

Aeterna Zentaris Inc.
Form 424B5
March 29, 2017

Use these links to rapidly review the document

[TABLE OF CONTENTS](#)

[TABLE OF CONTENTS](#)

[Table of Contents](#)

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-194547

PROSPECTUS SUPPLEMENT NO. 3

(To Prospectus dated March 28, 2014)

Up to \$9,000,000 of Common Shares

Aeterna Zentaris Inc. ("we", "us" or the "Company") is hereby offering up to 3,000,000 of our common shares (the "Common Shares") under this prospectus supplement and the accompanying prospectus. The offering is being conducted pursuant to our existing At Market Issuance Sales Agreement dated April 1, 2016 (the "Sales Agreement") with H.C. Wainwright & Co., LLC ("Wainwright"). In accordance with the terms of the Sales Agreement, we may offer and sell Common Shares having an aggregate offering price of up to \$9,000,000, from time to time through Wainwright, as agent. Unless otherwise stated, currency amounts in this prospectus supplement are presented in United States dollars, or "\$" or "US\$".

Our Common Shares are listed on the NASDAQ Capital Market ("NASDAQ") and on the Toronto Stock Exchange ("TSX") under the symbol "AEZS". On March 27, 2017, the last reported sales price of our Common Shares on NASDAQ was \$3.00 per share and on TSX was C\$4.01 per share. There is no arrangement for funds to be received in escrow, trust or similar arrangement. The TSX has conditionally approved the listing of the Common Shares offered for sale pursuant to this prospectus supplement. Listing on the TSX is subject to the Company fulfilling all of the requirements of the TSX on or before the business day immediately following the date on which this prospectus supplement is filed.

Upon delivery of a placement notice by us, if any, Wainwright may sell the Common Shares, in the United States ("U.S.") only, by any method permitted by law deemed to be an "at the market offering" as defined in Rule 415 of the U.S. Securities Act of 1933, as amended (the "Securities Act"), including, without limitation, sales made directly on NASDAQ, or on any other existing trading market for the Common Shares in the U.S. at market prices prevailing at the time of sale. Wainwright is not required to sell any specific number or dollar amount of our Common Shares, but Wainwright has agreed to seek to make all sales using commercially reasonable efforts consistent with its normal sales and trading practices and on mutually agreed upon terms between Wainwright and us. The Common Shares will be distributed at the market prices prevailing at the time of the sale of such Common Shares. As a result, prices may vary as between purchasers and during the period of distribution.

The compensation to Wainwright for sales of our Common Shares under this prospectus supplement will be equal to three percent (3.0%) of the gross proceeds from the sale of such Common Shares. In addition, Wainwright will be reimbursed for certain reasonable out-of-pocket expenses in connection with this offering. See "Plan of Distribution". The net proceeds, if any, from sales under this prospectus supplement will be used as described under the section titled "Use of Proceeds" in this prospectus supplement. The proceeds we receive from sales will depend on the number of Common Shares actually sold and the offering price of such Common Shares. Depending on the trading price of our Common Shares on NASDAQ, we may not be able to raise the full \$9,000,000 in gross proceeds permitted under this offering and the Sales Agreement and we may not sell all of the Common Shares offered hereby. The actual proceeds to us will vary. In connection with the sale of the Common Shares on our behalf, Wainwright will be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation of Wainwright will be deemed to be underwriting commissions or discounts. Pursuant to the Sales Agreement, we have agreed to provide indemnification and contribution to Wainwright against certain liabilities, including liabilities under the Securities Act.

Edgar Filing: Aeterna Zentaris Inc. - Form 424B5

The aggregate market value of our Common Shares held by non-affiliates pursuant to General Instruction I.B.5 of Form F-3 is \$45,819,347, which was calculated based on 13,677,417 of our Common Shares outstanding and held by non-affiliates as of the date of this prospectus supplement and a price of \$3.35 per share, the closing price of our Common Shares on NASDAQ on February 17, 2017. We have sold 1,706,968 Common Shares pursuant to General Instruction I.B.5 of Form F-3 during the twelve calendar month period that ends on and includes the date of this prospectus supplement and the aggregate value of the Common Shares sold was \$6,002,682.

Investing in our Common Shares involves a high degree of risk. See "Risk Factors" beginning on page S-7 of this prospectus supplement and the risk factors described in the documents incorporated by reference herein for information that should be considered before investing in our Common Shares.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR PASSED UPON THE ACCURACY OF THIS PROSPECTUS SUPPLEMENT AND THE ACCOMPANYING PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

H.C. Wainwright & Co.

The date of this prospectus supplement is March 28, 2017.

Table of Contents

TABLE OF CONTENTS

	Page
PROSPECTUS SUPPLEMENT	
<u>ABOUT THIS PROSPECTUS SUPPLEMENT</u>	<u>ii</u>
<u>PROSPECTUS SUPPLEMENT SUMMARY</u>	<u>S-1</u>
<u>SPECIAL NOTE ON FORWARD-LOOKING STATEMENTS</u>	<u>S-5</u>
<u>RISK FACTORS</u>	<u>S-7</u>
<u>USE OF PROCEEDS</u>	<u>S-30</u>
<u>PRICE RANGE AND TRADING VOLUME</u>	<u>S-30</u>
<u>PRIOR SALES</u>	<u>S-31</u>
<u>CONSOLIDATED CAPITALIZATION</u>	<u>S-31</u>
<u>DILUTION</u>	<u>S-32</u>
<u>DIVIDEND POLICY</u>	<u>S-33</u>
<u>DESCRIPTION OF SECURITIES OFFERED UNDER THIS PROSPECTUS SUPPLEMENT</u>	<u>S-33</u>
<u>PLAN OF DISTRIBUTION</u>	<u>S-34</u>
<u>CERTAIN INCOME TAX CONSIDERATIONS</u>	<u>S-35</u>
<u>LEGAL MATTERS</u>	<u>S-41</u>
<u>EXPERTS</u>	<u>S-42</u>
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	<u>S-42</u>
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	<u>S-42</u>

Table of Contents

This prospectus supplement is not an offer to sell or a solicitation of an offer to buy securities in any jurisdiction in which such offer or solicitation is illegal.

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a "shelf" registration statement on Form F-3 (File No. 333-194547) that was filed with the Securities and Exchange Commission ("SEC") on March 14, 2014 and was declared effective on March 28, 2014.

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of our Common Shares and supplements information contained in the accompanying prospectus and the documents incorporated by reference into the accompanying prospectus. The second part is the accompanying prospectus, which gives more general information about us and the Common Shares we may offer from time to time under our shelf registration statement.

We have not authorized any dealer, salesperson or other person to give any information or to make any representation other than those contained in or incorporated by reference into this prospectus supplement, the accompanying prospectus and any related free writing prospectus that we may authorize to be provided to you. You should not rely upon any information or representation not contained in or incorporated by reference into this prospectus supplement, the accompanying prospectus or any free writing prospectus that we may authorize to be provided to you. If information in this prospectus supplement is inconsistent with the accompanying prospectus or the information incorporated by reference, you should rely on this prospectus supplement. This prospectus supplement, the accompanying prospectus and any related free writing prospectus that we may authorize to be provided to you do not constitute an offer to sell or the solicitation of an offer to buy Common Shares in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus supplement, the accompanying prospectus and any related free writing prospectus that we may authorize to be provided to you is accurate on any date other than the date set forth on the front cover of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference regardless of the date of delivery of this prospectus supplement, the accompanying prospectus and any related free writing prospectus that we may authorize to be provided to you or any sale of Common Shares. Our business, financial condition, results of operations and prospects may have changed since those dates.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference into this prospectus supplement and the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

The financial statements included in or incorporated by reference into this prospectus supplement and the accompanying prospectus have been prepared in accordance with International Financial Reporting Standards as issued by the International Accounting Standards Board. Our consolidated financial statements are subject to Canadian generally accepted auditing standards and auditor independence standards, in addition to the standards of the Public Company Accounting Oversight Board (U.S.) and the SEC independence standards. This may not be comparable to financial statements of U.S. companies.

Except as otherwise indicated, all historical share, warrant and option data, including number of securities issued and outstanding and applicable exercise prices, in this prospectus supplement and in the documents incorporated by reference herein, have been retroactively adjusted to reflect and give effect to the share consolidation (reverse stock split) we effected on November 17, 2015 on a 100-for-1 basis. Our Common Shares commenced trading on a consolidated and adjusted basis on both NASDAQ and TSX on November 20, 2015.

In this prospectus supplement, unless otherwise indicated, references to "we", "us", "our", "Aeterna Zentaris" or the "Company" are to Aeterna Zentaris Inc., a Canadian corporation, and its consolidated subsidiaries, unless it is clear that such terms refer only to Aeterna Zentaris Inc. excluding its subsidiaries.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere in or incorporated by reference into this prospectus supplement and the accompanying prospectus. The summary may not contain all of the information that you should consider before investing in our Common Shares. You should read this entire prospectus supplement and the accompanying prospectus carefully, including "Risk Factors" contained in this prospectus supplement and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, before making an investment decision. This prospectus supplement may add to, update or change information in the accompanying prospectus.

Our Business

Overview. We are a specialty biopharmaceutical company engaged in developing and commercializing novel treatments in oncology, endocrinology and women's health. We are engaged in drug development activities and in the promotion of products for others. We recently completed two Phase 3 studies of internally developed components. The focus of our business development efforts is the acquisition of or licenses to products that are relevant to our therapeutic areas of focus. We also intend to license out certain commercial rights of internally developed products to licensees in non-U.S. territories where such out-licensing would enable us to ensure development, registration and launch of our product candidates. Our goal is to become a growth-oriented specialty biopharmaceutical company by pursuing successful development and commercialization of our product portfolio, achieving successful commercial presence and growth, while consistently delivering value to our shareholders, employees and the medical providers and patients who will benefit from our products.

Our Strategy. Our primary business strategy is to finalize the development and to pursue registration of our principal product candidates Zoptrex (zoptarelin doxorubicin) and Macrilen (macimorelin) in oncology and endocrinology, respectively and to commercialize oncology, endocrinology and women's health products that we may acquire, in-license or promote. The registration of Zoptrex and Macrilen are subject to the concurrence of the U.S. Food and Drug Administration (the "FDA") that top-line clinical trial data results have met FDA requirements. A meeting with the FDA to discuss the Macrilen clinical trial data results is scheduled for the end of March 2017.

Drug Development. Our drug development efforts are currently focused on two compounds, Zoptrex and Macrilen as well as on an LHRH-disorazol Z conjugate (AEZS-138), which is in pre-clinical development in oncology and is available for partnering. We made the decision to focus our efforts in pre-clinical development on one compound because we lack the resources to pursue other earlier-stage opportunities. As a result of this decision, we discontinued drug discovery efforts, including basic research activities in medicinal chemistry and biology and our high-throughput-screening operations, which resulted in a reduction of our research and development staff by approximately 29 personnel during 2014.

Zoptrex™ represents a new targeting concept in oncology using a hybrid molecule composed of a synthetic peptide carrier, zoptarelin, and a well-known chemotherapy agent, doxorubicin, resulting in a cytotoxic conjugate. Zoptarelin is a luteinizing hormone-releasing hormone ("LHRH") agonist, a modified natural hormone with affinity for the LHRH receptor. Most chemotherapeutic agents, including doxorubicin, are toxic to normally growing, healthy cells as well as to tumor cells that grow uncontrolled. Therefore, a method for targeting such drugs specifically to cancerous tissue offers a potential benefit for patients with tumors, and particularly patients with locally advanced, recurrent or metastatic tumors. Zoptrex is our proposed tradename for zoptarelin doxorubicin. The proposed tradename is subject to approval by the FDA.

Zoptrex is the first intravenous drug in advanced clinical development that is considered to direct the chemotherapy agent specifically to LHRH-receptor expressing tumors, which then could result in a more targeted treatment with less damage to healthy tissue. This design is believed to allow for the specific binding and selective uptake of the cytotoxic conjugate by LHRH receptor-positive tumors. Potential benefits of this targeted approach include better efficacy and a more favorable safety profile with lower incidence and severity of side effects as compared to doxorubicin. In addition, the targeted approach may enable treatment of LHRH receptor-positive cancers that have become resistant to doxorubicin.

Table of Contents

We are conducting a pivotal Phase 3 clinical study of Zoptrex[®] in women with locally advanced, recurrent or metastatic endometrial cancer who have progressed and who have received one chemotherapeutic regimen with platinum and taxane (either as adjuvant or first-line treatment). The clinical study is known as the "ZoptEC" study (zoptarelin doxorubicin in endometrial cancer). ZoptEC is a fully-recruited (over 500 patients), open-label, randomized-controlled study, comparing the efficacy and safety of Zoptrex[®] to doxorubicin alone. Patients were centrally randomized in a 1:1 ratio and received either Zoptrex[®] (267 mg/m²) or doxorubicin (60 mg/m²) intravenously, every three weeks and for up to nine cycles. Response was evaluated every three cycles during treatment and thereafter every 12 weeks until progression.

We are conducting the ZoptEC trial under a Special Protocol Assessment ("SPA") with the FDA. The SPA agreement states that the proposed trial protocol design, clinical endpoints and planned analyses are acceptable to the FDA to support a regulatory submission. Final marketing approval depends on the results of efficacy, the adverse event profile and an evaluation of the benefit/risk of treatment demonstrated in ZoptEC. The primary efficacy endpoint of the ZoptEC trial is improvement in median Overall Survival ("OS"). Secondary endpoints include progression-free survival, objective response rate and clinical benefit response rate.

The ZoptEC study was designed to permit the final analysis of the data from the study to occur following the deaths of 384 patients. On January 30, 2017, we announced the occurrence of the 384th death, representing the clinical endpoint of the study. We expect clinical database lock and reporting of top-line results to occur in April 2017. If the results of the ZoptEC study warrant doing so, we expect to file a new drug application ("NDA") in the United States for Zoptrex[®] in the third quarter of 2017. We are now moving forward with our planning to commercialize Zoptrex[®], looking toward commercial launch of the product in 2018, assuming positive Phase 3 results and that the NDA is granted.

We have licensed the development, commercialization and certain other rights to Zoptrex[®] to: (i) Sinopharm A-Think Pharmaceuticals Co., Ltd. for the People's Republic of China, including Hong Kong and Macau; (ii) Cyntec Co., Ltd., an affiliate of Orient EuroPharma Co., Ltd., for Taiwan and nine countries in southeast Asia; (iii) Rafa Laboratories Ltd for Israel and the Palestinian territories; and (iv) Specialised Therapeutics Asia Pte Ltd for Australia and New Zealand.

