualified for distribution by prospectus under the securities laws of any province or territory of Canada and are not being offered in Canada or to any resident of Canada. See "Plan of Distribution."

An investment in our securities involves a high degree of risk. Please read "Risk Factors" on page S-11 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement before investing in our securities.

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

The date of this prospectus supplement is December 4, 2020.

ENFORCEABILITY OF CIVIL LIABILITIES

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ABOUT THIS PROSPECTUS SUPPLEMENT

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

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

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

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

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

In this prospectus supplement and the accompanying base shelf prospectus, unless the context otherwise requires, references to "we," "us," "our" or similar terms, as well as references to "Zymeworks" or the "Company," refer to Zymeworks Inc., either alone or together with our wholly-owned subsidiary, Zymeworks Biopharmaceuticals Inc. Furthermore, except as otherwise indicated, references to "Merck," "Lilly," "Celgene," "GSK," "Daiichi Sankyo," "Janssen," "LEO," "BeiGene," "Iconic" and "Pfizer" refer to Merck Sharp & Dohme Research Ltd., Eli Lilly and Company, Celgene Corporation and Celgene Alpine Investment Co. LLC, GlaxoSmithKline Intellectual Property Development Limited, Daiichi Sankyo Co., Ltd., Janssen Biotech, Inc., LEO Pharma A/S, BeiGene Ltd., Iconic Therapeutics, Inc. and Pfizer Inc., respectively.

The names Azymetric, Zymeworks, ZymeCAD, EFECT, ZymeLink and the phrase "Building Better Biologics" are our registered trademarks. Other trademarks, product names and company names appearing in this prospectus

supplement, the accompanying base shelf prospectus and documents incorporated by reference herein and therein are the property of their respective owners. Solely for convenience, the trademarks, service marks, tradenames and copyrights referred to in this prospectus supplement are listed without the ©, ® and TM symbols, but we will assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensors to these trademarks, service marks and tradenames.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying base shelf prospectus, including the documents incorporated by reference herein or therein, contain "forward-looking statements" within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and "forward-looking information" within the meaning of Canadian securities laws, or collectively, forward-looking statements. Forward-looking statements include statements that may relate to our plans, objectives, goals, strategies, future events, future revenue or performance, capital expenditures, financing needs and other information that is not historical information. Forward-looking statements can often be identified by the use of terminology such as "subject to," "believe," "anticipate," "plan," "expect," "intend," "estimate," "project," "may," "will," "should," "would," "could," "can," the negatives thereof, variations thereon and similar expressions, or by discussions of strategy. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. In particular, forward-looking statements in this prospectus supplement, the accompanying base shelf prospectus and the documents incorporated by reference herein and therein include, but are not limited to, statements about:

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

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;
- our ability to understand and predict trends in our industry and markets;
- our ability to maintain good business relationships with our strategic partners;
- our ability to comply with current and future regulatory standards;
- our ability to protect our intellectual property rights;
- · our continued compliance with third-party license terms and the non-infringement of third-party intellectual property rights;
- our ability to manage and integrate acquisitions;
- our ability to retain key personnel; and
- our ability to raise sufficient debt or equity financing to support our continued growth.

We believe there is a reasonable basis for our expectations and beliefs, but they are inherently uncertain. We may not realize our expectations, and our beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements. The following uncertainties and factors, among others (including those set forth under "Risk Factors" in this prospectus supplement, the accompanying base shelf prospectus and in our Quarterly Report on Form 10-Q for the three and nine months ended September 30, 2020), could affect future performance and cause actual results to differ materially from those matters expressed in or implied by forward-looking statements:

• our ability to obtain regulatory approval for our product candidates without significant delays;

- the predictive value of our current or planned clinical trials;
- delays with respect to the development and commercialization of our product candidates, which may cause increased costs or delay receipt
 of product revenue;
- our, or any of our partners', ability to enroll subjects in clinical trials and thereby complete trials on a timely basis;
- the design or our execution of clinical trials may not support regulatory approval, including where clinical trials are conducted outside the United States;
- the extent to which our business may be adversely affected by the COVID-19 pandemic;
- the Fast Track designations for any of our product candidates may not expedite regulatory review or approval;
- the U.S. Food and Drug Administration ("FDA") may not accept data from trials we conduct outside the United States;
- disruptions at the FDA and other government agencies caused by funding shortages or global health concerns;
- our discretion to discontinue or reprioritize the development of any of our product candidates;
- the potential for our product candidates to have undesirable side effects;
- no regulatory agency has made a determination that any of our product candidates are safe or effective for use by the general public or for any indication;
- our ability to face significant competition;
- 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;
- the potential for foreign governments to impose strict price controls;
- the risk of security breaches or data loss, which could compromise sensitive business or health information;
- current and future legislation that may increase the difficulty and cost of commercializing our product candidates;

- economic, political, regulatory and other risks associated with international operations;
- our exposure to legal and reputational penalties as a result of any of our current and future relationships with various third parties;
- our ability to comply with export control and import laws and regulations;
- our history of significant losses since inception;
- our ability to generate revenue from product sales and achieve profitability;
- our requirement for substantial additional funding;
- the potential dilution to our shareholders associated with future financings;
- restrictions on our ability to seek financing, which may be imposed by future debt;
- unstable market, sociopolitical and economic conditions;
- currency fluctuations and changes in foreign currency exchange rates;
- our ability to maintain existing and future strategic partnerships;
- our ability to realize the anticipated benefits of our strategic partnerships;
- our ability to secure future strategic partners;
- our reliance on third-party manufacturers to produce our clinical product candidate supplies and on other third parties to store, monitor and transport bulk drug substance and drug product;
- risk related to the manufacture of product candidates and difficulties in production;
- our reliance on third parties to oversee clinical trials of our product candidates and, in some cases, maintain regulatory files for those product candidates;
- our reliance on the performance of independent clinical investigators and contract research organizations;
- our reliance on third parties for various operational and administrative aspects of our business including our reliance on third parties' cloud-based software platforms;
- the risk that natural disasters, public health crises, political crises, and other catastrophic events may damage the facilities or disrupt the
 operations of third parties upon which we rely;
- our ability to operate without infringing the patents and other proprietary rights of third parties;
- our ability to obtain and enforce patent protection for our product candidates and related technology;
- our patents could be found invalid or unenforceable if challenged;
- our intellectual property rights may not necessarily provide us with competitive advantages;
- we may become involved in expensive and time-consuming patent lawsuits;
- the risk that the duration of our patents will not adequately protect our competitive position;
- our ability to obtain protection under the Drug Price Competition and Patent Term Restoration Act of 1984 and similar foreign legislation;
- we may be unable to protect the confidentiality of our proprietary information;
- our ability to comply with procedural and administrative requirements relating to our patents;
- the risk of claims challenging the inventorship of our patents and other intellectual property;
- our intellectual property rights for some of our product candidates are dependent on the abilities of third parties to assert and defend such rights;

- patent reform legislation and court decisions can diminish the value of patents in general, thereby impairing our ability to protect our products;
- we may not be able to protect our intellectual property rights throughout the world;
- we will require FDA approval for any proposed product candidate names and any failure or delay associated with such approval may adversely affect our business;
- the risk of employee misconduct including noncompliance with regulatory standards and insider trading;
- our ability to market our products in a manner that does not violate the law and subject us to civil or criminal penalties;
- if we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected;
- our ability to retain key executives and attract and retain qualified personnel;
- our ability to manage organizational growth;
- additional costs and expenses related to no longer being considered an emerging growth company or a smaller reporting company;
- our exposure to potential securities class action litigation; and
- if securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

Consequently, forward-looking statements should be regarded solely as our current plans, estimates and beliefs. You should not place undue reliance on forward-looking statements. We cannot guarantee future results, events, levels of activity, performance or achievements. We do not undertake and specifically decline any obligation to update, republish or revise forward-looking statements to reflect future events or circumstances or to reflect the occurrences of unanticipated events, except as required by law.

EXCHANGE RATE INFORMATION

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

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

				Nine mont	hs ended
	Year er	Year ended December 31,		September 30,	
	2017	2018	2019	2019	2020
Highest rate during the period	1.3743	1.3642	1.3600	1.3600	1.4496
Lowest rate during the period	1.2128	1.2288	1.2988	1.3038	1.2970
Average exchange rate for the period(1)	1.2986	1.2957	1.3269	1.3292	1.3386
Rate at the end of the period	1.2545	1.3642	1.2988	1.3243	1.3339

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

On December 3, 2020, the Bank of Canada daily average rate of exchange was \$1.00 = C\$1.2880.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights key aspects of this offering and certain information contained elsewhere in this prospectus supplement and the documents incorporated by reference. This summary is not complete and does not contain all of the information that may be important to you or that you should consider before investing in our common shares. You should read carefully the other information included and incorporated by reference in this prospectus supplement and the accompanying base shelf prospectus before investing in our common shares. You should pay special attention to the risks and uncertainties identified under the captions "Risk Factors," "Cautionary Note Regarding Forward-Looking Statements" and elsewhere in this prospectus supplement, the accompanying base shelf prospectus and the documents incorporated by reference herein or therein, including our Quarterly Report on Form 10-Q for the three and nine months ended September 30, 2020, when determining whether an investment in our common shares is appropriate for you.

Our Company

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

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

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

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

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

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

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

Our 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.

Company information

We were incorporated on September 8, 2003 under the *Canada Business Corporations Act*, under the name "Zymeworks Inc." On October 22, 2003, we were registered as an extra-provincial company under the *Company Act* (British Columbia), the predecessor to the *Business Corporations Act* (British Columbia), or the BCBCA. Zymeworks continued to the BCBCA on May 2, 2017. Our principal 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 corporate website address is *www.zymeworks.com*. The references to *www.zymeworks.com* in this prospectus supplement, the accompanying base shelf prospectus and the documents incorporated by reference herein or therein are inactive textual references only, and the information found on our internet website is not incorporated by reference into, and should not be considered part of, this prospectus supplement, the accompanying base shelf prospectus or the documents incorporated by reference herein or therein. Investors should not rely on any such information in deciding whether to purchase our common shares.

OFFERING SUMMARY

The following summary contains basic information about the offering and is not intended to be complete. It does not contain all the information that is important to you. You should carefully read the entire prospectus supplement, the accompanying base shelf prospectus and the documents incorporated by reference herein and therein before making an investment decision.

Common Shares Offered by the

Selling Shareholders

6,950,433 common shares.

Use of Proceeds

We will not receive any proceeds from the sale of common shares covered by this

prospectus supplement.

Risk Factors

Investing in our common shares involves risks. See "Risk Factors" beginning on page S-11 of this prospectus supplement and on page 2 of the accompanying base shelf prospectus, as well as those risks and uncertainties identified in the documents incorporated by reference herein or therein, including our Quarterly Report on Form 10-Q for the three and nine

months ended September 30, 2020.

NYSE symbol

Our common shares are listed on the NYSE under the symbol "ZYME."

Income tax considerations

The common shares will be subject to special and complex tax rules for U.S. taxpayers. Holders are urged to consult their own tax advisors with respect to the U.S. and Canadian federal, state, provincial, territorial, local and foreign tax consequences of purchasing, owning and disposing of the common shares. See "Certain U.S. Federal Income Tax Considerations" and "Certain Canadian Income Tax Considerations" on pages S-20 and S-24 of this progressive suppliers ont

24 of this prospectus supplement.

The selling shareholders named in this prospectus supplement may offer and sell up to 6,950,433 of our common shares. Throughout this prospectus supplement, when we refer to common shares being registered on behalf of the selling shareholders, we are referring to common shares reported to us as held by the selling shareholders as of December 2, 2020. We agreed to file this prospectus supplement pursuant to a Registration Rights Agreement with the selling shareholders dated March 16, 2020, or the Registration Rights Agreement. Additional information with respect to the Registration Rights Agreement is contained in this prospectus supplement under the heading "Selling Shareholders" and in our current report on Form 8-K filed with the Securities and Exchange Commission on March 16, 2020.

When we refer to the selling shareholders in this prospectus supplement, we are referring to the entities named in this prospectus supplement as the selling shareholders and, as applicable, any donees, pledgees, transferees or other successors-in-interest selling shares received after the date of this prospectus supplement from the selling shareholders as a gift, pledge, partnership distribution or other non-sale related transfer.

RISK FACTORS

Investing in our common shares is speculative and involves a high degree of risk. The following risk factors, as well as risks currently unknown to us, could materially adversely affect our future business, operations and financial condition and could cause them to differ materially from the estimates described in forward-looking information relating to us, or our business, property or financial results, each of which could cause purchasers of our common shares to lose part or all of their investment. In addition to the other information contained in this prospectus supplement, the accompanying base shelf prospectus and the documents incorporated by reference herein and therein, prospective investors should carefully consider the factors set out under "Risk Factors" in the accompanying base shelf prospectus and our Quarterly Report on Form 10-Q for the three and nine months ended September 30, 2020 and the factors set out below in evaluating Zymeworks and its business before making an investment in our common shares.

Risks relating to the common shares and the offering

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

You should consider an investment in our common shares as risky and invest only if you can withstand a significant loss and wide fluctuations in the market value of your investment. In addition, the stock market has 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, such as the COVID-19 pandemic;
- period-to-period fluctuations in our financial condition and results of operations, including the timing of receipt of any milestone or other payments under commercialization or licensing agreements;
- general market conditions and market conditions for biopharmaceutical stocks;
- overall fluctuations in U.S. equity markets; and
- other factors that may be unanticipated or out of our control.

Substantial future sales of our common shares, including by the selling shareholders, 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 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. See "Description of Share Capital—Share Capital—Dividend Policy" in the accompanying base shelf prospectus.

We are at risk of securities class action litigation.

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

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, or DGCL, that may have the greatest such effect include, but are not limited to, the following: (i) for certain corporate transactions (such as mergers and amalgamations or amendments to our articles) the BCBCA generally requires the voting threshold to be a special resolution approved by 66 2/3% of shareholders, or as set out in the articles, as applicable, whereas DGCL generally only requires a majority vote; and (ii) under the BCBCA a holder of 5% or more of our common shares can requisition a special meeting of shareholders, whereas such right does not exist under the DGCL. Investors may find our company and our common shares less attractive because we are governed by foreign laws.

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

We are governed by the BCBCA and our principal place of business is in Canada. Some 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 British Columbia. Furthermore, provisions in our articles provide that, unless we consent in writing to the selection of an alternative forum, the Supreme Court of British Columbia and the appellate courts therefrom, to the fullest extent permitted by law, will be the sole and exclusive forum for certain actions or proceedings brought against us, our directors and/or our officers. These provisions may limit our shareholders' ability to bring a claim against us in a judicial forum that our shareholders consider favorable or convenient for such disputes and may discourage lawsuits with respect to such claims. See "Description of Share Capital" in the accompanying base shelf prospectus.

USE OF PROCEEDS

The selling shareholders will receive all of the net proceeds from sales of the common shares sold pursuant to this prospectus supplement. We will not receive any of the proceeds from the sale of the shares by the selling shareholders.

SELLING SHAREHOLDERS

The selling shareholders named in this prospectus supplement may offer and sell up to 6,950,433 of our common shares. Other than disclosed herein, the foregoing shares represent all the commons shares reported to us as held by the selling shareholders as of December 2, 2020.

On March 16, 2020, we entered into the Registration Rights Agreement with investment funds, including 667, L.P. ("667") and Baker Brothers Life Sciences, "and together with 667, the "Baker Funds"), for which Baker Bros. Advisors LP ("BBA") serves as investment adviser, pursuant to which we agreed that at any time subsequent to April 22, 2020, if the Baker Funds demand that we register common shares they hold for resale under the Securities Act, we would be obligated to effect such registration. Our registration obligations under the Registration Rights Agreement cover all of our common shares now held or later acquired by the Baker Funds, and will continue until the earlier of such time as all such common shares have been sold or may be sold freely without limitations or restrictions as to volume or manner of sale pursuant to Rule 144 of the Securities Act, or ten years after the date of the Registration Rights Agreement. In addition, under the Registration Rights Agreement, the Baker Funds have the right to request one underwritten public offering per calendar year, but no more than three underwritten public offerings in total, to effect the registered sale or distribution of their common shares, subject to certain exceptions, conditions and limitations. We are required to bear certain expenses in connection with any registration effected pursuant to the Registration Rights Agreement. We have also agreed to customary indemnification provisions in favor of the Baker Funds in connection with this prospectus supplement and all registrations effected pursuant to the Registration Rights Agreement. Additional information regarding the Registration Rights Agreement is available in our current report on Form 8-K filed with the Securities and Exchange Commission on March 16, 2020.