Macrilen (macimorelin acetate) is a novel orally available peptidomimetic ghrelin receptor agonist that stimulates the secretion of growth hormone by binding to the ghrelin receptor (GHSR-1a) and that has potential uses in both endocrinology and oncology indications. Macrilen[®] has been granted orphan-drug designation by the FDA for use in evaluating growth hormone deficiency ("GHD"). If approved by the FDA, Macrilen[®] would be the first orally administered drug indicated for the evaluation of adult growth hormone deficiency ("AGHD"). Macrilen[®] is our proposed proprietary trade name for macimorelin, being subject to approval by the FDA. On December 16, 2016 we were advised by the European Medicines Agency ("EMA") that Macrilen[®] was rejected as a proposed invented name for macimorelin because of its similarity to the names of other medicines. We intend to appeal this decision.

On January 4, 2017, we announced that, based on an analysis of top-line data, the confirmatory Phase 3 clinical trial of Macrilen[®] failed to achieve one of its co-primary endpoints. Under the study protocol, the evaluation of AGHD with Macrilen[®] would be considered successful, if the lower bound of the two-sided 95% confidence interval for the primary efficacy variables was 75% or higher for "percent negative agreement" with the insulin tolerance test (the "ITT"), and 70% or higher for the "percent positive agreement" with the ITT. While the estimated percent negative agreement met the success criteria, the estimated percent positive agreement did not reach the criteria for a successful outcome. Therefore, the results did not meet the pre-defined equivalence criteria which required success for both the percent negative agreement and the percent positive agreement.

On February 13, 2017, we announced that, after reviewing the raw data on which the top-line data were based, we concluded that Macrilen[®] had demonstrated performance supportive of achieving FDA registration and that we intended to pursue registration. The announcement set forth the facts on which our conclusion was based. We are scheduled to meet with the FDA at the end of March 2017 to discuss this position.

Edgar Filing: Aeterna Zentaris Inc. - Form 424B5

Table of Contents

On March 7, 2017, we announced that the Pediatric Committee ("PDCO") of the EMA agreed to our Pediatric Investigation Plan ("PIP") for Macrilen and agreed that we may defer conducting the PIP until after we file a Marketing Authorization Application ("MAA") seeking marketing authorization for the use of Macrilen for the evaluation of adult growth hormone deficiency. The decision will permit the us to file an MAA substantially earlier than if we were required to complete the PIP before filing.

Commercial Operations. Our commercial operations consist of a full-time sales force and a sales-management staff. We currently have 13 sales representatives in the United States, who provide services solely for us pursuant to our agreement with a contract-sales organization. Our sales force is managed by two Regional Sales Managers, a National Sales Director and led by our Senior Vice President and Chief Commercial Officer. Our sales force is currently promoting two products:

Saizen® [somatropin (rDNA origin) for injection] is a prescription medicine indicated for the treatment of growth hormone deficiency in children and adults. We promote Saizen® pursuant to our promotional services agreement (the "EMD Serono Agreement") with EMD Serono Inc. ("EMD Serono"), which we entered into in May 2015 and amended as of December 31, 2016. The EMD Serono Agreement, as amended, provides that we will promote Saizen® in specific agreed-upon US territories to adult and pediatric endocrinologists in exchange for a sales commission that is based upon new patient starts ("NPS") of the product. The EMD Serono Agreement has a five-year term that began in May 2015, which is not subject to a specified extension period, and is subject to customary termination provisions. Both parties to the EMD Serono Agreement have the right to terminate the EMD Serono Agreement for convenience at any time after October 31, 2017, by giving three months' advance written notice to the other party.

APIFINY® is the only cancer-specific, non-PSA blood test for the evaluation of the risk of prostate cancer. The test was developed by Armune BioScience, Inc. ("Armune"), a medical diagnostics company that develops and commercializes unique proprietary technology exclusively licensed from the University of Michigan for diagnostic and prognostic tests for cancer. We entered into a co-marketing agreement with Armune in November 2015 (the "Armune Agreement"), which was amended effective as of June 1, 2016, pursuant to which we have the exclusive right to promote APIFINY® throughout the entire United States. We receive a commission for each test performed resulting from our targeted promotion without regard to a baseline. The Armune Agreement, as amended, has a three-year term that renews automatically for successive one-year periods, unless either party terminates it by giving not less than 60 days' advance written notice to the other, which either party may do at any time with or without cause.

Our sales force will also be available for the launch of our own potential product candidates (i.e., Zoptrex and Macrilen) in the U.S., in the event the products may ultimately be approved for sale in the U.S.

We also continue to pursue opportunities to in-license or acquire additional commercial products that are relevant to our therapeutic areas of focus. Our preference is to in-license or acquire additional commercial products because we wish to control all aspects of the commercialization of the products and to record the sales revenue from the products.

Corporate Information

We were incorporated on September 12, 1990 under the *Canada Business Corporations Act* (the "CBCA") and continue to be governed by the CBCA. Our registered address is 1 Place Ville Marie, Suite 2500, Montreal, Quebec, Canada, H3B 1R1, c/o Norton Rose Fulbright Canada LLP. Our corporate head office is located at 315 Sigma Drive, Suite 302D, Summerville, South Carolina, USA, 29486; our telephone number is (843) 900-3223 and our website is www.aezsinc.com. None of the documents or information found on our website shall be deemed to be included in or incorporated by reference into this prospectus supplement, unless such document is specifically incorporated herein by reference.

We currently have three wholly owned direct and indirect subsidiaries, Aeterna Zentaris GmbH ("AEZS Germany"), based in Frankfurt, Germany, Zentaris IVF GmbH, a direct wholly owned subsidiary of AEZS Germany, based in Frankfurt, Germany, and Aeterna Zentaris, Inc., an entity incorporated in the State of Delaware based in the Charleston, South Carolina area in the U.S.

Our Common Shares are currently listed for trading on NASDAQ and on TSX under the trading symbol "AEZS".

Table of Contents

The Offering

Common Shares offered by us pursuant to this prospectus supplement:	A maximum of 3,000,000 Common Shares having an aggregate offering price of up to \$9,000,000.
Manner of offering:	"At-the-market" offering that may be made from time to time solely in the U.S. through our agent, Wainwright. See "Plan of Distribution" on page S-34.
Use of proceeds:	We intend to use the net proceeds from the sale of Common Shares under this prospectus supplement for general corporate purposes, which includes the funding of the preparation and submission of an NDA for Zoptrex , if the results of our recently completed clinical trial of such product warrants doing so, to pursue FDA registration for Macrilen , if we decide to seek registration after our upcoming meeting with the FDA, the potential in-licensing or acquisition of new commercial products or other corporate and business development activities, and the potential expansion of existing product candidates into other indications. See "Use of Proceeds" on page S-30 of this prospectus supplement.
NASDAQ Capital Market and TSX symbols:	NASDAQ, TSX: AEZS
Risk factors:	An investment in our Common Shares involves a high degree of risk. See "Risk Factors" beginning on page S-7 of this prospectus supplement as well as the other information included in or incorporated by reference into this prospectus supplement and the accompanying prospectus for a discussion of factors that you should consider carefully before making an investment decision.

Table of Contents

SPECIAL NOTE ON FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated herein by reference contain forward-looking statements concerning the business, operations, financial performance and condition of the Company. When used in this prospectus supplement, the accompanying prospectus and the documents incorporated herein by reference, words such as "may", "will", "should", "could", "expects", "plans", "seeks", "anticipates", "intends", "believes", "estimates", "predicts", "potential" or "continue" or the negative of these terms and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain such words. These forward-looking statements are based on current expectations and are naturally subject to uncertainty and changes in circumstances that may cause actual results to differ materially from those expressed or implied by such forward-looking statements. Such statements, based as they are on the current expectations of management, inherently involve numerous risks and uncertainties, known and unknown, many of which are beyond our control. Such risks include but are not limited to:

investments in biopharmaceutical companies are generally considered to be speculative;

we may not be able to continue as a going concern, if we are unsuccessful in generating new revenue, increasing our revenues and/or raising additional funding;

fluctuations in our revenues and expenses may disappoint securities analysts and investors, causing the price of our securities to decline;

our clinical trials may not yield results that will enable us to obtain regulatory approval for our products and a setback in any of our clinical trials would likely cause a drop in the price of our securities;

we may not be able to successfully complete our clinical trial programs, or such clinical trials could take longer to complete than we project;

we may not be able to realize any profit from our commercial operation;

we may not be able to acquire, in-license or otherwise obtain the right to sell other products;

we will require significant additional financing, and we may not have access to sufficient capital;

we may breach or fail to maintain a necessary license;

the impact of the stringent ongoing government regulations to which our product candidates are subject;

the impact of restrictions on, or withdrawals of, any product approvals and changes in regulatory requirements;

the impact of healthcare reform measures on the commercial success of our product candidates and on our business prospects or future financial condition;

Edgar Filing: Aeterna Zentaris Inc. - Form 424B5

the impact of healthcare fraud and abuse laws on our ability to market products;

we may not be able to generate significant revenues if our products do not gain market acceptance;

we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications for which there may be a greater likelihood of success;

the failure to achieve our projected development goals in the time-frames we announce and expect;

the impact of any failure on our part to obtain acceptable prices or adequate reimbursement for our products on our ability to generate revenues;

the impact of competition in our targeted markets;

we may not obtain adequate protection for our products through our intellectual property;

the impact of the recent expiration of certain of our patents;

we may infringe the intellectual property rights of others;

we may incur liabilities from our involvement in any patent litigation;

Table of Contents

we may not obtain trademark registrations in connection with our product candidates;

current and future collaborations for the development of our product candidates may not provide the benefits we expect;

the failure to perform satisfactorily by third parties upon which we rely to conduct, supervise and monitor our clinical trials;

our ability to obtain a stable and consistent supply of ingredients and raw materials;

the failure to perform satisfactorily by third parties upon which we expect to rely to manufacture and supply products;

our ability to retain or attract key personnel;

we use hazardous materials and are subject to environmental and occupational safety laws;

the impact of securities class-action litigation or other litigation on our cash flow, results of operations and financial position;

risks relating to product liability and other claims;

risks relating to our holding company structure and inter-company funding agreements;

it may be difficult for U.S. investors to obtain and enforce judgments against us;

we may not be able to maintain effective internal controls;

the possibility that we may be a passive foreign investment company, which could result in adverse tax consequences to U.S. investors;

fluctuations in currency exchange rates;

the impact of legislative actions, new accounting pronouncements and higher insurance costs on our future financial position or results of operations;

security breaches may disrupt our operations and adversely affect our operating results;

the possibility that our Common Shares may be delisted from the stock exchanges on which they currently trade;

Edgar Filing: Aeterna Zentaris Inc. - Form 424B5

our share price is volatile;

we do not intend to pay dividends;

future issuances of securities and hedging activities may depress the price of our securities;

our status as a foreign private issuer could be lost in future periods which could increase certain legal, financial and accounting compliance costs;

we are permitted to issue "blank check" preferred shares; and

our business could be negatively affected as a result of the actions of activist shareholders.

More detailed information about these and other factors is included under "Risk Factors" in this prospectus supplement, the accompanying prospectus as well as in other documents incorporated herein by reference. Many of these factors are beyond our control. Future events may vary substantially from what we currently foresee. You should not place undue reliance on such forward-looking statements. The Company disavows and is under no obligation to update or alter such forward-looking statements whether as a result of new information, future events or otherwise, other than as required by applicable securities legislation.

Table of Contents

RISK FACTORS

Before making an investment decision, you should carefully consider the risks described in this prospectus supplement, together with all of the other information incorporated by reference into this prospectus supplement and the accompanying prospectus, including the risks described in our most recent Annual Report on Form 20-F and subsequent Reports on Form 6-K furnished to the SEC, including our audited consolidated financial statements and corresponding management's discussion and analysis. The risks mentioned below are presented as of the date of this prospectus supplement and we expect that these will be updated from time to time in our periodic and current reports filed with or furnished to the SEC, as applicable, which will be incorporated herein by reference. Please refer to these subsequent reports for additional information relating to the risks associated with investing in our Common Shares.

Our business, financial condition or results of operations could be materially adversely affected by any of these risks. Additional risks not presently known to us or that we currently deem immaterial may also impair our business operations. The trading price of our Common Shares could decline due to any of these risks, and you may lose part or all of your investment. This prospectus supplement, the accompanying prospectus and the incorporated documents also contain forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks mentioned below. Forward-looking statements included in this prospectus supplement are based on information available to us on the date hereof, and all forward-looking statements in documents incorporated by reference are based on information available to us as of the date of each such document. The Company disavows and is under no obligation to update or alter such forward-looking statements whether as a result of new information, future events or otherwise, other than as required by applicable securities legislation.

Risks Relating to Us and Our Business

Investments in biopharmaceutical companies are generally considered to be speculative.

The prospects for companies operating in the biopharmaceutical industry are uncertain, given the very nature of the industry, and, accordingly, investments in biopharmaceutical companies should be considered to be speculative assets.

We have a history of operating losses and we may never achieve or maintain operating profitability. In addition, if we are unsuccessful in generating new revenue, increasing our revenue and/or raising additional funding, we may not be able to continue as a going concern.

We have incurred, and expect to continue to incur, substantial expenses in our efforts to develop and market products. Consequently, we have incurred operating losses historically and in each of the last several years. As at December 31, 2016, we had an accumulated deficit of approximately \$298 million. Our operating losses have adversely impacted, and will continue to adversely impact, our working capital, total assets, operating cash flow and shareholders' equity. We do not expect to reach operating profitability in the immediate future, and our operating expenses are likely to continue to represent a significant component of our overall cost profile as we seek regulatory approval for our product candidates and carry out commercial activities. Even if we succeed in developing, acquiring or in-licensing new commercial products, we could incur additional operating losses for at least the next several years. If we do not ultimately generate sufficient revenue from commercialized products to achieve or maintain operating profitability, an investment in our Common Shares could result in a significant or total loss.

Our ability to continue as a going concern is dependent on the successful execution of our business plan, which will require an increase in revenue and/or additional funding to be provided by potential investors and/or non-traditional sources of financing. We did not have, as at December 31, 2016, sufficient liquidity and financial resources to fund planned expenditures and other working capital needs for the 12-month period following such date. Therefore, our audited consolidated financial statements as at December 31, 2016 include a footnote disclosing material uncertainties related to events and conditions that may cast significant doubt about our ability to continue as a going concern for at least twelve months from December 31, 2016.

Additional funding may be in the form of debt or equity or a hybrid instrument depending on our needs, the demands of investors and market conditions. Depending on the prevailing global economic and credit market

Table of Contents

conditions, we may not be able to raise additional cash through these traditional sources of financing. Although we may also pursue non-traditional sources of financing with third parties, the global equity and credit markets may adversely affect the ability of potential third parties to pursue such transactions for us. Accordingly, as a result of the foregoing, we continue to review traditional sources of financing, such as private and public debt or various equity financing alternatives, as well as other alternatives to enhance shareholder value, including, but not limited to, non-traditional sources of financing, such as strategic alliances with third parties, the sale of assets or licensing of our technology or intellectual property, a combination of operating and related initiatives or a substantial reorganization of our business.

There can be no assurance that we will achieve profitability or positive cash flows or be able to obtain additional funding or that, if obtained, the additional funding will be sufficient, or whether any other initiatives will be successful such that we may continue as a going concern. There could also be material uncertainties related to certain adverse conditions and events that could impact our ability to remain a going concern. If the going concern assumptions were deemed no longer appropriate for our consolidated financial statements, adjustments to the carrying value of assets and liabilities, reported expenses and consolidated statement of financial position classifications would be necessary. Such adjustments could be material.

Our revenues and expenses may fluctuate significantly, and any failure to meet financial expectations may disappoint securities analysts or investors and result in a decline in the price of our Common Shares.

We have a history of operating losses. Our revenues and expenses have fluctuated in the past and may continue to do so in the future. These fluctuations could cause our share price to decline. Some of the factors that could cause our revenues and expenses to fluctuate include but are not limited to:

the inability to complete product development in a timely manner that results in a failure or delay in receiving the required regulatory approvals to commercialize our product candidates;

the timing of regulatory submissions and approvals;

the timing and willingness of any current or future collaborators to invest the resources necessary to commercialize our product candidates;

the nature and timing of licensing fee revenues;

the outcome of litigation, including the securities class-action litigation pending against us that is described elsewhere in this prospectus supplement;

foreign currency fluctuations;

the timing of the achievement and the receipt of milestone payments from current or future collaborators; and

failure to enter into new or the expiration or termination of current agreements with collaborators.

Due to fluctuations in our revenues and expenses, we believe that period-to-period comparisons of our results of operations are not necessarily indicative of our future performance. It is possible that in some future periods, our revenues and expenses will be above or below the expectations of securities analysts or investors. In this case, the price of our Common Shares could fluctuate significantly or decline.

Our clinical trials may not yield results that will enable us to obtain regulatory approval for our products, and a setback in any of our clinical trials would likely cause a drop in the price of our Common Shares.

We will only receive regulatory approval for a product candidate if we can demonstrate, in carefully designed and conducted clinical trials, that the product candidate is both safe and effective. We do not know whether our pending or any future clinical trials will demonstrate sufficient

Edgar Filing: Aeterna Zentaris Inc. - Form 424B5

safety and efficacy to obtain the requisite regulatory approvals or will result in marketable products.

Unfavorable data from those studies could result in our failure to obtain regulatory and marketing approval for our product candidates, the withdrawal of such approval for approved products or an extension of the review period for developmental products. Preclinical testing and clinical development are inherently lengthy, complex, expensive and uncertain processes and have a high risk of failure. It typically takes many years to complete

S-8

Table of Contents

testing, and failure can occur at any stage of testing. Results attained in preclinical testing and early clinical studies, or trials, may not be indicative of results that are obtained in later studies. In addition, we have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approval and, accordingly, may encounter unforeseen problems and delays in the approval process. Furthermore, errors in the conduct, monitoring and/or auditing of a clinical trial, whether made by us or by a contract research organization (a "CRO") that we retain, could invalidate the results from a regulatory perspective.

None of our current product candidates has to date received regulatory approval for their intended commercial sale. We cannot market a pharmaceutical product in any jurisdiction until it has completed rigorous preclinical testing and clinical trials and passed such jurisdiction's extensive regulatory approval process. In general, significant research and development ("R&D") and clinical studies are required to demonstrate the safety and efficacy of our product candidates before we can submit regulatory applications. Even if a product candidate is approved by the applicable regulatory authority, we may not obtain approval for an indication whose market is large enough to recover our investment in that product candidate. In addition, there can be no assurance that we will ever obtain all or any required regulatory approvals for any of our product candidates.

We are currently developing our product candidates based on R&D activities, preclinical testing and clinical trials conducted to date, and we may not be successful in developing or introducing to the market these or any other new products or technology. If we fail to develop and deploy new products successfully and on a timely basis, we may become non-competitive and unable to recover the R&D and other expenses we incur to develop and test new products.

Interim results of preclinical or clinical studies do not necessarily predict their final results, and acceptable results in early studies might not be obtained in later studies. Safety signals detected during clinical studies and preclinical animal studies may require us to perform additional studies, which could delay the development of the drug or lead to a decision to discontinue development of the drug. Product candidates in the later stages of clinical development may fail to show the desired safety and efficacy traits despite positive results in initial clinical testing. Results from earlier studies may not be indicative of results from future clinical trials and the risk remains that a pivotal program may generate efficacy data that will be insufficient for the approval of the drug, or may raise safety concerns that may prevent approval of the drug. Interpretation of the prior preclinical and clinical safety and efficacy data of our product candidates may be flawed and there can be no assurance that safety and/or efficacy concerns from the prior data were not overlooked or misinterpreted, which in subsequent, larger studies appear and prevent approval of such product candidates.

Furthermore, we may suffer significant setbacks in advanced clinical trials, even after promising results in earlier studies. Based on results at any stage of clinical trials, we may decide to repeat or redesign a trial or discontinue development of one or more of our product candidates. Further, actual results may vary once the final and quality-controlled verification of data and analyses has been completed. If we fail to adequately demonstrate the safety and efficacy of our products under development, we will not be able to obtain the required regulatory approvals to commercialize our product candidates.

By way of example, on February 13, 2017, we announced that, after reviewing the raw top-line data on which the confirmatory Phase 3 clinical trial of Macrilen were based, we had concluded that Macrilen had, despite not having attained one of its co-primary endpoints in the Phase 3 study, demonstrated performance supportive of achieving FDA registration and that we intended to pursue registration of Macrilen with the FDA and, to that end, the Company will meet with the FDA at the end of March 2017 to confirm this position. There can be no assurance, however, that the FDA will agree, in whole or in part, with our conclusions regarding Macrilen, particularly in light of the infrequency with which the FDA has in the past agreed to reassess portions of clinical trial data and elements of the design of a clinical trial following the conclusion of such trial.

A failure in the development of any one of our programs or product candidates could have a negative impact on the development of the others. Setbacks in any phase of the clinical development of our product candidates would have an adverse financial impact (including with respect to any agreements and partnerships that may exist between us and other entities), could jeopardize regulatory approval and would likely cause a drop in the price of our Common Shares.

Table of Contents

If we are unable to successfully complete our clinical trial programs, or if such clinical trials take longer to complete than we project, our ability to execute our current business strategy will be adversely affected.

Whether or not and how quickly we complete our clinical trial of Zoptrex[®], which is the only clinical trial that we are conducting, is dependent in part upon the rate at which we are able to collect, clean, lock and analyze the clinical trial database. The ZoptEC (zoptarelin doxorubicin in endometrial cancer) trial was designed to continue until a pre-determined number of events occur to the patients enrolled. On January 30, 2017, we announced the occurrence of the requisite pre-determined number of events in the ZoptEC trial, representing the clinical endpoint of the study. We expect to lock the clinical database and to report top-line results in April 2017.

We have no plans to conduct another Phase 3 clinical trial but we may decide to do so in the future. If we experience delays in identifying and contracting with sites and/or in patient enrollment in our future clinical trial programs, we may incur additional costs and delays in our development programs, and may not be able to complete our clinical trials on a cost-effective or timely basis. In addition, conducting multi-national studies adds another level of complexity and risk as we are subject to events affecting countries other than the U.S. and Canada. Moreover, negative or inconclusive results from the clinical trials we conduct or adverse medical events could cause us to have to repeat or terminate the clinical trials. Accordingly, we may not be able to complete the clinical trials within an acceptable time-frame, if at all. If we or our CRO have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay or terminate ongoing clinical trials.

Clinical trials are subject to continuing oversight by governmental regulatory authorities and institutional review boards and must meet requirements of such authorities for informed consent and for good clinical practices. We may not be able to comply with these requirements in respect of one or more of our product candidates.

Additionally, we have limited experience in filing an NDA or similar application for approval in the U.S. or in any other country for our current product candidates, which may result in a delay in, or the rejection of, our filing of an NDA or similar application. During the drug development process, regulatory agencies will typically ask questions of drug sponsors. While we endeavor to answer all such questions in a timely fashion, some questions may not be answered in time to prevent the delay of acceptance of an NDA or the rejection of an NDA.

We have incurred, and expect to continue to incur, substantial expenses, and we have made, and expect to continue to make, substantial financial commitments to establish a commercial operation. There can be no assurance how quickly, if ever, we will realize a profit from our commercial operation.

Our business strategy is to become a specialty biopharmaceutical company with commercial operations to market and sell products that we may develop internally, acquire or in-license. To that end, our commercial operations consist of 13 full-time staff, who provide services pursuant to our agreement with a contract sales organization, and our sales-management staff. We have to date incurred, and expect to continue to incur, substantial expenses, and we have made, and expect to continue to make, substantial financial commitments to maintain our commercial operations. Establishing a commercial operation is expensive and time-consuming, and there can be no assurance how quickly, if ever, we will realize a profit from our commercial operations. Factors that may inhibit our efforts to realize a profit from our commercial operations include:

our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel and representatives;

the inability of our sales personnel to obtain access to or to persuade adequate numbers of physicians to prescribe our products or the products that we in-license or co-promote;

the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and

unforeseen costs and expenses associated with creating an independent sales and marketing organization.

Table of Contents

Implementation of our business strategy depends, in part, on our ability to acquire, in-license or otherwise obtain the right to sell other products. If we are unable to do so, our business, financial condition and results of operations may be materially adversely affected.

In connection with our strategy to further transform the Company into a commercially operating specialty biopharmaceutical organization, we may enter into commercial arrangements with third parties, including but not limited to promotion, co-promotion, acquisition or in-licensing agreements, in efforts to establish and expand our commercial revenue base. These business activities entail numerous operational and financial risks, including:

the difficulty of securing or the inability to secure financing to acquire or in-license products;

the incurrence of substantial debt or dilutive issuances of securities to pay for the acquisition or in-licensing of new products;

the disruption of our business and diversion of our management's time and attention;

higher than expected development, acquisition or in-license and integration costs;

exposure to unknown liabilities; and

the difficulty in locating products that are in our targeted therapeutic areas and that are compatible with other products in our portfolio.

We can provide no assurance that we will be able to identify potential product candidates or strategic commercial partners or, if we identify such product candidates or partners, that any related commercial arrangements will be consummated on terms that are favorable to us. To the extent that we are successful in entering into any strategic commercial arrangements, including promotional, co-promotional or marketing agreements, or acquisition or in-licensing agreements with third parties, we cannot provide any assurance that any resulting initiatives or activities will be successful. To the extent that any related investments in such arrangements do not yield the expected benefits, our business, financial condition and results of operations may be materially adversely affected.

We have limited resources to identify and execute the procurement of additional products and to integrate them into our current commercial operations. The failure to successfully integrate the personnel and operations of businesses that we may acquire or of products that we may in-license in the future with our existing operations, business and products could have a material adverse effect on our operations and results. We compete with larger pharmaceutical companies and other competitors in our efforts to acquire, in-license, and/or obtain the right to market and/or detail new products. Our competitors likely will have access to greater financial resources than us and may have greater expertise in identifying and evaluating new opportunities. Moreover, we may devote resources to potential acquisition, in-licensing, promotion or co-promotion opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts.

We will require significant additional financing, and we may not have access to sufficient capital.

We will require significant additional capital to fund our commercial operations and may require additional capital to pursue planned clinical trials and regulatory approvals, as well as further R&D and marketing efforts for our product candidates and potential products. We do not anticipate generating significant revenues from operations in the near future, and we currently have no committed sources of capital.

We may attempt to raise additional funds through public or private financings, collaborations with other pharmaceutical companies or from other sources, including, without limitation, through at-the-market offerings and issuances of Common Shares. Additional funding may not be available on terms that are acceptable to us. If adequate funding is not available to us on reasonable terms, we may need to delay, reduce or eliminate one or more of our product development programs or obtain funds on terms less favorable than we would otherwise accept. To the extent that additional capital is raised through the sale of equity securities or securities convertible into or exchangeable or exercisable for equity securities (collectively, "Convertible Securities"), the issuance of those securities would result in dilution to our shareholders. Moreover, the incurrence of debt financing or the issuance of dividend-paying preferred shares, could result in a substantial portion of our future operating cash flow, if any, being dedicated to the payment of principal and interest on such indebtedness or the payment of

Edgar Filing: Aeterna Zentaris Inc. - Form 424B5

Table of Contents

dividends on such preferred shares and could impose restrictions on our operations and on our ability to make certain expenditures and/or to incur additional indebtedness, which could render us more vulnerable to competitive pressures and economic downturns.

Our future capital requirements are substantial and may increase beyond our current expectations depending on many factors, including:

the results of our recently completed clinical trials;

unexpected delays or developments in seeking regulatory approvals;

the time and cost involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;

unexpected developments encountered in implementing our business development and commercialization strategies;

the potential addition of commercialized products to our portfolio;

lower revenues from sales commission than expected;

the outcome of litigation, including the securities class-action litigation pending against us that is described elsewhere in this prospectus supplement; and

further arrangements, if any, with collaborators.

In addition, global economic and market conditions as well as future developments in the credit and capital markets may make it even more difficult for us to raise additional financing in the future.

We are and will be subject to stringent ongoing government regulation for our products and our product candidates, even if we obtain regulatory approvals for the latter.

The manufacture, marketing and sale of our products and product candidates are and will be subject to strict and ongoing regulation, even if regulatory authorities approve any of the latter. Compliance with such regulation will be expensive and consume substantial financial and management resources. For example, an approval for a product may be conditioned on our agreement to conduct costly post-marketing follow-up studies to monitor the safety or efficacy of the product. In addition, as clinical experience with a drug expands after approval because the drug is used by a greater number and more diverse group of patients than during clinical trials, side effects or other problems may be observed after approval that were not observed or anticipated during pre-approval clinical trials. In such a case, a regulatory authority could restrict the indications for which the product may be sold or revoke the product's regulatory approval.