One of our directors, Dr. Kelvin Neu, is an employee of BBA, which is a significant beneficial owner of our common shares and investment advisor to, and affiliate of, the Baker Funds. In June 2019, we issued and sold 7,013,892 common shares and, in lieu of common shares, 4,166,690 pre-funded warrants to purchase common shares in a registered public offering, at prices to the public of \$18.00 per common share and \$17.9999 per pre-funded warrant, respectively, which we refer to as the June 2019 Public Offering. The Baker Funds purchased 4,166,690 pre-funded warrants at the price to the public in the June 2019 Public Offering. In January 2020, the Company issued and sold 5,824,729 common shares and, in lieu of common shares, 1,075,271 pre-funded warrants to purchase common shares in a registered public offering, at prices to the public of \$46.50 per common share and \$46.4999 per pre-funded warrant, respectively, which we refer to as the January 2020 Public Offering and the Baker Funds purchased 1,075,271 pre-funded warrants at the price to the public in the January 2020 Public Offering. The common shares issuable upon exercise of the pre-funded warrants purchased by the Baker Funds in the June 2019 Public Offering and January 2020 Public Offering are included in the common shares offered by this prospectus supplement.

Except for beneficial ownership of our securities, the Registration Rights Agreement, Dr. Neu's position on our Board of Directors and the participation by entities affiliated with Dr. Neu and BBA in the June 2019 Public Offering and January 2020 Public Offering, BBA and its affiliates, including the Baker Funds, have not had any material relationship with us or our affiliates within the past three years.

The table below, including the footnotes, lists BBA and certain of its affiliates and other information regarding the beneficial ownership of our common shares held by the Baker Funds based on information provided to us by BBA. Generally, a person "beneficially owns" our common shares if the person has or shares with others the right to vote those shares or to dispose of them, or if the person has the right to acquire voting or disposition rights within 60 days. The percentages of shares beneficially owned prior to and after the offering are based on 45,945,913 common shares outstanding as of December 2, 2020, which includes the outstanding common shares offered by this prospectus supplement and the accompanying prospectus and other shares reported to us as beneficially owned by BBA and its affiliates. The number of common shares beneficially owned prior to the offering indicates the number of common shares reported to us as beneficially owned by BBA and its affiliates as of December 2, 2020.

The maximum number of shares to be sold column indicates the total number of common shares that BBA and its affiliates may offer under this prospectus supplement and the accompanying prospectus.

The shares beneficially owned after offering number assumes the sale of all of the common shares offered by BBA and its affiliates pursuant to this prospectus supplement and the accompanying prospectus. However, because BBA and its affiliates may sell all or some of their shares under this prospectus supplement and the accompanying prospectus from time to time, or in another permitted manner, we cannot assure you as to the actual number of shares that will be sold by BBA and its affiliates or that will be held by the Baker Funds after completion of any sales. We do not know how long either of the Baker Funds will hold the shares before selling them.

BBA and its affiliates may sell all, some or none of their shares in this offering. See "Plan of Distribution."

	owned	Shares beneficially owned prior to offering		Shares beneficially owned after offering(1)	
Name of Selling Shareholder	Number	Percent	supplement	Number	Percent
Baker Bros. Advisors LP(2)	4,909,810(2)	9.99%	6,950,433(2)	5,000	*

- * Represents beneficial ownership of less than 1% of our outstanding common shares.
- (1) Assumes the sale of all common shares covered by this prospectus supplement. The selling shareholders may offer and sell all or part of the common shares covered by this prospectus supplement.
- Current beneficial ownership consists of (i) 168,252 common shares and 264,518 common shares issuable upon exercise of pre-funded warrants held by 667, L.P. ("667"), (ii) 1,540,220 common shares and 2,931,820 common shares issuable upon exercise of pre-funded warrants held by Baker Brothers Life Sciences, L.P. ("Life Sciences," and together with 667, the "Baker Funds"), in each case, in accordance with the limitations imposed by the Maximum Percentage (as defined below) and (iii) 5,000 common shares issuable upon exercise of options to purchase common shares held by Dr. Kelvin Neu, a member of our Board of Directors. The common shares being offered consist of (i) 168,252 common shares and 433,807 common shares issuable upon exercise of pre-funded warrants held by 667 and (ii) 1,540,220 common shares and 4,808,154 common shares issuable upon exercise of pre-funded warrants held by Life Sciences. The pre-funded warrants held by 667 and Life Sciences discussed above are only exercisable to the extent that after giving effect to such exercise the holders thereof and their affiliates would beneficially own, for purposes of Rule 13d-3 under the Securities Exchange Act of 1934, as amended, no more than 9.99% of the Company's outstanding common shares (the "Maximum Percentage"). By written notice to the Company, the Baker Funds may from time to time increase or decrease the Maximum Percentage applicable to that Baker Fund to any other percentage not in excess of 19.99%. Any such change will not be effective until the 61st day after such notice is delivered to us. As a result of this restriction, the number of common shares that may be issued upon exercise of the pre-funded warrants by the above holders may change depending upon changes in the outstanding common shares. Due to the effect of the Maximum Percentage, the amount of current beneficial ownership in the table above differs from the amount of common shares being offered. Baker Bros. Advisors LP ("BBA") is the investment adviser to the Baker Funds and has the sole voting and investment power with respect to the securities held by the Baker Funds and thus may be deemed to beneficially own such securities. Baker Bros. Advisors (GP) LLC ("BBA GP") is the sole general partner of BBA and thus may be deemed to beneficially own the securities held by the Baker Funds. The principals of BBA GP are Julian C. Baker and Felix J. Baker, who may be deemed to beneficially own the securities held by the Baker Funds. Dr. Neu, an employee of BBA, serves on our Board of Directors as a representative of the Baker Funds and BBA may be deemed to beneficially own the securities received by Dr. Neu as compensation for serving as a director. Pursuant to the policies of BBA, Dr. Neu does not have any right to the pecuniary interest in securities received as compensation for serving as a director and the BBA Funds are entitled to an indirect proportionate pecuniary interest in such securities. The business address for BBA, BBA GP, Julian C. Baker and Felix J. Baker is 860 Washington Street, 3rd Floor, New York, NY 10014.

PLAN OF DISTRIBUTION

The selling shareholders may sell the shares offered by this prospectus supplement and the accompanying prospectus. The selling shareholders, including their donees, pledgees, transferees or other successors-in-interest selling common shares received after the date of this prospectus supplement from a selling shareholder as a gift, pledge, partnership distribution or other non-sale related transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their common shares or interests in common shares on any stock exchange, market or trading facility on which the common shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices. To the extent any of the selling shareholders gift, pledge, grant a security interest in, or otherwise transfer the shares offered hereby, such transferees may offer and sell the shares from time to time under this prospectus supplement, provided that this prospectus supplement has been amended under Rule 424(b) or other applicable provision of the Securities Act to include the name of such transferee in the list of selling shareholders under this prospectus supplement if and when necessary or required.

The selling shareholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. They may use any one or more of the following methods when disposing of shares or interests therein:

- oordinary brokerage transactions and transactions in which a broker-dealer solicits purchasers;
- block trades in which a 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 under this prospectus supplement;
- an over-the-counter distribution:
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- "at the market" or through market makers or into an existing market for the shares;
- delivery of securities in settlement of short sales;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- through the distribution of the common shares by any selling shareholder to its partners, members or shareholders;
- through broker-dealers that agree with the selling shareholders to sell a specified number of such shares at a stipulated price per share;
- through one or more underwritten offerings on a firm commitment or best efforts basis;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

In connection with the sale of the common shares, the selling shareholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common shares in the course of hedging the positions they assume. The selling shareholders may also sell our common shares short and deliver these securities to close out their short positions, or loan or pledge the common shares to broker dealers that in turn may sell these securities. The selling shareholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities

which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus supplement (as amended to reflect such transaction).