We and our contract manufacturers will be required to comply with applicable current Good Manufacturing Practice regulations for the manufacture of our products. These regulations include requirements relating to quality assurance, as well as the corresponding maintenance of rigorous records and documentation. Manufacturing facilities must be approved before we can use them in the commercial manufacturing of our products and are subject to subsequent periodic inspection by regulatory authorities. In addition, material changes in the methods of manufacturing or changes in the suppliers of raw materials are subject to further regulatory review and approval.

If we, or if any future marketing collaborators or contract manufacturers, fail to comply with applicable regulatory requirements, we may be subject to sanctions including fines, product recalls or seizures and related publicity requirements, injunctions, total or partial suspension of production, civil penalties, suspension or withdrawals of previously granted regulatory approvals, warning or untitled letters, refusal to approve pending applications for marketing approval of new products or of supplements to approved applications, import or export bans or restrictions, and criminal prosecution and penalties. Any of these penalties could delay or prevent the promotion, marketing or sale of our products and product candidates.

Even if we receive marketing approval for our product candidates, such product approvals could be subject to restrictions or withdrawals. Regulatory requirements are subject to change.

Regulatory authorities generally approve products for particular indications. If an approval is for a limited indication, this limitation reduces the size of the potential market for that product. Product approvals, once

S-12

Table of Contents

granted, are subject to continual review and periodic inspections by regulatory authorities. Our operations and practices are subject to regulation and scrutiny by the U.S. government, as well as governments of any other countries in which we do business or conduct activities. Later discovery of previously unknown problems or safety issues and/or failure to comply with domestic or foreign laws, knowingly or unknowingly, can result in various adverse consequences, including, among other things, a possible delay in the approval or refusal to approve a product, warning letters, fines, injunctions, civil penalties, recalls or seizures of products, total or partial suspension of production, refusal of the government to renew marketing applications, complete withdrawal of a marketing application, criminal prosecution, withdrawal of an approved product from the market and/or exclusion from government healthcare programs. Such regulatory enforcement could have a direct and negative impact on the product for which approval is granted, but also could have a negative impact on the approval of any pending applications for marketing approval of new drugs or supplements to approved applications.

Because we operate in a highly regulated industry, regulatory authorities could take enforcement action against us in connection with our, or our licensees' or collaborators', business and marketing activities for various reasons.

From time to time, new legislation is passed into law that could significantly change the statutory provisions governing the approval, manufacturing, and marketing of products regulated by the FDA and other health authorities. Additionally, regulations and guidance are often revised or reinterpreted by health agencies in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted, or whether regulations, guidance, or interpretations will change, and what the impact of such changes, if any, may be.

Healthcare reform measures could hinder or prevent the commercial success of our product candidates and adversely affect our business.

The business prospects and financial condition of pharmaceutical and biotechnology companies are affected by the efforts of governmental and third-party payers to contain or reduce the costs of healthcare. The U.S. government and other governments have shown significant interest in pursuing healthcare reform and reducing healthcare costs. Any government-adopted reform measures could cause significant pressure on the pricing of healthcare products and services, including our product candidates, both in the U.S. and internationally, as well as the amount of reimbursement available from governmental agencies and other third-party payers. If reimbursement for our product candidates is substantially less than we expect, our revenue prospects could be materially and adversely impacted.

In the U.S. and in other jurisdictions there have been, and we expect that there will continue to be, a number of legislative and regulatory proposals aimed at changing the healthcare system, such as proposals relating to the pricing of healthcare products and services in the U.S. or internationally, the re-importation of drugs into the U.S. from other countries (where they are then sold at a lower price), and the amount of reimbursement available from governmental agencies or other third party payers. Furthermore, the pricing of pharmaceutical products, in general, and specialty drugs, in particular, has been a topic of concern in the U.S. Congress, where hearings on the topic have been held, and has been a topic of speeches given by political figures, including President Trump. There can be no assurance as to how this scrutiny on pricing of pharmaceutical products will impact future pricing of our products or orphan drugs, or pharmaceutical products generally.

The *Patient Protection and Affordable Care Act* and the *Healthcare and Education Affordability Reconciliation Act of 2010* (collectively, the "ACA") has had far-reaching consequences for most healthcare companies, including specialty biopharmaceutical companies like us. The future of the ACA is, however, uncertain. In January 2017, the U.S. Congress voted to adopt a budget resolution for fiscal year 2017, that while not law, is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the ACA. Further, on January 20, 2017, President Trump signed an executive order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On March 6, 2017, members of the U.S. House of Representatives released

Table of Contents

proposed legislation, the American Healthcare Act ("AHCA"), that was intended to replace the ACA. On March 24, 2017, U.S. House of Representatives Speaker Paul Ryan announced that he, with agreement from President Donald Trump, was withdrawing the AHCA. We cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

In addition, the *Food and Drug Administration Amendments Act of 2007* gives the FDA enhanced post-market authority, including the authority to require post-marketing studies and clinical trials, labeling changes based on new safety information, and compliance with risk evaluations and mitigation strategies approved by the FDA. The FDA's exercise of this authority may result in delays or increased costs during the period of product development, clinical trials and regulatory review and approval, which may also increase costs related to complying with new post-approval regulatory requirements, and increase potential FDA restrictions on the sale or distribution of approved products.

If we market products in a manner that violates healthcare fraud and abuse laws, we may be subject to civil or criminal penalties, including exclusion from participation in government healthcare programs.

As a pharmaceutical company, even though we do not provide healthcare services or receive payments directly from or bill directly to Medicare, Medicaid or other third-party payers for our products, certain federal and state healthcare laws and regulations pertaining to fraud and abuse are and will be applicable to our business. We are subject to healthcare fraud and abuse regulation by both the federal government and the states in which we conduct our business.

The laws that may affect our ability to operate include the federal healthcare program anti-kickback statute, which prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce, or in return for, the purchase, lease, order, or arrangement for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute applies to arrangements between pharmaceutical manufacturers and prescribers, purchasers and formulary managers. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny, if they do not qualify for an exception or safe harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to get a false claim paid. Pharmaceutical companies have been prosecuted under these laws for a variety of alleged promotional and marketing activities, such as providing free product to customers with the expectation that the customers would bill federal programs for the product; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in off-label promotion that caused claims to be submitted to Medicaid for non-covered off-label uses; and submitting inflated best price information to the Medicaid Drug Rebate Program.

The *Health Insurance Portability and Accountability Act of 1996* also created prohibitions against healthcare fraud and false statements relating to healthcare matters. The healthcare fraud statute prohibits knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private payers. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians. The *Physician Payments Sunshine Act* imposed new requirements on manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the Centers for Medicare and Medicaid Services ("CMS") information related to payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and applicable manufacturers and group purchasing organizations to report annually to CMS ownership and investment interests held by physicians (as defined above) and their immediate family members and payments or

Edgar Filing: Aeterna Zentaris Inc. - Form 424B5

Table of Contents

other "transfers of value" to such physician owners and their immediate family members. Manufacturers are required to report such data to the government by the 90th calendar day of each year.

The majority of states also have statutes or regulations similar to these federal laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. In addition, some states have laws that require pharmaceutical companies to adopt comprehensive compliance programs. For example, under California law, pharmaceutical companies must comply with both the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and the PhRMA Code on Interactions with Healthcare Professionals, as amended. Certain states also mandate the tracking and reporting of gifts, compensation, and other remuneration paid by us to physicians and other healthcare providers.

Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state laws may prove costly.

Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of such laws. The ACA also made several important changes to the federal Anti-Kickback Statute, false claims laws, and healthcare fraud statute by weakening the intent requirement under the anti-kickback and healthcare fraud statutes that may make it easier for the government or whistleblowers to charge such fraud and abuse violations. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. In addition, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the false claims statutes. The ACA increases penalties for fraud and abuse violations. If our past, present or future operations are found to be in violation of any of the laws described above or other similar governmental regulations to which we are subject, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and negatively impact our financial results.

If our products do not gain market acceptance, we may be unable to generate significant revenues.

Even if our products are approved for commercialization, they may not be successful in the marketplace. Market acceptance of any of our products will depend on a number of factors, including, but not limited to:

demonstration of clinical efficacy and safety;

the prevalence and severity of any adverse side effects;

limitations or warnings contained in the product's approved labeling;

availability of alternative treatments for the indications we target;

the advantages and disadvantages of our products relative to current or alternative treatments;

the availability of acceptable pricing and adequate third-party reimbursement; and

the effectiveness of marketing and distribution methods for the products.

If our products do not gain market acceptance among physicians, patients, healthcare payers and others in the medical community, who may not accept or utilize our products, our ability to generate significant revenues from our products would be limited, and our financial condition could be materially adversely affected. In addition, if we fail to further penetrate our core markets and existing geographic markets or to successfully expand our business into new markets, the growth in sales of our products, along with our operating results, could be negatively

impacted.

Our ability to further penetrate our core markets and existing geographic markets in which we compete or to successfully expand our business into additional countries in Europe, Asia or elsewhere is subject to

S-15

Table of Contents

numerous factors, many of which are beyond our control. Our products, if successfully developed, may compete with a number of drugs, therapies, products and tests currently manufactured and marketed by major pharmaceutical and other biotechnology companies. Our products may also compete with new products currently under development by others or with products which may be less expensive than our products. There can be no assurance that our efforts to increase market penetration in our core markets and existing geographic markets will be successful. Our failure to do so could have an adverse effect on our operating results and would likely cause a drop in the price of our Common Shares.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications for which there may be a greater likelihood of success.

Because we have limited financial and managerial resources, we are currently focusing our efforts on our lead, clinical-stage development compounds, Zoptrex (zoptarelin doxorubicin) and Macrilen (macimorelin), and we are doing so for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications for which there may be a greater likelihood of success or may prove to have greater commercial potential. Notwithstanding our investment to date and anticipated future expenditures on Zoptrex, Macrilen and any earlier-stage programs, we have not yet developed, and may never successfully develop, any marketed treatments using these products. Research programs to identify new product candidates or pursue alternative indications for current product candidates require substantial technical, financial and human resources. These activities may initially show promise in identifying potential product candidates or indications, yet fail to yield product candidates or indications for further clinical development.

We may not achieve our projected development goals in the time-frames we announce and expect.

We set goals and make public statements regarding the timing of the accomplishment of objectives material to our success, such as the commencement, enrollment and anticipated completion of clinical trials, anticipated regulatory submission and approval dates and time of product launch. The actual timing of these events can vary dramatically due to factors such as delays or failures in our clinical trials, the uncertainties inherent in the regulatory approval process and delays in achieving manufacturing or marketing arrangements sufficient to commercialize our products. There can be no assurance that we will make regulatory submissions based on our recently completed clinical trials or receive regulatory approvals as planned or that we will be able to adhere to our current schedule for the launch of any of our products. If we fail to achieve one or more of these milestones as planned, the price of our Common Shares would likely decline.

If we fail to obtain acceptable prices or adequate reimbursement for our products, our ability to generate revenues will be diminished.

Our ability to successfully commercialize our products will depend significantly on our ability to obtain acceptable prices and the availability of reimbursement to the patient from third-party payers, such as governmental and private insurance plans. These third-party payers frequently require companies to provide predetermined discounts from list prices, and they are increasingly challenging the prices charged for pharmaceuticals and other medical products. For example, drug manufacturers are required to have a national rebate agreement with the U.S. Department of Health and Human Services in order to obtain state Medicaid coverage, which requires manufacturers to pay a rebate on drugs dispensed to Medicaid patients. Our products may not be considered cost-effective, and reimbursement to the patient may not be available or sufficient to allow us to sell our products on a competitive basis. It may not be possible to negotiate favorable reimbursement rates for our products. Adverse pricing and reimbursement conditions would also likely diminish our ability to induce third parties to co-promote our products.

In addition, the continuing efforts of third-party payers to contain or reduce the costs of healthcare through various means may limit our commercial opportunity and reduce any associated revenue and profits. We expect proposals to implement similar government controls to continue. The pricing of pharmaceutical products, in general, and specialty drugs, in particular, has been a topic of concern in the U.S. Congress, where hearings on the topic have been held, and has been a topic of speeches given by political figures, including President Trump. Specifically, there have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer

Table of Contents

patient programs, and reform government program reimbursement methodologies for drugs. Additionally, on the state level, many U.S. states are proposing and passing laws that seek to control drug pricing through increased transparency and other means that may impact future revenues and profits for drug makers. Further, third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical drug products and medical services, in addition to questioning their safety and efficacy. There can be no assurance as to how this scrutiny on pricing of pharmaceutical products will impact future pricing of our products or orphan drugs or pharmaceutical products generally. In addition, increasing emphasis on managed care will continue to put pressure on the pricing of pharmaceutical and biopharmaceutical products. Cost control initiatives could decrease the price that we or any current or potential collaborators could receive for any of our products and could adversely affect our profitability. In addition, in the U.S., in Canada and in many other countries, pricing and/or profitability of some or all prescription pharmaceuticals and biopharmaceuticals are subject to government control. If we fail to obtain acceptable prices or adequate levels of reimbursement for our products, the sales of our products would be adversely affected or there may be no commercially viable market for our products.

Competition in our targeted markets is intense, and development by other companies could render our products or technologies non-competitive.

The biopharmaceutical field is highly competitive. New products developed by other companies in the industry could render our products or technologies non-competitive. Competitors are developing and testing products and technologies that would compete with the products that we are developing. Some of these products may be more effective or have an entirely different approach or means of accomplishing the desired effect than our products. We expect competition from pharmaceutical and biopharmaceutical companies and academic research institutions to continue to increase over time. Many of our competitors and potential competitors have substantially greater product development capabilities and financial, scientific, marketing and human resources than we do. Our competitors may succeed in developing products earlier and in obtaining regulatory approvals and patent protection for such products more rapidly than we can or at a lower price.

We may not obtain adequate protection for our products through our intellectual property.

We rely heavily on our proprietary information in developing and manufacturing our product candidates. Our success depends, in large part, on our ability to protect our competitive position through patents, trade secrets, trademarks and other intellectual property rights. The patent positions of pharmaceutical and biopharmaceutical firms, including us, are uncertain and involve complex questions of law and fact for which important legal issues remain unresolved. We have filed and are pursuing applications for patents and trademarks in many countries. Pending patent applications may not result in the issuance of patents and we may not be able to obtain additional issued patents relating to our technology or products.