The aggregate proceeds to the selling shareholders from the sale of the shares offered by them will be the purchase price of the common shares less discounts or commissions, if any. Each of the selling shareholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common shares to be made directly or through agents. We will not receive any of the proceeds from this offering.

The selling shareholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided that they meet the criteria and conform to the requirements of that rule.

The selling shareholders and any broker-dealers that act in connection with the sale of securities may be deemed to be "underwriters" within the meaning of Section 2(11) of the Securities Act in connection with such sales, and any commissions received by such broker-dealers and any profit on the resale of the securities sold by them while acting as principals may be deemed to be underwriting discounts or commissions under the Securities Act. In the event that any selling shareholder is deemed to be an "underwriter" within the meaning of Section 2(11) of the Securities Act, the selling shareholders will be subject to the prospectus delivery requirements of the Securities Act. The selling shareholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act. To our knowledge, none of the selling shareholders received any shares as underwriting compensation.

To the extent required, our common shares to be sold, the names of the selling shareholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, any applicable commissions or discounts with respect to a particular offer will be set forth in an amendment to this prospectus supplement.

To comply with the securities laws of some states, if applicable, the shares may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the shares may not be sold unless they have been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling shareholders that the anti-manipulation rules of Regulation M under the Securities Exchange Act of 1934, as amended, or the Exchange Act, may apply to sales of our common shares in the market and to the activities of the selling shareholders and their affiliates. These rules may limit the timing of purchases and sales of the shares by such selling shareholders. Regulation M may also restrict the ability of any person engaged in the distribution of the common shares to engage in market-making activities with respect to the 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 the common shares.

We will bear all of the costs, expenses and fees in connection with the registration of the common shares, other than any commissions, discounts or other fees payable to underwriters or broker-dealers in connection with any sale of shares, which will be borne by the selling shareholder selling such common shares. We have agreed to bear legal expenses of the selling shareholders of up to \$50,000 per underwritten public offering of the shares offered by this prospectus supplement and the accompanying prospectus, and legal expenses of the selling shareholders of up to \$50,000 in connection with filing of a shelf registration statement, if required, pursuant to the Registration Rights Agreement. We have agreed to indemnify the selling shareholders against certain liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus supplement and the accompanying prospectus. Our common shares are listed on the NYSE under the symbol "ZYME."

The offer and sale of our common shares under this prospectus supplement to any person or company outside of Canada is not subject to the prospectus requirements under applicable Canadian securities laws. The common shares offered hereby have not been qualified for distribution by prospectus under the securities laws of any province or territory of Canada and are not being offered in Canada or to any resident of Canada.

There can be no assurance that any selling shareholder will sell any or all of the common shares registered pursuant to this prospectus supplement.

CERTAIN U.S. FEDERAL INCOME TAX CONSIDERATIONS

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

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

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

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

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

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

Distributions on the common shares

Subject to the PFIC rules discussed below, the gross amount of any distribution received by a U.S. Holder with respect to the common shares (including any amounts withheld to pay Canadian withholding taxes) will be included in the gross income of the U.S. Holder as a dividend to the extent attributable to the Company's current or accumulated earnings and profits, as determined under U.S. federal income tax principles. The Company does not intend to calculate its earnings and profits under U.S. federal income tax rules. Accordingly, U.S. Holders should expect that a distribution generally will be treated as a dividend for U.S. federal income tax purposes. Unless the Company is treated as a PFIC for the taxable year in which it pays a distribution or in the preceding

taxable year (see "Passive Foreign Investment Company Rules" below), the Company believes that it may qualify as a "qualified foreign corporation," in which case distributions treated as dividends and received by non-corporate U.S. Holders may be eligible for a preferential tax rate. Distributions on the common shares generally will not be eligible for the dividends received deduction available to U.S. Holders that are corporations.

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

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

Sale, exchange or other taxable disposition of the common shares

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

Passive foreign investment Company rules

A foreign corporation will be considered a PFIC for any taxable year in which (i) 75% or more of its gross income is "passive income" under the PFIC rules or (ii) 50% or more of the average quarterly value of its assets produce (or are held for the production of) "passive income." For this purpose, "passive income" generally includes interest, dividends, certain rents and royalties, and certain gains. Royalties derived in the active conduct of a trade or business by a corporation in the licensing of property developed or created through its own officers or staff of employees is generally excluded from passive income, and interest, dividends, rents and royalties received from a related person (within the meaning of the PFIC rules) are excluded from passive income to the extent such payments are properly allocable to the active income of such related person. Moreover, for purposes of determining if the foreign corporation is a PFIC, if the foreign corporation owns, directly or indirectly, at least 25%, by value, of the shares of another corporation, it will be treated as if it holds directly its proportionate share of the assets and receives directly its proportionate share of the income of such other corporation. If a corporation is treated as a PFIC with respect to a U.S. Holder for any taxable year, the corporation will continue to be treated

as a PFIC with respect to that U.S. Holder in all succeeding taxable years, regardless of whether the corporation continues to meet the PFIC requirements in such years, unless certain elections are made.

The determination as to whether a foreign corporation is a PFIC is based on the application of complex U.S. federal income tax rules, which are subject to differing interpretations, and the determination will depend on the composition of the income, expenses and assets of the foreign corporation from time to time and the nature of the activities performed by its officers and employees. The Company believes that it was not classified as a PFIC for the taxable year ended December 31, 2019. However, the Company cannot provide any assurance regarding its PFIC status for the current or future taxable years given that the determination of PFIC status is fact-intensive and made on an annual basis. Neither the Company's U.S. counsel nor U.S. tax advisor expresses any opinion with respect to the Company's PFIC status or with respect to the Company's expectations regarding its PFIC status.

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

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

The adverse tax consequences described above may be mitigated if a U.S. Holder makes a timely "qualified electing fund" election, or a QEF election, with respect to its interest in the PFIC. Consequently, if the Company is classified as a PFIC, it may be advantageous for a U.S. Holder to elect to treat the Company as a "qualified electing fund" with respect to such U.S. Holder in the first year in which it holds common shares. If a U.S. Holder makes a timely QEF election with respect to the Company, the electing U.S. Holder would be required in each taxable year that the Company is considered a PFIC to include in gross income (i) as ordinary income, the U.S. Holder's pro rata share of the ordinary earnings of the Company and (ii) as capital gain, the U.S. Holder's pro rata share of the net capital gain (if any) of the Company, whether or not the ordinary earnings or net capital gain are distributed. An electing U.S. Holder's basis in common shares will be increased to reflect the amount of any taxed but undistributed income. Distributions of income that had previously been taxed will result in a corresponding reduction of basis in the common shares and will not be taxed again as distributions to the U.S. Holder.

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

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

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

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

Required disclosure with respect to foreign financial assets

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

CERTAIN CANADIAN INCOME TAX CONSIDERATIONS

The following is, as of the date hereof, a general summary of the principal Canadian federal income tax considerations under the *Income Tax Act* (Canada), or the Tax Act, and the regulations thereunder, or the Regulations, generally applicable to a holder who acquires common shares issued pursuant to this prospectus supplement (the "Offered Shares"), as beneficial owner and who, at all relevant times, for the purposes of the Tax Act, deals at arm's length with the Company and the selling shareholders, is not affiliated with the Company or the selling shareholders, and will acquire and hold such Offered Shares as capital property (each, a "Holder"), all within the meaning of the Tax Act. Offered Shares will generally be considered to be capital property to a Holder unless the Holder holds or uses the Offered Shares or is deemed to hold or use the Offered Shares in the course of carrying on a business of trading or dealing in securities or has acquired the Offered Shares or is deemed to have acquired them in a transaction or transactions considered to be an adventure or concern in the nature of trade.