The laws of some countries do not protect intellectual property rights to the same extent as the laws of the U.S. and Canada. Many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. Many countries, including certain countries in Europe, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of the patent. Compulsory licensing of life-saving drugs is also becoming increasingly popular in developing countries either through direct legislation or international initiatives. Such compulsory licenses could be extended to include some of our product candidates, which could limit our potential revenue opportunities. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the aggressive enforcement of patent and other intellectual property protection, which makes it difficult to stop infringement.

Our patents and/or the patents that we license from others may be challenged, narrowed, invalidated, held to be unenforceable or circumvented, which could limit our ability to stop competitors from marketing similar products or limit the length of term of patent protection we may have for our products. Changes in either patent laws or in interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection. The patents issued or to be issued to us may not provide us with any competitive advantage or protect us against competitors with similar technology. In

Table of Contents

addition, it is possible that third parties with products that are very similar to ours will circumvent our patents by means of alternate designs or processes. We may have to rely on method-of-use, methods of manufacture and/or new-formulation protection for our compounds in development, and any resulting products, which may not confer the same protection as claims to compounds *per se*.

In addition, our patents may be challenged by third parties in patent litigation, which is becoming widespread in the biopharmaceutical industry. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There may also be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that our patents would, if challenged, be held by a court to be valid or enforceable or that a competitor's technology or product would be found by a court to infringe our patents. Our granted patents could also be challenged and revoked in U.S. post-grant proceedings as well as in opposition or nullity proceedings in certain countries outside the U.S. In addition, we may be required to disclaim part of the term of certain patents.

Patent applications relating to or affecting our business have been filed by a number of pharmaceutical and biopharmaceutical companies and academic institutions. A number of the technologies in these applications or patents may conflict with our technologies, patents or patent applications, and any such conflict could reduce the scope of patent protection that we could otherwise obtain. Because patent applications in the U.S. and many other jurisdictions are typically not published until eighteen months after their first effective filing date, or in some cases not at all, and because publications of discoveries in the scientific literature often lag behind actual discoveries, we cannot be certain that we were the first to make the inventions claimed in issued patents or pending patent applications, or that we were the first to file for protection of the inventions set forth in the patent applications. If a third party has also filed a patent application in the U.S. covering our product candidates or a similar invention, we may have to participate in adversarial proceedings, such as interferences and deviation proceedings, before the United States Patent and Trademark Office to determine which party is entitled to a U.S. patent claiming the disputed invention. The costs of these proceedings could be substantial and it is possible that our efforts could be unsuccessful, resulting in a loss of our U.S. patent position.

We also rely on trade secrets and proprietary know-how to protect our intellectual property. If we are unable to protect the confidentiality of our proprietary information and know-how, the value of our technology and products could be adversely affected. We seek to protect our unpatented proprietary information in part by requiring our employees, consultants, outside scientific collaborators and sponsored researchers and other advisors to enter into confidentiality agreements. These agreements provide that all confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of our employees, the agreements provide that all of the technology that is conceived by the individual during the course of employment is our exclusive property.

These agreements may not provide meaningful protection or adequate remedies in the event of unauthorized use or disclosure of our proprietary information. In addition, it is possible that third parties could independently develop proprietary information and techniques substantially similar to ours or otherwise gain access to our trade secrets. If we are unable to protect the confidentiality of our proprietary information and know-how, competitors may be able to use this information to develop products that compete with our products and technologies, which could adversely impact our business.

We currently have the right to use certain patents and technologies under license agreements with third parties. Our failure to comply with the requirements of one or more of our license agreements could result in the termination of such agreements, which could cause us to terminate the related development program and cause a complete loss of our investment in that program. Inventions claimed in certain in-licensed patents may have been made with funding from the U.S. government and may be subject to the rights of the U.S. government and we may be subject to additional requirements in the event we seek to commercialize or manufacture product candidates incorporating such in-licensed technology.

As a result of the foregoing factors, we may not be able to rely on our intellectual property to protect our products in the marketplace.

Table of Contents

Some of our patents have recently expired.

The product development timelines for our products are lengthy and it is possible that our issued patents covering our product candidates in the U.S. and other jurisdictions may expire prior to commercial launch of the products. The patent that covers Zoptrex and other related targeted cytotoxic anthracycline analogues, pharmaceutical compositions comprising the compounds and their medical use for the treatment of cancer expired in the U.S. in November 2015 and expired in the European Union, Japan, China and Hong Kong in November 2016. We did not apply for patent term extensions for the U.S. patent. As a result, our ability to protect this compound from competition will be based on the protections provided in the U.S. for new chemical entities and similar protections, if any, provided in other countries. We cannot assure you that Zoptrex or any of our other drug candidates will obtain new chemical entity exclusivity or any other market exclusivity in the U.S., the European Union or any other territory, or that we will be the first to receive the respective regulatory approval for such drugs so as to be eligible for any market exclusivity protection.

We may infringe the intellectual property rights of others.

Our commercial success depends significantly on our ability to operate without infringing the patents and other intellectual property rights of third parties. There could be issued patents of which we are not aware that our products or methods may be found to infringe, or patents of which we are aware and believe we do not infringe but which we may ultimately be found to infringe. Moreover, patent applications and their underlying discoveries are in some cases maintained in secrecy until patents are issued. Because patents can take many years to issue, there may be currently pending applications of which we are unaware that may later result in issued patents that our products or technologies are found to infringe. Moreover, there may be published pending applications that do not currently include a claim covering our products or technologies but which nonetheless provide support for a later drafted claim that, if issued, our products or technologies could be found to infringe.

If we infringe or are alleged to infringe intellectual property rights of third parties, it will adversely affect our business. Our research, development and commercialization activities, as well as any product candidates or products resulting from these activities, may infringe or be accused of infringing one or more claims of an issued patent or may fall within the scope of one or more claims in a published patent application that may subsequently be issued and to which we do not hold a license or other rights. Third parties may own or control these patents or patent applications in the U.S. and abroad. These third parties could bring claims against us or our collaborators that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages. Further, if a patent infringement suit were brought against us or our collaborators, we or they could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit.

The biopharmaceutical industry has produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of products. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. In the event of infringement or violation of another party's patent or other intellectual property rights, we may not be able to enter into licensing arrangements or make other arrangements at a reasonable cost. Any inability to secure licenses or alternative technology could result in delays in the introduction of our products or lead to prohibition of the manufacture or sale of products by us or our partners and collaborators.

Patent litigation is costly and time consuming and may subject us to liabilities.

If we become involved in any patent litigation, interference, opposition or other administrative proceedings we will likely incur substantial expenses in connection therewith, and the efforts of our technical and management personnel will be significantly diverted. In addition, an adverse determination in litigation could subject us to significant liabilities.

We may not obtain trademark registrations for our product candidates.

We have filed applications for trademark registrations in connection with Zoptrex and Macrilen in various jurisdictions, including the U.S. We may file applications for other possible trademarks for our product

Table of Contents

candidates in the future. No assurance can be given that any of our trademarks will be registered in the U.S. or elsewhere, or that the use of any registered or unregistered trademarks will confer a competitive advantage in the marketplace. Furthermore, even if we are successful in our trademark registrations, the FDA and regulatory authorities in other countries have their own process for drug nomenclature and their own views concerning appropriate proprietary names. The FDA and other regulatory authorities also have the power, even after granting market approval, to request a company to reconsider the name for a product because of evidence of confusion in the marketplace. No assurance can be given that the FDA or any other regulatory authority will approve any of our trademarks or will not request reconsideration of one of our trademarks at some time in the future. On December 16, 2016, we learned that the EMA had rejected the "Macrilen " as the proposed invented name for macimorelin. We intend to appeal the EMA's determination. The loss, abandonment, or cancellation of any of our trademarks or trademark applications could negatively affect the success of the product candidates to which they relate.

We are currently dependent on certain strategic relationships with third parties and we may enter into future collaborations for the development of our product candidates.

We are currently dependent on certain strategic relationships with third parties and may enter into future collaborations for the development of our product candidates. Our arrangements with these third parties may not provide us with the benefits we expect and may expose us to a number of risks.

We are dependent on, and rely upon, third parties to perform various functions related to our business, including, but not limited to, development of some of our product candidates. Our reliance on these relationships poses a number of risks.

We may not realize the contemplated benefits of such agreements nor can we be certain that any of these parties will fulfill their obligations in a manner which maximizes our revenue. These arrangements may also require us to transfer certain material rights or to issue our equity, voting or other securities to third parties. Any license or sublicense of our commercial rights may reduce our product revenue.

These agreements create certain additional risks. The occurrence of any of the following or other events may delay product development or impair commercialization of our products:

not all of the third parties are contractually prohibited from developing or commercializing, either alone or with others, products and services that are similar to or competitive with our product candidates and, with respect to our contracts that do contain such contractual prohibitions or restrictions, prohibitions or restrictions do not always apply to the affiliates of the third parties and they may elect to pursue the development of any additional product candidates and pursue technologies or products either on their own or in collaboration with other parties, including our competitors, whose technologies or products may be competitive with ours;

the third parties may under-fund or fail to commit sufficient resources to marketing, distribution or other development of our products;

the third parties may cease to conduct business for financial or other reasons;

we may not be able to renew such agreements;

the third parties may not properly maintain or defend certain intellectual property rights that may be important to the commercialization of our products;

the third parties may encounter conflicts of interest, changes in business strategy or other issues which could adversely affect their willingness or ability to fulfill their obligations to us (for example, pharmaceutical companies historically have re-evaluated their priorities following mergers and consolidations, which have been common in recent years in this industry);

Edgar Filing: Aeterna Zentaris Inc. - Form 424B5

delays in, or failures to achieve, scale-up to commercial quantities, or changes to current raw material suppliers or product manufacturers (whether the change is attributable to us or the supplier or manufacturer) could delay clinical studies, regulatory submissions and commercialization of our product candidates; and

S-20

Table of Contents

disputes may arise between us and the third parties that could result in the delay or termination of the development or commercialization of our product candidates, resulting in litigation or arbitration that could be time-consuming and expensive, or causing the third parties to act in their own self-interest and not in our interest or those of our shareholders or other stakeholders.

In addition, the third parties can terminate our agreements with them for a number of reasons based on the terms of the individual agreements that we have entered into with them. If one or more of these agreements were to be terminated, we would be required to devote additional resources to developing and commercializing our product candidates, seek a new third party with which to contract or abandon the product candidate, which would likely cause a drop in the price of our Common Shares.

We rely on third parties to conduct, supervise and monitor our clinical trials, and those third parties may not perform satisfactorily.

We rely on third parties such as CROs, medical institutions and clinical investigators to enroll qualified patients and conduct, supervise and monitor our clinical trials. Our reliance on these third parties for clinical development activities reduces our control over these activities. Our reliance on these third parties, however, does not relieve us of our regulatory responsibilities, including ensuring that our clinical trials are conducted in accordance with Good Clinical Practice guidelines and the investigational plan and protocols contained in an Investigational New Drug application, or a comparable foreign regulatory submission. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. In addition, they may not complete activities on schedule, or may not conduct our preclinical studies or clinical trials in accordance with regulatory requirements or our trial design. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, our efforts to obtain regulatory approvals for, and to commercialize, our product candidates may be delayed or prevented.

In carrying out our operations, we are dependent on a stable and consistent supply of ingredients and raw materials.

There can be no assurance that we, our contract manufacturers or our licensees, will be able, in the future, to continue to purchase products from our current suppliers or any other supplier on terms similar to current terms or at all. An interruption in the availability of certain raw materials or ingredients, or significant increases in the prices we pay for them, could have a material adverse effect on our business, financial condition, liquidity and operating results.

The failure to perform satisfactorily by third parties upon which we expect to rely to manufacture and supply products may lead to supply shortfalls.

We expect to rely on third parties to manufacture and supply marketed products. We also have or may have certain supply obligations vis-à-vis our existing and potential licensees, who are or will be responsible for the marketing of the products. To be successful, our products have to be manufactured in commercial quantities in compliance with quality controls and regulatory requirements. Even though it is our objective to minimize such risk by introducing alternative suppliers to ensure a constant supply at all times, there are a limited number of contract manufacturers or suppliers that are capable of manufacturing our product candidates or the materials used in their manufacture. If we are unable to do so ourselves or to arrange for third-party manufacturing or supply of these product candidates or materials, or to do so on commercially reasonable terms, we may not be able to complete development of these product candidates or to commercialize them ourselves or through our licensees. Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured products ourselves, including reliance on the third party for regulatory compliance, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control, and the possibility of termination or non-renewal of the agreement by the third party, based on its own business priorities, at a time that is costly or inconvenient for us.

Table of Contents

We are subject to intense competition for our skilled personnel, and the loss of key personnel or the inability to attract additional personnel could impair our ability to conduct our operations.

We are highly dependent on our management and our clinical, regulatory and scientific staff, the loss of whose services might adversely impact our ability to achieve our objectives. Recruiting and retaining qualified management and clinical, scientific and regulatory personnel is critical to our success. Reductions in our staffing levels have eliminated redundancies in key capabilities and skill sets among our full-time staff and required us to rely more heavily on outside consultants and third parties. We have been unable to increase the compensation of our associates to the extent required to remain fully competitive for their services, which increases our employee retention risk. The competition for qualified personnel in the biopharmaceutical field is intense, and if we are not able to continue to attract and retain qualified personnel and/or maintain positive relationships with our outside consultants, we may not be able to achieve our strategic and operational objectives.

We are currently subject to securities class-action litigation and we may be subject to similar or other litigation in the future.

We and certain of our current and former officers are defendants in a purported class-action lawsuit pending in the U.S. District Court for the District of New Jersey (the "Court"), brought on behalf of shareholders of the Company. The lawsuit alleges violations of the *Securities Exchange Act of 1934* (the "Exchange Act") in connection with allegedly false and misleading statements made by the defendants between April 2, 2012 and November 6, 2014, or the Class Period, regarding the safety and efficacy of Macrilen, a product we developed for use in the diagnosis of AGHD, and the prospects for the approval of the Company's NDA for the product by the FDA. The plaintiffs seek to represent a class comprised of purchasers of our Common Shares during the Class Period and seek damages, costs and expenses and such other relief as determined by the Court. On September 14, 2015, the Court dismissed the lawsuit stating that the plaintiffs failed to state a claim, but granted the plaintiffs leave to amend. On October 14, 2015, the plaintiffs filed a Second Amended Complaint against us. We subsequently filed a motion to dismiss because we believed that the Second Amended Complaint also failed to state a claim.

On March 2, 2016, the Court issued an order granting our motion to dismiss the complaint in part and denying it in part. The Court dismissed certain of our current and former officers from the lawsuit. The Court allowed the claim that we omitted material facts from our public statements during the Class Period to proceed against us and our former CEO who departed in 2013, while dismissing such claims against other current and former officers. The Court also allowed a claim for "controlling person" liability to proceed against certain current and former officers. On March 16, 2016, we filed a motion for reconsideration of the Court's March 2, 2016 order and on April 6, 2016 we filed an answer to the second amended complaint. On June 30, 2016, the Court issued an order denying our motion for reconsideration. As a result, the lawsuit will proceed to the class certification phase and the discovery process has commenced.

While we believe we have meritorious defenses and intend to continue to defend this lawsuit vigorously, we cannot predict the outcome. Furthermore, we may, from time to time, be a party to other litigation in the normal course of business. Monitoring and defending against legal actions, whether or not meritorious, is time-consuming for our management and detracts from our ability to fully focus our internal resources on our business activities. In addition, legal fees and costs incurred in connection with such activities may be significant and we could, in the future, be subject to judgments or enter into settlements of claims for significant monetary damages. A decision adverse to our interests could result in the payment of substantial damages and could have a material adverse effect on our cash flow, results of operations and financial position.

With respect to any litigation, our insurance may not reimburse us or may not be sufficient to reimburse us for the expenses or losses we may suffer in contesting and concluding such lawsuit. Substantial litigation costs, including the substantial self-insured retention that we were required to satisfy before any insurance applied to the claim, or an adverse result in any litigation may adversely impact our business, operating results or financial condition. We believe that our directors' and officers' liability insurance will cover our potential liability with respect to the securities class-action lawsuit described above; however, the insurer has reserved its rights to contest the applicability of the insurance to such claim and the limits of the insurance may be insufficient to cover our eventual liability.

Table of Contents

We are subject to the risk of product liability claims, for which we may not have or may not be able to obtain adequate insurance coverage.

The use of Zoptrex and Macrilen on human participants in our clinical trials subjects us to the risk of liability to such participants, who may suffer unintended consequences. If Zoptrex and/or Macrilen are approved for commercialization or if we acquire a marketed product from a third party, the sale and use of such products will involve the risk of product liability claims and associated adverse publicity. Product liability claims might be made against us directly by patients, healthcare providers or pharmaceutical companies or others selling, buying or using our products. We attempt to manage our liability risks by means of insurance. We maintain insurance covering our liability for our preclinical and clinical studies. However, we may not have or be able to obtain or maintain sufficient and affordable insurance coverage, including coverage for potentially very significant legal expenses, and without sufficient coverage any claim brought against us could have a materially adverse effect on our business, financial condition or results of operations. We do not currently maintain product liability insurance because we do not currently market, sell, distribute or handle any products. We may not be able to obtain product liability insurance on reasonable terms, if at all, when we begin to market, sell, distribute or handle products.

Our business involves the use of hazardous materials. We are required to comply with environmental and occupational safety laws regulating the use of such materials. If we violate these laws, we could be subject to significant fines, liabilities or other adverse consequences.

Our discovery and development processes involve the controlled use of hazardous materials. We are subject to federal, provincial and local laws and regulations governing the use, manufacture, storage, handling and disposal of such materials and certain waste products. The risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of an accident or a failure to comply with environmental or occupational safety laws, we could be held liable for any damages that result, and any such liability could exceed our resources. We may not be adequately insured against this type of liability. We may be required to incur significant costs to comply with environmental laws and regulations in the future, and our operations, business or assets may be materially adversely affected by current or future environmental laws or regulations.

We are a holding company, and claims of creditors of our subsidiaries will generally have priority as to the assets of such subsidiaries over our claims and those of our creditors and shareholders. In addition, we may be required to fund obligations of AEZS Germany under a Letter of Comfort provided by us to AEZS Germany.

Aeterna Zentaris Inc. is a holding company and a substantial portion of our non-cash assets is the share capital of our subsidiaries. AEZS Germany, our principal operating subsidiary, based in Frankfurt, Germany, holds most of our intellectual property rights, which represent the principal non-cash assets of our business. Because Aeterna Zentaris Inc. is a holding company, our obligations to our creditors are structurally subordinated to all existing and future liabilities of our subsidiaries, which may incur additional or other liabilities and/or obligations. Therefore, our rights and the rights of our creditors to participate in any distribution of the assets of any subsidiary in the event that such subsidiary were to be liquidated or reorganized or in the event of any bankruptcy or insolvency proceeding relating to or involving such subsidiary, and therefore the rights of the holders of our Common Shares to participate in those assets, are subject to the prior claims of such subsidiary's creditors. To the extent that we may be a creditor with recognized claims against any such subsidiary, our claims would still be subject to the prior claims of our subsidiary's creditors to the extent that they are secured or senior to those held by us.

Holders of our Common Shares are not creditors of our subsidiaries. Claims to the assets of our subsidiaries will derive from our own ownership interest in those operating subsidiaries. Claims of our subsidiaries' creditors will generally have priority as to the assets of such subsidiaries over our own ownership interest claims and will therefore have priority over the holders of our Common Shares. Our subsidiaries' creditors may from time to time include general creditors, trade creditors, employees, secured creditors, taxing authorities, and creditors holding guarantees. Accordingly, in the event of any foreclosure, dissolution, winding-up, liquidation or reorganization, or a bankruptcy, insolvency or creditor protection proceeding relating to us or our property, or any subsidiary, there can be no assurance as to the value, if any, that would be available to holders of our

Table of Contents

Common Shares. In addition, any distributions to us by our subsidiaries could be subject to monetary transfer restrictions in the jurisdictions in which our subsidiaries operate.

At the present time, AEZS Germany does not generate any revenue and, therefore, it depends on cash advances or contributions from Aeterna Zentaris Inc. to finance its operations. For the reasons described in the following paragraph, we issued a written undertaking, called a "Letter of Comfort" to AEZS Germany. The Letter of Comfort provides that we will furnish to AEZS Germany the necessary funds to ensure that it will always be able to fulfill all of its financial and economic obligations to its third party creditors. Our advances to AEZS Germany are characterized by the Letter of Comfort as loans that are subordinated to all present and future creditors of AEZS Germany.

We provided the Letter of Comfort to AEZS Germany because German law imposes an obligation on the managing director of AEZS Germany to institute insolvency proceedings if the managing director concludes that AEZS Germany is insolvent because it is either illiquid or "over-indebted". The purpose of the Letter of Comfort is to preclude the managing director from determining that AEZS Germany is illiquid or over-indebted. The Letter of Comfort will be sufficient for that purpose only as long as the managing director reasonably believes that we will be able to honor our obligations under the Letter of Comfort. If we fail to renew the Letter of Comfort or if the managing director concludes that we will be unable to honor our obligations under the Letter of Comfort, the managing director of AEZS Germany may determine that he or she is obligated to institute insolvency proceedings in Germany for AEZS Germany.

Because we are a holding company and because we have an obligation to advance funds to AEZS Germany to prevent it from becoming either illiquid or over-indebted, we may be required to use our cash, which may include a substantial portion of the proceeds of this offering, to fund payments by AEZS Germany to its creditors. Therefore, in the event of any winding-up, liquidation or reorganization, or a bankruptcy or insolvency proceeding relating to us or our property, there can be no assurance as to the value or assets, if any, that would be available to holders of our Common Shares because we may be required to advance cash to AEZS Germany under the Letter of Comfort.

It may be difficult for U.S. investors to obtain and enforce judgments against us because of our Canadian incorporation and German presence.

We are a company existing under the laws of Canada. A number of our directors and officers, and certain of the experts named herein, are residents of Canada or otherwise reside outside the U.S., and all or a substantial portion of their assets, and a substantial portion of our assets, are located outside the U.S. Consequently, although we have appointed an agent for service of process in the U.S., it may be difficult for investors in the U.S. to bring an action against such directors, officers or experts or to enforce against those persons or us a judgment obtained in a U.S. court predicated upon the civil liability provisions of federal securities laws or other laws of the U.S. Investors should not assume that foreign courts (1) would enforce judgments of U.S. courts obtained in actions against us or such directors, officers or experts predicated upon the civil liability provisions of the U.S. federal securities laws or the securities or "blue sky" laws of any state within the U.S. or (2) would enforce, in original actions, liabilities against us or such directors, officers or experts predicated upon the U.S. federal securities laws or any such state securities or "blue sky" laws. In addition, we have been advised by our Canadian counsel that in normal circumstances, only civil judgments and not other rights arising from U.S. securities legislation (for example, penal or similar awards made by a court in a regulatory prosecution or proceeding) are enforceable in Canada and that the protections afforded by Canadian securities laws may not be available to investors in the U.S.

We are subject to various internal control reporting requirements under applicable Canadian securities laws and the Sarbanes-Oxley Act in the U.S. We can provide no assurance that we will at all times in the future be able to report that our internal controls over financial reporting are effective.

As a public company, we are required to comply with Section 404 of the U.S. *Sarbanes-Oxley Act* ("Section 404") and National Instrument 52-109 *Certification of Disclosure in Issuers' Annual and Interim Filings*. In any given year, we cannot be certain as to the time of completion of our internal control evaluation, testing and remediation actions or of their impact on our operations. Upon completion of this process, we may

Table of Contents

identify control deficiencies of varying degrees of severity under applicable SEC and Public Company Accounting Oversight Board (U.S.) rules and regulations. As a public company, we are required to report, among other things, control deficiencies that constitute material weaknesses or changes in internal controls that, or that are reasonably likely to, materially affect internal controls over financial reporting. A "material weakness" is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual consolidated financial statements will not be prevented or detected on a timely basis. If we fail to comply with the requirements of Section 404 or similar Canadian requirements or if we report a material weakness, we might be subject to regulatory sanction and investors may lose confidence in our consolidated financial statements, which may be inaccurate if we fail to remedy such material weakness.

It is possible that we may be a passive foreign investment company, which could result in adverse tax consequences to U.S. investors.

Adverse U.S. federal income tax rules apply to "U.S. Holders" (as defined below in "Certain Material U.S. Federal Income Tax Considerations") who directly or indirectly hold common shares of a passive foreign investment company ("PFIC"). We will be classified as a PFIC for U.S. federal income tax purposes for a taxable year if (i) at least 75% of our gross income is "passive income" or (ii) at least 50% of the average value of our assets, including goodwill (based on annual quarterly average), is attributable to assets which produce passive income or are held for the production of passive income.

We believe that we were not a PFIC for the 2016 taxable year and we may not be a PFIC for the 2017 taxable year. However, the PFIC determination depends on the application of complex U.S. federal income tax rules concerning the classification of our assets and income for this purpose, and these rules are uncertain in some respects. In addition, the fair market value of our assets may be determined in large part by the market price of our Common Shares, which is likely to fluctuate, and the composition of our income and assets will be affected by how, and how quickly, we spend any cash that is raised in any financing transaction. No assurance can be provided that we will not be classified as a PFIC for the 2017 taxable year and for any future taxable year.

If we are a PFIC for any taxable year during which a U.S. Holder holds Common Shares, we generally would continue to be treated as a PFIC with respect to that U.S. Holder for all succeeding years during which the U.S. Holder holds such Common Shares, even if we ceased to meet the threshold requirements for PFIC status. PFIC characterization could result in adverse U.S. federal income tax consequences to U.S. Holders. In particular, absent certain elections, a U.S. Holder would generally be subject to U.S. federal income tax at ordinary income tax rates, plus a possible interest charge, in respect of a gain derived from a disposition of our Common Shares, as well as certain distributions by us. If we are treated as a PFIC for any taxable year, a U.S. Holder may be able to make an election to "mark to market" Common Shares each taxable year and recognize ordinary income pursuant to such election based upon increases in the value of the Common Shares. In addition, U.S. Holders may mitigate the adverse tax consequences of the PFIC rules by making a "qualified electing fund" ("QEF") election; however, there can be no assurance that the Company will satisfy the record keeping requirements applicable to a QEF or that it will provide the information regarding its income that would be necessary for a U.S. Holder to make a QEF election.

If the Company is a PFIC, U.S. Holders will generally be required to file an annual information return with the Internal Revenue Service (the "IRS") (on IRS Form 8621, which PFIC shareholders will be required to file with their U.S. federal income tax or information returns) relating to their ownership of Common Shares. This filing requirement is in addition to any preexisting reporting requirements that apply to a U.S. Holder's interest in a PFIC (which this requirement does not affect).

For a more detailed discussion of the potential tax impact of us being a PFIC, see "Certain Material U.S. Federal Income Tax Considerations" below. The PFIC rules are complex. U.S. Holders should consult their tax advisors regarding the potential application of the PFIC regime and any reporting obligations to which they may be subject under that regime.

Table of Contents

We may incur losses associated with foreign currency fluctuations.

Our operations are in many instances conducted in currencies other than our functional currency or the functional currencies of our subsidiaries. Fluctuations in the value of currencies could cause us to incur currency exchange losses. We do not currently employ a hedging strategy against exchange rate risk. We cannot assert with any assurance that we will not suffer losses as a result of unfavorable fluctuations in the exchange rates between the U.S. dollar, the euro, the Canadian dollar and other currencies.

Legislative actions, new accounting pronouncements and higher insurance costs may adversely impact our future financial position or results of operations.

Changes in financial accounting standards or implementation of accounting standards may cause adverse, unexpected revenue or expense fluctuations and affect our financial position or results of operations. New pronouncements and varying interpretations of pronouncements have occurred with greater frequency and are expected to occur in the future, and we may make or be required to make changes in our accounting policies in the future. Compliance with changing regulations of corporate governance and public disclosure, notably with respect to internal controls over financial reporting, may result in additional expenses. Changing laws, regulations and standards relating to corporate governance and public disclosure are creating uncertainty for companies such as ours, and insurance costs are increasing as a result of this uncertainty.

Security breaches may disrupt our operations and adversely affect our operating results.

Our network security and data recovery measures and those of third parties with which we contract, may not be adequate to protect against computer viruses, cyber-attacks, breaches, and similar disruptions from unauthorized tampering with our computer systems. The misappropriation, theft, sabotage or any other type of security breach with respect to any of our proprietary and confidential information that is electronically stored, including research or clinical data, could cause interruptions in our operations, could result in a material disruption of our clinical activities and business operations and could expose us to third-party legal claims. Furthermore, we could be required to make substantial expenditures of resources to remedy the cause of cyber-attacks or break-ins. This disruption could have a material adverse impact on our business, operating results and financial condition. Additionally, any break-in or trespass of our facilities that results in the misappropriation, theft, sabotage or any other type of security breach with respect to our proprietary and confidential information, including research or clinical data, or that results in damage to our R&D equipment and assets could have a material adverse impact on our business, operating results, and financial condition.