This summary does not apply to a Holder (a) that is a "financial institution" for purposes of the mark-to-market rules contained in the Tax Act; (b) an interest in which is or would constitute a "tax shelter investment" as defined in the Tax Act; (c) that is a "specified financial institution" as defined in the Tax Act; (d) that is a corporation resident in Canada (for the purpose of the Tax Act) or a corporation that does not deal at arm's length (for purposes of the Tax Act) with a corporation resident in Canada, and that is or becomes as part of a transaction or event or series of transactions or events that includes the acquisition of the Offered Shares, controlled by a non-resident person, or group of non-resident persons not dealing with each other at arm's length, for the purposes of the foreign affiliate dumping rules in Section 212.3 of the Tax Act; (e) that reports its "Canadian tax results" in a currency other than Canadian currency in accordance with the rules in the Tax Act; (f) that is exempt from tax under the Tax Act; or (g) that has entered into, or will enter into, a "synthetic disposition arrangement" or a "derivative forward agreement" with respect to the Offered Shares, as those terms are defined in the Tax Act. In addition, this summary does not address the deductibility of interest by a Holder that will borrow money or otherwise incur indebtedness in connection with the acquisition of the Offered Shares. Such Holders should consult their own tax advisors with respect to an investment in Offered Shares.

This summary is based upon the current provisions of the Tax Act and the Regulations in force as of the date hereof, specific proposals to amend the Tax Act and the Regulations, or the Tax Proposals, which have been publicly announced by or on behalf the Minister of Finance (Canada) prior to the date hereof, the current provisions of the *Canada-United States Income Tax Convention* (1980), or the Canada-U.S. Tax Convention, and counsel's understanding of the current published administrative policies and assessing practices of the Canada Revenue Agency, or the CRA.

This summary assumes that the Tax Proposals will be enacted in the form proposed, and does not take into account or anticipate any other changes in law, whether by way of judicial, legislative or governmental decision or action, or any changes in administrative policy or assessing practice. No assurances can be given that the Tax Proposals will be enacted as proposed or at all, or that legislative, judicial or administrative changes will not modify or change the statements expressed herein. This summary does not take into account provincial, territorial or foreign income tax legislation or considerations, which may differ from the Canadian federal income tax considerations discussed herein. This summary is not exhaustive of all possible Canadian federal income tax considerations applicable to an investment in Offered Shares. This summary is of a general nature only and is not intended to be, nor should it be construed to be, legal or income tax advice to any particular Holder. Holders should consult their own income tax advisors with respect to the tax consequences applicable to them based on their own particular circumstances.

Amounts determined in Canadian dollars

For purposes of the Tax Act, all amounts relating to the acquisition, holding or disposition of Offered Shares must be expressed in Canadian dollars, including cost, adjusted cost base, proceeds of disposition and dividends, and amounts denominated in U.S. dollars must be converted to Canadian dollars using the daily exchange rate

published by the Bank of Canada on the particular date the particular amount arose or such other rate of exchange as may be accepted by the CRA.

Residents of Canada

The following portion of this summary is generally applicable to a Holder who, for the purposes of the Tax Act, is resident or deemed to be resident in Canada at all relevant times (each, a "Resident Holder"). Certain Resident Holders whose Offered Shares might not otherwise qualify as capital property may be entitled to make an irrevocable election pursuant to subsection 39(4) of the Tax Act to have the Offered Shares, and every other "Canadian security" (as defined by the Tax Act) owned or subsequently acquired by such Resident Holder in the taxation year of the election and in all subsequent taxation years, deemed to be capital property. Resident Holders should consult their own tax advisors for advice as to whether an election under subsection 39(4) of the Tax Act is available or advisable in their particular circumstances.

Taxation of dividends

In the case of a Resident Holder who is an individual (including certain trusts), dividends (including deemed dividends) received on the Offered Shares will be included in the Resident Holder's income and be subject to the gross-up and dividend tax credit rules applicable to taxable dividends received by an individual from taxable Canadian corporations, including the enhanced gross-up and dividend tax credit for "eligible dividends" properly designated as such by the Company. There may be limitations on the ability of the Company to designate dividends as "eligible dividends."

In the case of a Resident Holder that is a corporation, such dividends (including deemed dividends) received on the Offered Shares will be included in the Resident Holder's income and will normally be deductible in computing such Resident Holder's taxable income. In certain circumstances, subsection 55(2) of the Tax Act will treat a taxable dividend received or deemed to be received by a Resident Holder that is a corporation as proceeds of disposition or a capital gain. Resident Holders that are corporations should consult their own tax advisors having regard to their own particular circumstances.

A Resident Holder that is a "private corporation" or "subject corporation" (as such terms are defined in the Tax Act) may be liable to pay a refundable tax under Part IV of the Tax Act on dividends received or deemed to be received on the Offered Shares to the extent that such dividends are deductible in computing the Resident Holder's taxable income for the year.

Disposition of offered shares

A Resident Holder who disposes of, or is deemed to have disposed of, an Offered Share (other than to the Company, unless purchased by the Company in the open market in the manner in which shares are normally purchased by any member of the public in the open market) will realize a capital gain (or incur a capital loss) equal to the amount by which the proceeds of disposition in respect of the Offered Share exceed (or are exceeded by) the aggregate of the adjusted cost base to the Resident Holder of such Offered Share immediately before the disposition or deemed disposition and any reasonable expenses incurred for the purpose of making the disposition. The adjusted cost base to a Resident Holder of an Offered Share will be determined by averaging the cost of that Offered Share with the adjusted cost base of all other Common Shares held as capital property at that time by the Resident Holder. The tax treatment of capital gains and capital losses is discussed in greater detail below under the subheading "Taxation of Capital Gains and Losses."

Refundable tax

A Resident Holder that is throughout the year a "Canadian-controlled private corporation" (as defined in the Tax Act) may be liable to pay an additional refundable tax on its "aggregate investment income" (as defined in the

Tax Act) for the year, including taxable capital gains (as defined below), but excluding dividends or deemed dividends deductible in computing taxable income.

Taxation of capital gains and losses

Generally, one-half of any capital gain, or a taxable capital gain, realized by a Resident Holder must be included in the Resident Holder's income for the taxation year in which the disposition occurs. Subject to and in accordance with the provisions of the Tax Act, one-half of any capital loss incurred by a Resident Holder, or an "allowable capital loss," must generally be deducted from taxable capital gains realized by the Resident Holder in the taxation year in which the disposition occurs. Allowable capital losses in excess of taxable capital gains for the taxation year of disposition generally may be carried back and deducted in the three preceding taxation years or carried forward and deducted in any subsequent year against taxable capital gains realized in such years (but not against other income), in the circumstances and to the extent provided in the Tax Act.

A capital loss realized on the disposition of an Offered Share by a Resident Holder that is a corporation may in certain circumstances be reduced by the amount of dividends which have previously been received or deemed to have been received by the Resident Holder on the Offered Share. Similar rules may apply where a corporation is, directly or indirectly through a trust or partnership, a member of a partnership or a beneficiary of a trust that owns Offered Shares. A Resident Holder to which these rules may be relevant is urged to consult its own tax advisor.

Minimum tax

Individuals, including certain trusts, may be subject to a minimum tax. Generally, dividends received or deemed to be received on Offered Shares and capital gains realized on the disposition of Offered Shares may result in a Resident Holder being liable for minimum tax under the Tax Act. Resident Holders should consult with their own tax advisors with respect to the potential application of the minimum tax.

Non-residents of Canada

The following portion of this summary is generally applicable to a Holder who, for purposes of the Tax Act and at all relevant times, is neither resident nor deemed to be resident in Canada and does not use or hold, and will not be deemed to use or hold, Offered Shares in a business carried on in Canada (each, a "Non-Resident Holder"). The term "U.S. Resident Holder," for the purposes of this summary, means a Non-Resident Holder who, for purposes of the Canada-U.S. Tax Convention, is at all relevant times both a resident of the United States within the meaning of the Canada-U.S. Tax Convention and a "qualifying person" within the meaning of Article XXIX-A of the Convention. In some circumstances, persons deriving amounts through fiscally transparent entities (including limited liability companies) may be entitled to benefits under the Canada-U.S. Tax Convention. U.S. Resident Holders are urged to consult their own tax advisors to determine their entitlement to benefits under the Canada-U.S. Tax Convention based on their particular circumstances.

Special considerations, which are not discussed in this summary, may apply to a Non-Resident Holder that is an insurer that carries on, or is deemed to carry on, an insurance business in Canada and elsewhere or an authorized foreign bank (as defined in the Tax Act). Such Non-Resident Holders should consult their own advisors.