Risks Relating to our Common Shares and the Offering

Our Common Shares may be delisted from NASDAQ or TSX, which could affect their market price and liquidity. If our Common Shares were to be delisted, investors may have difficulty in disposing of their shares.

Our Common Shares are currently listed on both NASDAQ and TSX under the symbol "AEZS". We must meet continuing listing requirements to maintain the listing of our Common Shares on NASDAQ and TSX. For continued listing, NASDAQ requires, among other things, that listed securities maintain a minimum closing bid price of not less than \$1.00 per share. There can be no assurance that the market price of our Common Shares will not fall below \$1.00 in the future or that, if it does, we will regain compliance with the minimum bid price requirement.

In addition to the minimum bid price requirement, the continued listing rules of NASDAQ require us to meet at least one of the following listing standards: (i) stockholders' equity of at least \$2.5 million, (ii) market value of listed securities (calculated by multiplying the daily closing bid price of our Common Shares by our total outstanding Common Shares) of at least \$35 million or (iii) net income from continuing operations (in the latest fiscal year or in two of the last three fiscal years) of at least \$500,000 (collectively, the "Additional Listing Standards"). If we fail to meet at least one of the Additional Listing Standards, our Common Shares may be subject to delisting after the expiration of the period of time, if any, that we are allowed for regaining compliance.

Table of Contents

There can be no assurance that our Common Shares will remain listed on NASDAQ or TSX. If we fail to meet any of NASDAQ's or TSX's continued listing requirements, our Common Shares may be delisted. Any delisting of our Common Shares may adversely affect a shareholder's ability to dispose, or obtain quotations as to the market value, of such shares.

Our share price is volatile, which may result from factors outside of our control.

Our valuation and share price since the beginning of trading after our initial listings, first in Canada and then in the U.S., have had no meaningful relationship to current or historical financial results, asset values, book value or many other criteria based on conventional measures of the value of shares.

Between March 1, 2016 and March 27, 2017, the closing price of our Common Shares ranged from \$2.45 to \$4.94 per share on NASDAQ and from C\$3.24 to C\$6.62 per share on TSX. See "Price Range and Trading Volume" on page S-30 of this prospectus supplement. Our share price may be affected by developments directly affecting our business and by developments out of our control or unrelated to us. The stock market generally, and the biopharmaceutical sector in particular, are vulnerable to abrupt changes in investor sentiment. Prices of shares and trading volume of companies in the biopharmaceutical industry can swing dramatically in ways unrelated to, or that bear a disproportionate relationship to, operating performance. Our share price and trading volume may fluctuate based on a number of factors including, but not limited to:

clinical and regulatory developments regarding our product candidates;

delays in our anticipated development or commercialization timelines;

developments regarding current or future third-party collaborators;

announcements by us regarding technological, product development or other matters;

arrivals or departures of key personnel;

governmental or regulatory action affecting our product candidates and our competitors' products in the U.S., Canada and other countries;

developments or disputes concerning patent or proprietary rights;

actual or anticipated fluctuations in our revenues or expenses;

general market conditions and fluctuations for the emerging growth and biopharmaceutical market sectors; and

economic conditions in the U.S., Canada or abroad.

Our listing on both NASDAQ and TSX may increase price volatility due to various factors, including different ability to buy or sell our Common Shares, different market conditions in different capital markets and different trading volumes. In addition, low trading volume may increase the price volatility of our Common Shares. A thin trading market could cause the price of our Common Shares to fluctuate significantly more than the stock market as a whole.

You will experience immediate and substantial dilution.

Edgar Filing: Aeterna Zentaris Inc. - Form 424B5

Since the public offering price of the Common Shares offered pursuant to this prospectus supplement and the accompanying prospectus is higher than the net tangible book value per Common Share, you will suffer substantial dilution in the net tangible book value of the Common Shares you purchase in this offering.

We do not intend to pay dividends in the near future.

To date, we have not declared or paid any dividends on our Common Shares. We currently intend to retain our future earnings, if any, to finance further research and the overall commercial expansion of our business. As a result, the return on an investment in our Common Shares will depend upon any future appreciation in value. There is no guarantee that our Common Shares will appreciate in value or even maintain the price at which shareholders have purchased them.

S-27

Table of Contents

Management will have broad discretion as to the use of the proceeds of any offering. We may invest or spend the proceeds of any offering in ways with which investors may not agree and in ways that may not earn a profit.

Our management team will have broad discretion concerning the use of the proceeds of any offering of Common Shares under this prospectus supplement and the accompanying prospectus as well as the timing of their expenditure. As a result, investors will be relying on the judgment of management for the application of the proceeds of any offering of Common Shares under the Sales Agreement and under this prospectus supplement and the accompanying prospectus. We intend to use the proceeds from any offering for general corporate purposes, which includes the funding of the preparation and submission of an NDA for Zoptrex, if the results of our recently completed clinical trial of such product warrants doing so, to pursue FDA registration for Macrilen, if we decide to seek registration after our upcoming meeting with the FDA, the potential in-licensing or acquisition of new commercial products or other corporate and business development activities, and the potential expansion of existing product candidates into other indications. See "Use of Proceeds" on page S-30 of this prospectus supplement. Investors may not agree with the ways we decide to use these proceeds, and our use of the proceeds may not yield any results or profits.

Future issuances of securities and hedging activities may depress the trading price of our Common Shares.

Any issuance of equity securities or Convertible Securities after the offering of Common Shares under this prospectus supplement, including the issuance of Common Shares upon the exercise of stock options and upon the exercise of warrants or other Convertible Securities, could dilute the interests of our existing shareholders, and could substantially decrease the trading price of our Common Shares.

Apart from the Common Shares offered under this prospectus supplement, we may issue equity securities in the future for a number of reasons, including to finance our operations and business strategy, to satisfy our obligations upon the exercise of options or warrants or for other reasons. Our stock option plan generally permits us to have outstanding, at any given time, stock options that are exercisable for a maximum number of Common Shares equal to 11.4% of all then issued and outstanding Common Shares. As at December 31, 2016, there were:

12,917,995 Common Shares issued and outstanding;

no issued and outstanding Preferred Shares;

3,779,245 Common Shares issuable upon exercise of warrants that we previously issued in an underwritten public offering in October 2012, in a registered direct offering in July 2013, in an underwritten public offering in March 2015, in an underwritten public offering in December 2015, as well as in a registered direct offering in November 2016, which had a weighted average exercise price as of December 31, 2016 of \$9.94 per Common Share;

966,539 Common Shares that underlie outstanding stock options granted under our stock option plan as at December 31, 2016, having a weighted average exercise price of \$7.23 per Common Share, and an additional 1,858 Common Shares that underlie outstanding stock options granted under our stock option plan as at December 31, 2016, having a weighted average exercise price of C\$820.27 per Common Share; and

an aggregate of 504,254 additional Common Shares available for future grants under our stock option plan, which provides that the maximum number of Common Shares issuable under the plan may equal 11.4% of the issued and outstanding Common Shares at any given time.

In addition, the price of our Common Shares could also be affected by possible sales of Common Shares by investors who view other investment vehicles as more attractive means of equity participation in us and by hedging or arbitrage trading activity that may develop involving our Common Shares. This hedging or arbitrage could, in turn, affect the trading price of our Common Shares.

Table of Contents

In the event we were to lose our foreign private issuer status as of June 30 of a given financial year, we would be required to comply with the Exchange Act's domestic reporting regime, which could cause us to incur additional legal, accounting and other expenses.

In order to maintain our current status as a foreign private issuer, either (1) a majority of our Common Shares must not be either directly or indirectly owned of record by residents of the U.S. or (2) (a) a majority of our executive officers and of our directors must not be U.S. citizens or residents, (b) more than 50 percent of our assets cannot be located in the U.S. and (c) our business must be administered principally outside the U.S.

In 2016, our management conducted its annual assessment of the various facts and circumstances underlying the determination of our status as a foreign private issuer and, based on the foregoing, our management has determined that, as of the date of such determination and as of June 30, 2016, we continued to be a foreign private issuer.

There can be no assurance, however, that we will remain a foreign private issuer either in 2017 or in future financial years.

If we were to lose our foreign private issuer status as of June 30 of any given financial year, we would be required to comply with the Exchange Act reporting and other requirements applicable to U.S. domestic issuers, which are more detailed and extensive than the requirements for foreign private issuers. We may also be required to make changes in our corporate governance practices in accordance with various SEC rules and NASDAQ listing standards. The regulatory and compliance costs to us of complying with the reporting requirements applicable to a U.S. domestic issuer under U.S. securities laws may be higher than the cost we have historically incurred as a foreign private issuer. In addition, if we were to lose our foreign private issuer status, we would no longer qualify under the Canada-U.S. multijurisdictional disclosure system to benefit from being able to file registration statements on Form F-10 (even if we satisfy the other conditions to eligibility), which could make it longer and more difficult to register our securities and raise funds by way of public, registered offerings in the U.S., and we would become subject to "baby shelf" rules that place limitations on our ability to issue an amount of securities above a certain threshold depending on our market capitalization and public float at a given point in time. As a result, we would expect that a potential loss of foreign private issuer status at some future point in time could increase our legal, financial reporting and accounting compliance costs, and it is difficult at this time to estimate by how much our legal, financial reporting and accounting compliance costs may increase in such eventuality.

Our articles of incorporation contain "blank check" preferred share provisions, which could delay or impede an acquisition of our company.

Our articles of incorporation, as amended, authorize the issuance of an unlimited number of "blank check" preferred shares, which could be issued by our board of directors without shareholder approval and which may contain liquidation, dividend and other rights equivalent or superior to our Common Shares. In addition, we have implemented in our constating documents an advance notice procedure for shareholder approvals to be brought before an annual meeting of our shareholders, including proposed nominations of persons for election to our board of directors. These provisions, among others, whether alone or together, could delay or impede hostile takeovers and changes in control or changes in our management. Any provision of our constating documents that has the effect of delaying or deterring a change in control could limit the opportunity for our shareholders to receive a premium for their Common Shares and could also affect the price that some investors are willing to pay for our Common Shares.

Our business could be negatively affected as a result of the actions of activist shareholders.

Proxy contests have been waged against many companies in the biopharmaceutical industry over the last few years. If faced with a proxy contest, we may not be able to successfully respond to the contest, which would be

Table of Contents

disruptive to our business. Even if we are successful, our business could be adversely affected by a proxy contest because:

responding to proxy contests and other actions by activist shareholders may be costly and time-consuming, and may disrupt our operations and divert the attention of management and our employees;

perceived uncertainties as to the potential outcome of any proxy contest may result in our inability to consummate potential acquisitions, collaborations or in-licensing opportunities and may make it more difficult to attract and retain qualified personnel and business partners; and

if individuals that have a specific agenda different from that of our management or other members of our board of directors are elected to our board as a result of any proxy contest, such an election may adversely affect our ability to effectively and timely implement our strategic plan and to create value for our shareholders.

USE OF PROCEEDS

Except as otherwise provided in any free writing prospectus that we may authorize to be provided to you, we intend to use the net proceeds from the sale of the Common Shares under this prospectus supplement for general corporate purposes, which includes the funding of the preparation and submission of an NDA for Zoptrex, if the results of our recently completed clinical trial of such product warrants doing so, to pursue FDA registration for Macrilen, if we decide to seek registration after our upcoming meeting with the FDA, the potential in-licensing or acquisition of new commercial products or other corporate and business development activities, and the potential expansion of existing product candidates into other indications. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds we will have upon completion of this offering. Accordingly, our management will have broad discretion in the application of net proceeds.

PRICE RANGE AND TRADING VOLUME

Our Common Shares are listed on NASDAQ and on TSX under the symbol "AEZS". The following table indicates the monthly range of high and low closing prices of a Common Share and the average daily volumes traded on NASDAQ and on TSX during the period beginning on March 1, 2016 and ending on March 27, 2017:

	NASDAQ (US\$)			TSX (C\$)		
	High	Low	Volume	High	Low	Volume
2016						
March	3.99	3.08	371,706	5.33	4.16	29,661
April	4.38	3.36	265,606	5.69	4.45	22,374
May	3.92	3.27	161,335	4.95	4.24	13,274
June	3.65	3.01	126,649	4.62	3.90	12,882
July	3.62	3.30	322,087	4.71	4.26	13,583
August	3.72	3.40	85,023	4.83	4.45	12,323
September	3.73	3.35	95,411	4.82	4.39	9,776
October	4.94	3.34	782,079	6.62	4.46	67,219
November	4.00	3.25	223,123	5.30	4.40	17,056
December	4.10	3.40	264,323	5.52	4.45	25,539
2017						
January	3.65	2.45	499,639	4.81	3.24	58,622
February	3.35	2.80	201,259	4.43	3.62	26,392
March ⁽¹⁾	3.10	2.70	139,441	4.26	3.60	11,095

(1) Up to and including March 27, 2017.

Table of Contents

PRIOR SALES

During the twelve-month period preceding the date of this prospectus supplement, we issued or granted, as applicable:

an aggregate of 2,100,000 units consisting of either one Common Share or one pre-funded warrant to acquire one Common Share and 0.45 of a warrant to purchase one Common Share, at a purchase price of \$3.60 per unit, in connection with our registered direct offering completed in November 2016, which generated net proceeds of approximately \$6.7 million;

an aggregate of 1,706,968 Common Shares issued under our "at-the-market" issuance program implemented in April 2016 pursuant to a prospectus supplement at an average issuance and sales price of \$3.52 per share (the "April 2016 ATM Program"); and

713,573 stock options exercisable at a weighted average price of \$3.47 per share.

CONSOLIDATED CAPITALIZATION

The following table presents the number of our issued and outstanding Common Shares and our consolidated cash and cash equivalents and capitalization as at December 31, 2016 on an actual basis and on an as adjusted basis assuming that an aggregate of 3,000,000 Common Shares are sold at a price of \$3.00, being the last reported sale price of our Common Shares on NASDAQ on March 27, 2017, for aggregate gross proceeds of \$9.0 million. The adjustments present the expected impact on the number of our issued and outstanding Common Shares, our consolidated cash and cash equivalents and our capitalization as at December 31, 2016 of the issuances described above and after the payment by us of Wainwright's compensation and our estimated transaction expenses. Except for the issuance by the Company of an aggregate of 817,670 Common Shares under the April 2016 ATM Program between January 1, 2017 and the date of this prospectus supplement, there has been no material change to our share and loan capital since December 31, 2016. In addition, as at December 31, 2016, we had no outstanding long-term third-party debt.