Taxation of dividends

Subject to an applicable tax treaty or convention, dividends paid or credited, or deemed to be paid or credited, to a Non-Resident Holder on the Offered Shares will be subject to Canadian withholding tax under the Tax Act at the rate of 25% of the gross amount of the dividend. Such rate is generally reduced under the Canada-U.S. Tax Convention to 15% if the beneficial owner of such dividend is a U.S. Resident Holder. The rate of withholding tax is instead reduced to 5% if the beneficial owner of such dividend is a U.S. Resident Holder that is a company

that owns, directly or indirectly, at least 10% of the voting stock of the Company. In addition, under the Canada-U.S. Tax Convention, dividends may be exempt from such Canadian withholding tax if paid to certain U.S. Resident Holders that are qualifying religious, scientific, literary, educational or charitable organizations to the extent such dividends are exempt from tax in the United States or that are qualifying trusts, companies, organizations or arrangements operated exclusively to administer or provide pension, retirement or employee benefits or benefits for the self-employed under one or more funds or plans established to provide pension or retirement benefits or other employee benefits that are exempt from tax in the United States and that have complied with specific administrative procedures.

Disposition of offered shares

A Non-Resident Holder will not be subject to tax under the Tax Act in respect of any capital gain realized by such Non-Resident Holder on a disposition of Offered Shares, unless the Offered Shares constitute "taxable Canadian property" (as defined in the Tax Act) of the Non-Resident Holder at the time of the disposition and are not "treaty-protected property" (as defined in the Tax Act) of the Non-Resident Holder at the time of the disposition.

Generally, provided that the Offered Shares are then listed on a designated stock exchange (which currently includes the NYSE), the Offered Shares will not constitute taxable Canadian property of a Non-Resident Holder, unless at any time during the 60-month period immediately preceding the disposition the following two conditions are met concurrently: (a) the Non-Resident Holder, persons with which the Non-Resident Holder does not deal at arm's length, partnerships whose members include, either directly or indirectly through one or more partnerships, the Non-Resident Holder or persons which do not deal at arm's length with the Non-Resident Holder, or any combination of them, owned 25% or more of the issued shares of any class or series of shares of the capital stock of the Company, and (b) more than 50% of the fair market value of the shares of the Company was derived, directly or indirectly, from one or any combination of real or immovable property situated in Canada, "Canadian resource properties," "timber resource properties" (each as defined in the Tax Act), and options in respect of or interests in, or for civil law rights in, any such property (whether or not such property exists). The Offered Shares may also be deemed to be taxable Canadian property in certain circumstances.

In the case of a U.S. Resident Holder, the Offered Shares of such U.S. Resident Holder will generally constitute "treaty-protected property" for purposes of the Tax Act unless the value of the Offered Shares is derived principally from real property situated in Canada. For this purpose, "real property" has the meaning that term has under the laws of Canada and includes any option or similar right in respect thereof and usufruct of real property, rights to explore for or to exploit mineral deposits, sources and other natural resources and rights to amounts computed by reference to the amount or value of production from such resources.

If Offered Shares are taxable Canadian property of a Non-Resident Holder and are not treaty-protected property of the Non-Resident Holder at the time of their disposition, the consequences above under "Residents of Canada—Disposition of Offered Shares" and "Residents of Canada—Taxation of Capital Gains and Losses" will generally apply.

Non-Resident Holders whose Offered Shares may be taxable Canadian property should consult their own advisors.

LEGAL MATTERS

Certain legal matters in connection with the securities offered hereby will be passed upon on behalf of the Company by Blake, Cassels & Graydon LLP with respect to Canadian legal matters and by Skadden, Arps, Slate, Meagher & Flom LLP with respect to U.S. legal matters.

EXPERTS

The consolidated financial statements of Zymeworks Inc. as of December 31, 2019 and 2018 and for each of the years in the three-year period ended December 31, 2019, appearing in our Annual Report on Form 10-K for the year ended December 31, 2019, have been incorporated herein by reference in reliance upon the report of KPMG LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference, and upon the authority of said firm as experts in accounting and auditing.

The audit report covering the consolidated financial statements as of December 31, 2019 and 2018 and for each of the years in the three-year period ended December 31, 2019, refers to a change in our accounting policies for revenue recognition as of January 1, 2018 due to the adoption of ASC 606—Revenue from Contracts with Customers.

ENFORCEABILITY OF CIVIL LIABILITIES

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

pending or time for appeal has not expired; and except that any court in the Province of British Columbia may give judgment only in Canadian dollars. We have also been advised by Blake, Cassels & Graydon LLP, however, that there is substantial doubt whether an action could be brought in Canada in the first instance on the basis of liability predicated solely upon U.S. federal securities laws. See "Risk factors."

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and accompanying base shelf prospectus are part of the registration statement on Form S-3 (File No. 333-234517) that we filed with the Securities and Exchange Commission, or SEC, under the Securities Act and do not contain all of the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or accompanying base shelf prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus supplement and the accompanying base shelf prospectus for a copy of such contract, agreement or other document.

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

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus supplement which has been previously filed with the SEC, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement, except for any information superseded by information included or subsequently incorporated by reference in this prospectus supplement. We have filed the documents listed below with the SEC under the Exchange Act, and these documents are incorporated herein by reference:

- (a) our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, filed with the SEC on March 3, 2020;
- (b) our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2020, June 30, 2020 and September 30, 2020, filed with the SEC on May 7, 2020, August 5, 2020 and November 3, 2020, respectively;
- (c) our Current Reports on Form 8-K filed with the SEC on <u>January 7, 2020, January 24, 2020</u> (other than the information furnished under Item 7.01 and exhibits related thereto), <u>January 27, 2020</u> (other than the information furnished under Item 7.01 and exhibits related thereto), <u>May 8, 2020</u> (other than the information furnished under Item 7.01 and exhibits related thereto), <u>May 8, 2020</u> (other than the information furnished under Item 7.01 and exhibits related thereto), <u>November 30, 2020</u> (other than the information furnished under Item 7.01 and exhibits related thereto) and <u>December 1, 2020</u> (other than the information furnished under Item 7.01 and exhibits related thereto);
- (d) the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2019 from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on March 23, 2020; and
- (e) the description of our common shares set forth in our registration statement on <u>Form 8-A</u>, filed with the SEC on April 24, 2017, including any amendments or reports filed for the purpose of updating such description.

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

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

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

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PROSPECTUS



Common Shares
Preferred Shares
Debt Securities
Warrants
Subscription Receipts
Units

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

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

Our common shares are listed and posted for trading on the New York Stock Exchange ("NYSE"), under the symbol "ZYME." On November 4, 2019, the last reported sale price of the common shares on the NYSE was \$35.39 per common share. Unless otherwise specified in the applicable prospectus supplement, securities other than the common shares will not be listed on any securities exchange. There is currently no market through which the securities, other than the common shares, may be sold and you may not be able to resell such securities purchased under this prospectus and any applicable prospectus supplement. This may affect the pricing of such securities in the secondary market, the transparency and availability of trading prices, the liquidity of the securities, and the extent of issuer regulation.

Investing in our securities involves a high degree of risk. You should carefully read the "Risk Factors" section beginning on page 2 of this prospectus and carefully consider the discussion of risks and uncertainties under the heading "Risk Factors" contained in any applicable prospectus supplement and in the documents that are incorporated by reference.

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

The date of this prospectus is November 5, 2019.

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ABOUT THIS PROSPECTUS

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

You should rely only on the information contained or incorporated by reference in this prospectus or any applicable prospectus supplement and on the other information included in the registration statement of which this prospectus forms a part. We have not authorized anyone to provide you with different or additional information, 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," "Janssen," "LEO," "BeiGene" and "Iconic" 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., Janssen Biotech, Inc., LEO Pharma A/S, BeiGene Ltd. and Iconic Therapeutics, Inc., respectively.

The names Azymetric, Zymeworks, ZymeCAD, EFECT, ZymeLink and the phrase "Building Better Biologics" are our registered trademarks. Other trademarks, product names and company names appearing in this prospectus and any prospectus supplement and documents incorporated by reference in this prospectus and any prospectus supplement are the property of their respective owners. Solely for convenience, the trademarks, service marks, tradenames and copyrights referred to in this prospectus are listed without the ©, ® and TM symbols, but we will assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensors to these trademarks, service marks and tradenames.

RISK FACTORS

Investing in our securities is speculative and involves a high degree of risk. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the any applicable prospectus supplement and any free writing prospectus, together with all the information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus, including the risks, uncertainties and assumptions discussed under the heading "Risk Factors" in our annual report on Form 10-K for the year ended December 31, 2018, as revised or supplemented by our subsequent quarterly reports on Form 10-Q or our current reports on Form 8-K, which are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. These risks, as well as risks currently unknown to us, could materially adversely affect our future business, operations and financial condition and could cause purchasers of securities to lose all or part of their investments. The risks and uncertainties we have described are not the only risks we face; risks and uncertainties not currently known to us or that we currently deem to be immaterial may also materially and adversely affect our business, financial condition, results of operations and prospects.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents incorporated by reference herein, includes and incorporates by reference "forward-looking statements" within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and "forward-looking information" within the meaning of Canadian securities laws, or collectively, forward-looking statements. Forward-looking statements include statements that may relate to our plans, objectives, goals, strategies, future events, future revenue or performance, capital expenditures, financing needs and other information that is not historical information. Forward-looking statements can often be identified by the use of terminology such as "subject to," "believe," "anticipate," "plan," "expect," "intend," "estimate," "project," "may," "will," "should," "could," "can," the negatives thereof, variations thereon and similar expressions, or by discussions of strategy. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. In particular, forward-looking statements in this prospectus and the documents incorporated by reference herein include, but are not limited to, statements about:

- the size of our addressable markets and our ability to commercialize product candidates;
- the achievement of advances in and expansion of our therapeutic platforms and antibody engineering expertise;
- · the likelihood of product candidate development and clinical trial progression, initiation or success; 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 referred to under "Risk Factors," above), could affect future performance and cause actual results to differ materially from those matters expressed in or implied by forward-looking statements:

- our ability to obtain regulatory approval for our product candidates without significant delays;
- the predictive value of our current or planned clinical trials;
- delays with respect to the development and commercialization of our product candidates, which may cause increased costs or delay receipt of product revenue;
- our or any of our partners' ability to enroll subjects in clinical trials and thereby complete trials on a timely basis;
- the design or our execution of clinical trials may not support regulatory approval, including where clinical trials are conducted outside the United States;
- our discretion to discontinue or reprioritize the development of any of our product candidates;
- the potential for our product candidates to have undesirable side effects;
- no regulatory agency has made a determination that any of our product candidates are safe or effective for use by the general public or for any indication;
- our ability to face significant competition;
- 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;
- the potential for foreign governments to impose strict price controls;

- the risk of security breaches or data loss, which could compromise sensitive business or health information;
- · current and future legislation that may increase the difficulty and cost of commercializing our product candidates;
- economic, political, regulatory and other risks associated with international operations;
- our exposure to legal and reputational penalties as a result of any of our current and future relationships with various third parties;
- our ability to comply with export control and import laws and regulations;
- our history of significant losses since inception;
- our ability to generate revenue from product sales and achieve profitability;
- our requirement for substantial additional funding;
- the potential dilution to our shareholders associated with future financings;
- restrictions on our ability to seek financing, which may be imposed by future debt;
- unstable market and economic conditions;
- currency fluctuations and changes in foreign currency exchange rates;
- our ability to maintain existing and future strategic partnerships;
- our ability to realize the anticipated benefits of our strategic partnerships;
- our ability to secure future strategic partners;
- our reliance on third-party manufacturers to produce our clinical product candidate supplies and on other third parties to store, monitor and transport bulk drug substance and drug product;
- risk related to the manufacture of product candidates and difficulties in production;
- our reliance on third parties to oversee clinical trials of our product candidates and, in some cases, maintain regulatory files for those product candidates;
- our reliance on the performance of independent clinical investigators and contract research organizations;
- our reliance on third parties for various operational and administrative aspects of our business including our reliance on third parties' cloud-based software platforms;
- our ability to operate without infringing the patents and other proprietary rights of third parties;
- our ability to obtain and enforce patent protection for our product candidates and related technology;
- our patents could be found invalid or unenforceable if challenged;
- our intellectual property rights may not necessarily provide us with competitive advantages;
- we may become involved in expensive and time-consuming patent lawsuits;
- the risk that the duration of our patents will not adequately protect our competitive position;
- our ability to obtain protection under the Drug Price Competition and Patent Term Restoration Act of 1984 and similar foreign legislation;
- we may be unable to protect the confidentiality of our proprietary information;
- our ability to comply with procedural and administrative requirements relating to our patents;
- the risk of claims challenging the inventorship of our patents and other intellectual property;

- our intellectual property rights for some of our product candidates are dependent on the abilities of third parties to assert and defend such rights;
- patent reform legislation and court decisions can diminish the value of patents in general, thereby impairing our ability to protect our products;
- we may not be able to protect our intellectual property rights throughout the world;
- we will require U.S. Food and Drug Administration approval for any proposed product candidate names and any failure or delay associated with such approval may adversely affect our business;
- the risk of employee misconduct including noncompliance with regulatory standards and insider trading;
- our ability to market our products in a manner that does not violate the law and subject us to civil or criminal penalties;
- if we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected:
- our ability to retain key executives and attract and retain qualified personnel;
- our ability to manage organizational growth;
- additional costs and expenses related to the change from foreign private issuer to U.S. domestic issuer status and no longer being considered an emerging growth company or a smaller reporting company;
- our exposure to potential securities class action litigation; and
- if securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

Consequently, forward-looking statements should be regarded solely as our current plans, estimates and beliefs. You should not place undue reliance on forward-looking statements. We cannot guarantee future results, events, levels of activity, performance or achievements. We do not undertake and specifically decline any obligation to update, republish or revise forward-looking statements to reflect future events or circumstances or to reflect the occurrences of unanticipated events, except as required by law.

EXCHANGE RATE INFORMATION

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

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

				Nine Months Ended	
	Year Ended December 31,			September 30,	
	2016	2017	2018	2018	2019
Highest rate during the period	1.4589	1.3743	1.3642	1.3310	1.3600
Lowest rate during the period	1.2544	1.2128	1.2288	1.2288	1.3038
Average exchange rate for the period(1)	1.3231	1.2986	1.2957	1.2876	1.3292
Rate at the end of the period	1.3427	1.2545	1.3642	1.2945	1.3243

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

On November 4, 2019 the Bank of Canada daily average rate of exchange was \$1.00 = C\$1.3148.

ZYMEWORKS INC.

The following description of the Company is, in some instances, derived from selected information about us contained in the documents incorporated by reference into this prospectus. This description does not contain all of the information about us and our business that you should consider before investing in any securities. You should carefully read the entire prospectus and the applicable prospectus supplement, including the section titled "Risk Factors" above, as well as the documents incorporated by reference into this prospectus and the applicable prospectus supplement, before making an investment decision.

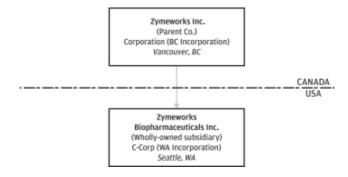
Corporate Structure

Name, address and incorporation

We were incorporated on September 8, 2003 under the Canada Business Corporations Act, under the name "Zymeworks Inc." On October 22, 2003, we were registered as an extra-provincial company under the Company Act (British Columbia), the predecessor to the Business Corporations Act (British Columbia) ("BCBCA"). Zymeworks continued to the BCBCA on May 2, 2017. 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.

Intercorporate relationships

The following reflects our organizational structure. We have one wholly-owned subsidiary located in Seattle, Washington named Zymeworks Biopharmaceuticals Inc.



Description of the Business

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

Our lead product candidate, ZW25, is a novel bispecific (dual-targeting) antibody which targets two distinct domains of the human epidermal growth factor receptor 2 ("HER2"). The unique mechanism of action of ZW25 may enable it to address unmet need in patient populations with HER2-expressing cancers, including those with lower levels of expression, for which there are no approved HER2-targeted agents. In clinical trials, single agent ZW25 and ZW25 in combination with chemotherapy have been well tolerated with promising anti-tumor activity in patients with heavily pretreated HER2-expressing cancers that have progressed after standard of care,

including multiple HER2-targeted regimens. In 2019, we initiated a global multicenter Phase 2 clinical trial evaluating ZW25 in combination with standard of care chemotherapy for the first-line treatment of HER2-positive metastatic gastric, gastroesophageal junction and esophageal adenocarcinomas. In addition, ZW25 continues to be evaluated in multiple expansion cohorts in the ongoing Phase 1 trial as a single agent in several niche indications including biliary tract, colorectal, gynecological and other HER2-expressing cancers. Our second product candidate, ZW49, capitalizes on the unique design of ZW25 and is a bispecific antibody-drug conjugate ("ADC") based on the same antibody framework as ZW25 but armed with our proprietary ZymeLink-cytotoxic (potent cancer cell-killing) payload. We designed ZW49 to be a best-in-class HER2-targeting ADC to further address unmet need across a range of HER2 expressing cancers. A Phase 1 clinical trial to establish safety and anti-tumor activity of ZW49 began in 2019. We are also advancing a deep pipeline of preclinical product candidates and discovery-stage programs in oncology (including immuno-oncology agents) and other therapeutic areas. In addition to our robust pipeline, our Azymetric, EFECT and ZymeLink therapeutic platforms have been further leveraged through multiple revenue-generating strategic partnerships with the following global pharmaceutical companies: Merck, Lilly, Celgene, GSK, Daiichi Sankyo, Janssen, LEO, BeiGene and Iconic.

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

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

EARNINGS COVERAGE

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

USE OF PROCEEDS

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

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

As we currently have no revenues from product sales, we experienced a negative operating cash flow for the year ended December 31, 2018 and expect to experience a negative operating cash flow for the 2019 fiscal year. In order to raise additional funds to finance future growth opportunities, we may, from time to time, issue securities (including debt securities). See "Risk Factors."

CONSOLIDATED CAPITALIZATION

There have been no material changes in our share and loan capital, on a consolidated basis, since September 30, 2019, the date of our most recently filed financial statements.

PRIOR SALES

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

MARKET FOR SECURITIES

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

DESCRIPTION OF SHARE CAPITAL

General

The following 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 of October 31, 2019, 39,387,339 common shares and no preferred shares were issued and outstanding. Our common shares are listed on the NYSE under the symbol "ZYME."

Common Shares

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

Dividend Policy

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

Preferred Shares

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

DESCRIPTION OF DEBT SECURITIES

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

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 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 is 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;
- 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.

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 depositary, 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 depositary for such global security to a nominee of the depositary, by a nominee of the depositary to the depositary or another nominee of the depositary or any such nominee to a successor of the depositary or a nominee of the successor.

The specific terms of the depositary 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 depositary arrangements.

Upon the issuance of a global security, the depositary 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 depositary 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 depositary 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.

So long as the depositary for a global security or its nominee is the registered owner of the global security, such depositary 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 depositary or its nominee will be made to the depositary 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 depositary 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 depositary 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 Depositary's Services

If a depositary for a global security representing a particular series of the debt securities is at any time unwilling or unable to continue as depositary and a successor depositary 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 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, 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 U.S. Securities Exchange Act of 1934, as amended (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 10-K or any successor form, quarterly reports on Form 10-Q or any successor form and current reports of Form 8-K or any successor form.

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.

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

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

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

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

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

Equity Warrants

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

- the designation and aggregate number of equity warrants;
- the price at which the equity warrants will be offered;
- the currency or currencies in which the equity warrants will be offered;
- the date on which the right to exercise the equity warrants will commence and the date on which the right will expire;
- the number of common shares 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.

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.

SELLING SECURITYHOLDERS

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

PLAN OF DISTRIBUTION

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

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

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

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

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

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

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

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

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

CANADIAN AND U.S. FEDERAL INCOME TAX CONSIDERATIONS

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

LEGAL MATTERS

Certain legal matters in connection with the securities offered hereby will be passed upon on behalf of the Company by Blake, Cassels & Graydon LLP with respect to Canadian legal matters, and by Skadden, Arps, Slate, Meagher & Flom LLP with respect to U.S. legal matters.

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 2017 and 2018 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 Code 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.

INTEREST OF EXPERTS

The consolidated financial statements of Zymeworks for the years ended December 31, 2018 and 2017, and for each of the years in the three year period ended December 31, 2018, have been incorporated by reference herein in reliance upon the report of KPMG LLP, independent registered public accounting firm, also incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

The audit report covering the consolidated financial statements as of December 31, 2018 and 2017 and for each of the years in the three-year period ended December 31, 2018, refers to a change in our accounting policies for revenue recognition as of January 1, 2018 due to the adoption of ASC 606 – Revenue from Contracts with Customers.

DOCUMENTS INCORPORATED BY REFERENCE

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

We incorporate by reference the documents listed below and future filings we make with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (excluding, unless otherwise provided therein or herein,

documents not deemed "filed" with the SEC and information furnished pursuant to Item 2.02 and Item 7.01 on any Current Report on Form 8-K or certain exhibits furnished pursuant to Item 9.01 of Form 8-K) after the date of the initial filing of this registration statement on Form S-3 to which this prospectus relates until the termination of any offering under this prospectus or such time as all securities offered by this prospectus have been sold and all conditions to the consummation of such sales have been satisfied.

- (a) annual report on Form 10-K for the fiscal year ended December 31, 2018, filed with the SEC on March 6, 2019;
- (b) quarterly reports on Form 10-Q for the quarterly periods ended March 31, 2019, June 30, 2019 and September 30, 2019, filed with the SEC on May 2, 2019, August 2, 2019 and November 5, 2019, respectively;
- (c) current reports on Form 8-K, filed with the SEC on <u>January 7, 2019, January 17, 2019, January 31, 2019, March 5, 2019, April 15, 2019, April 23, 2019, April 25, 2019, April 30, 2019, May 3, 2019, May 15, 2019, May 17, 2019, May 24, 2019, May 28, 2019, May 29, 2019, May 30, 2019, June 5, 2019, June 13, 2019, June 20, 2019, June 25, 2019, July 16, 2019, August 28, 2019, September 18, 2019, September 20, 2019, September 30, 2019, October 16, 2019, October 28, 2019 and November 4, 2019;</u>
- (d) The description of our common shares contained in our registration statement on Form 8-A filed on April 24, 2017, including any amendments or reports filed for the purpose of updating such description; and
- (e) all other documents filed by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, after December 31, 2018, but before the end of the offering of the securities made by this prospectus.

WHERE YOU CAN FIND MORE INFORMATION

We are required to file with the securities commission or authority in each of the provinces and territories of Canada annual and quarterly reports, material change reports and other information. 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 the SEC.

You may read any document we file with or furnish to the securities commissions and authorities of the provinces and territories of Canada through SEDAR at https://www.sedar.com. The SEC maintains an internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, where our SEC filings are also available. The address of the SEC's website is http://www.sec.gov. We maintain a website at http://www.zymeworks.com. The references to our website in this prospectus or the documents incorporated by reference herein are inactive textual references only and information contained in or accessible through our website does not constitute a part of this prospectus.

ENFORCEABILITY OF CIVIL LIABILITIES

We are a corporation existing under the BCBCA. Some of our directors, officers, and the experts named in this prospectus, are residents of Canada or otherwise reside outside the United States, and all or a substantial portion of their assets may be, and a substantial portion our assets are, located outside the United States. We have appointed an agent for service of process in the United States, but it may be difficult for holders of common shares who reside in the United States to effect service within the United States upon those directors, officers and experts who are not residents of the United States. It may also be difficult for holders of common shares who reside in the United States to realize in the United States upon judgments of courts of the United States

predicated upon our civil liability and the civil liability of our directors, officers and experts under the U.S. federal securities laws. We have been advised by our Canadian counsel, Blake, Cassels & Graydon LLP, that a judgment of a U.S. court predicated solely upon civil liability under U.S. federal securities laws or the securities or "blue sky" laws of any state within the United States, would probably be enforceable in Canada if the U.S. court in which the judgment was obtained has a basis for jurisdiction in the matter that would be recognized by a Canadian court for the same purposes. We have also been advised by Blake, Cassels & Graydon LLP, however, that there is substantial doubt whether an action could be brought in Canada in the first instance on the basis of liability predicated solely upon U.S. federal securities laws.



6,950,433 Common shares

PROSPECTUS SUPPLEMENT