The information below has been derived from and should be read in conjunction with, and is qualified in its entirety by, our audited consolidated financial statements as at December 31, 2016 and December 31, 2015 and for the years ended December 31, 2016, 2015 and 2014 and Management's Discussion and Analysis thereon, incorporated by reference into this prospectus supplement. Figures are in thousands of U.S. dollars except share data.

	As at December 31, 2016	
	Actual	As Adjusted ⁽¹⁾
Number of Common Shares issued and outstanding	12,917,995 ⁽²⁾	15,917,995 ⁽²⁾
Cash and cash equivalents	\$ 21,999	\$ 30,504
Shareholders' equity:		
Share capital	\$ 213,980	\$ 222,485
Other capital	\$ 88,590	\$ 88,590
Deficit	\$ (298,059)	\$ (298,059)
Accumulated other comprehensive income	\$ 1,701	\$ 1,701
Total shareholders' equity and total capitalization	\$ 6,212	\$ 14,717

(1)

As adjusted assumes and gives effect to the issuance of 3,000,000 Common Shares to be offered from time to time under this prospectus supplement at an assumed price of \$3.00 per Common Share (being the last reported sale price of our Common Shares on NASDAQ on March 27, 2017) and the payment by us of Wainwright's compensation and our estimated transaction expenses. In light of the continuous distribution nature of this at-the-market

Edgar Filing: Aeterna Zentaris Inc. - Form 424B5

offering, there can be no assurance that we will in fact issue all or any number of the 3,000,000 Common Shares offered under this prospectus supplement or, if we do issue any Common Shares under this prospectus supplement, that they will be issued at \$3.00 per share. The figures provided in the "as adjusted" column are thus solely for illustrative purposes.

S-31

Table of Contents

(2)

The number of our Common Shares that will be outstanding both before and immediately after this offering is based on shares outstanding as of December 31, 2016 and excludes as of such date:

3,779,245 Common Shares issuable upon exercise of warrants that we previously issued in an underwritten public offering in October 2012, in a registered direct offering in July 2013, in an underwritten public offering in March 2015, in an underwritten public offering in December 2015, as well as in a registered direct offering in November 2016, which had a weighted average exercise price as of December 31, 2016 of \$9.94 per Common Share;

966,539 Common Shares that underlie outstanding stock options granted under our stock option plan as at December 31, 2016, having a weighted average exercise price of \$7.23 per Common Share, and an additional 1,858 Common Shares that underlie outstanding stock options granted under our stock option plan as at December 31, 2016, having a weighted average exercise price of C\$820.27 per Common Share

an aggregate of 504,254 additional Common Shares available for future grants under our stock option plan, which provides that the maximum number of Common Shares issuable under the plan may equal 11.4% of the issued and outstanding Common Shares at any given time; and

817,670 Common Shares issued under the April 2016 ATM Program between January 1, 2017 and the date of this prospectus supplement.

DILUTION

If you purchase Common Shares in this offering, your interest will be diluted to the extent of the excess of the public offering price per Common Share over the as adjusted net tangible book value per Common Share after this offering. Net tangible book value per share represents the amount of our total tangible assets (which include unrestricted and restricted cash and cash equivalents, accounts receivable, prepaid property, plant and equipment, and other non-current assets) reduced by the amount of our total liabilities, divided by the total number of Common Shares issued and outstanding.

As at December 31, 2016, we had a net tangible book value of approximately \$(1.4) million, or approximately \$(0.11) per Common Share. Net tangible book value per share is calculated by subtracting our total liabilities from our total tangible assets, which is total assets less intangible assets, and dividing this amount by the number of Common Shares issued and outstanding. After giving effect to the sale of our Common Shares in the aggregate amount of \$9.0 million at an assumed offering price of \$3.00 per share, being the last reported sale price of our Common Shares on NASDAQ on March 27, 2017, and after deducting estimated offering commissions and expenses of \$0.5 million, or \$0.17 per share, payable by us, we would have had a net tangible book value as at December 31, 2016 of \$7.1 million, or \$0.45 per Common Share. This represents an immediate increase in the net tangible book value of \$0.56 per share attributable to this offering. The following table illustrates this per share dilution:

Assumed offering price per share	\$ 3.00
Net tangible book value per share as at December 31, 2016	\$ (0.11)
Increase in net tangible book value per share attributable to this offering	\$ 0.56
As-adjusted net tangible book value per share after this offering	\$ 0.45
Net dilution per share to new investors	\$ 2.55

The table above assumes for illustrative purposes that an aggregate of 3,000,000 of our Common Shares are sold at a price of \$3.00 per share, being the last reported sale price of our Common Shares on NASDAQ on March 27, 2017, for aggregate gross proceeds of \$9,000,000. The Common Shares sold in this offering, if any, will be sold from time to time at various prices. An increase of \$0.30 per share in the price at which the Common Shares are sold from the assumed offering price of \$3.00 per share shown in the table above, assuming all of our Common Shares in the aggregate amount of \$9,000,000 are sold at that price, would increase the dilution in net tangible book value per share to new investors in this offering to \$2.85 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$0.30 per share in the price at which the Common Shares are sold from the assumed offering price of \$3.00 per share shown in the table above, assuming all of our Common Shares in the aggregate amount of \$9,000,000 are sold at that price, would decrease the dilution in net tangible book value per share to new investors in this offering to \$2.26 per share, after deducting

Edgar Filing: Aeterna Zentaris Inc. - Form 424B5

Table of Contents

commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

The calculations above are based upon 12,917,995 Common Shares issued and outstanding as at December 31, 2016 and exclude as of such date:

3,779,245 Common Shares issuable upon exercise of warrants that we previously issued in an underwritten public offering in October 2012, in a registered direct offering in July 2013, in an underwritten public offering in March 2015, in an underwritten public offering in December 2015, as well as in a registered direct offering in November 2016, which had a weighted average exercise price as of December 31, 2016 of \$9.94 per Common Share;

966,539 Common Shares that underlie outstanding stock options granted under our stock option plan as at December 31, 2016, having a weighted average exercise price of \$7.23 per Common Share, and an additional 1,858 Common Shares that underlie outstanding stock options granted under our stock option plan as at December 31, 2016, having a weighted average exercise price of C\$820.27 per Common Share

an aggregate of 504,254 additional Common Shares available for future grants under our stock option plan, which provides that the maximum number of Common Shares issuable under the plan may equal 11.4% of the issued and outstanding Common Shares at any given time; and

817,670 Common Shares issued under the April 2016 ATM Program between January 1, 2017 and the date of this prospectus supplement.

DIVIDEND POLICY

We have never declared or paid dividends on our Common Shares. We currently expect to retain future earnings, if any, for use in the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends on our Common Shares is subject to the discretion of our board of directors and will depend upon various factors, including, without limitation, our results of operations and financial condition.

DESCRIPTION OF SECURITIES OFFERED UNDER THIS PROSPECTUS SUPPLEMENT

Share Capital

Our authorized share capital structure consists of an unlimited number of shares of the following classes (all classes are without nominal or par value): Common Shares; first preferred shares (the "First Preferred Shares") and second preferred shares (the "Second Preferred Shares" and, together with the First Preferred Shares, the "Preferred Shares"), each issuable in series. As at March 27, 2017 there were 13,735,665 Common Shares issued and outstanding. No Preferred Shares of the Company have been issued to date.

Common Shares

The holders of the Common Shares are entitled to one vote for each Common Share held by them at all meetings of shareholders, except meetings at which only shareholders of a specified class of shares are entitled to vote. In addition, the holders are entitled to receive dividends if, as and when declared by the Company's board of directors on the Common Shares. Finally, the holders of the Common Shares are entitled to receive the remaining property of the Company upon any liquidation, dissolution or winding-up of the affairs of the Company, whether voluntary or involuntary. Shareholders have no liability to further capital calls as all issued and outstanding shares are fully paid and non-assessable.

Additional information on our share capital is provided in "Item 10. Additional Information" in our Annual Report on Form 20-F for the financial year ended December 31, 2016, incorporated by reference into this prospectus supplement.

Table of Contents

PLAN OF DISTRIBUTION

Pursuant to our existing Sales Agreement with Wainwright, we may issue and sell Common Shares under this prospectus supplement from time to time through Wainwright, acting as agent. A form of the Sales Agreement was furnished to the SEC as Exhibit 99.2 to our Report on Form 6-K on April 1, 2016. Additional sales, if any, of Common Shares made under the Sales Agreement will be made in the U.S. and will only be made by any method permitted by law deemed to be an "at the market offering" as defined in Rule 415 of the Securities Act, including without limitation sales made directly on NASDAQ or on any other existing trading market for the Common Shares in the U.S. at market prices prevailing at the time of sale. We may instruct Wainwright not to sell Common Shares if the sales cannot be effected at or above the price designated by us from time to time. We or Wainwright may suspend the offering of Common Shares upon notice and subject to other conditions.

We will pay Wainwright commissions for its services in acting as agent in the sale of Common Shares. Wainwright is entitled to compensation at a fixed commission rate of three percent (3.0%) of the gross proceeds from the sale of such Common Shares. In connection with this offering, we have agreed to reimburse Wainwright up to \$50,000 for its reasonable legal fees and expenses incidental to the offering. We estimate that the total expenses for the offering, excluding compensation payable to Wainwright incidental to the offering, will be approximately \$0.2 million.

Settlement for sales of Common Shares will occur on the third business day following the date on which any sales are made, or on some other date that is agreed upon by us and Wainwright in connection with a particular transaction, in return for payment of the net proceeds to us.

The Common Shares will be listed on NASDAQ. The TSX has conditionally approved the listing of the Common Shares offered for sale pursuant to this prospectus supplement. Listing is subject to the Company fulfilling all of the requirements of the TSX on or before the business day immediately following the date on which this prospectus supplement is filed.

The aggregate market value of our Common Shares held by non-affiliates pursuant to General Instruction I.B.5 of Form F-3 is \$45,819,347, which was calculated based on 13,677,417 of our Common Shares outstanding and held by non-affiliates as of the date of this prospectus supplement and a price of \$3.35 per share, the closing price of our Common Shares on NASDAQ on February 17, 2017. We have sold 1,706,968 Common Shares pursuant to General Instruction I.B.5 of Form F-3 during the twelve calendar month period that ends on and includes the date of this prospectus supplement and the aggregate value of the Common Shares sold was \$6,002,682.

Wainwright is not required to sell any specific number or dollar amount of our Common Shares. Wainwright will act as sales agent and will use its commercially reasonable efforts consistent with its normal trading and sales practices to sell the Common Shares offered hereunder. In connection with the sale of the Common Shares on our behalf, Wainwright will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Wainwright will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to Wainwright against certain civil liabilities, including liabilities under the Securities Act.

The Sales Agreement further provides that, during its term, neither Wainwright nor any of its affiliates or subsidiaries shall engage in (i) any short sale of any security of the Company, or (ii) any sale of any security of the Company that Wainwright does not own or any sale which is consummated by the delivery of a security of the Company borrowed by, or for the account of, Wainwright, and that neither Wainwright nor any of its affiliates or subsidiaries shall engage in any proprietary trading or trading for Wainwright's (or its affiliates' or subsidiaries') own account.

Any offering pursuant to the Sales Agreement will terminate on the two-year anniversary of the date of the Sales Agreement or earlier upon (i) the sale of all Common Shares subject to the agreement (which includes all of the Common Shares that may be sold pursuant to this offering), or (ii) termination of the Sales Agreement by the Company or Wainwright as permitted therein.

Table of Contents

Wainwright and its affiliates may in the future provide various investment banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. The principal business address of Wainwright is 430 Park Avenue, 4th Floor, New York, New York 10022.

To the extent required by Regulation M, Wainwright will not engage in any market making activities involving our Common Shares while the offering is ongoing under this prospectus supplement.

CERTAIN INCOME TAX CONSIDERATIONS

Certain Material U.S. Federal Income Tax Considerations

The following discussion is a summary of certain material U.S. federal income tax consequences applicable to the purchase, ownership and disposition of Common Shares being offered by this prospectus supplement and the accompanying prospectus by a U.S. Holder (as defined below), but does not purport to be a complete analysis of all potential U.S. federal income tax effects.

This summary is based on the Internal Revenue Code of 1986, as amended (the "Code"), U.S. Treasury regulations promulgated thereunder, IRS rulings and judicial decisions in effect as of the date of this prospectus supplement. All of these are subject to change, possibly with retroactive effect, or different interpretations. This summary does not discuss the potential effects, whether adverse or beneficial, of any proposed legislation that, if enacted, could be applied on a retroactive basis. This summary is not binding on the IRS, and the IRS is not precluded from taking a position that is different from, and contrary to, the positions taken in this summary.

This summary does not address all aspects of U.S. federal income taxation that may be relevant to particular U.S. Holders in light of their specific circumstances (for example, U.S. Holders subject to the alternative minimum tax or the Medicare contribution tax on net investment income under the Code) or to holders that may be subject to special rules under U.S. federal income tax law, including:

dealers in stocks, securities or currencies;

securities traders that use a mark-to-market accounting method;

banks and financial institutions;

insurance companies;

regulated investment companies;

real estate investment trusts;

tax-exempt organizations;

retirement plans, individual plans, individual retirement accounts and tax-deferred accounts;

partnerships or other pass-through entities for U.S. federal income tax purposes and their partners or members;

persons holding Common Shares as part of a hedging or conversion transaction straddle or other integrated or risk reduction transaction;

Edgar Filing: Aeterna Zentaris Inc. - Form 424B5

persons who or that are, or may become, subject to the expatriation provisions of the Code;

persons whose functional currency is not the U.S. dollar; and

direct, indirect or constructive owners of 10% or more of the total combined voting power of all classes of our voting stock.

This summary also does not discuss any aspect of state, local or foreign law, or estate or gift tax law as applicable to U.S. Holders. In addition, this discussion is limited to U.S. Holders purchasing Common Shares pursuant to this prospectus supplement and that will hold such Common Shares as capital assets. For purposes of this summary, "U.S. Holder" means a beneficial holder of Common Shares who or that for U.S. federal income tax purposes is:

an individual citizen or resident of the U.S.;

S-35

Table of Contents

a corporation or other entity classified as a corporation for U.S. federal income tax purposes created or organized in or under the laws of the U.S., any state thereof or the District of Columbia;

an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or

a trust, if (a) a court within the U.S. is able to exercise primary supervision over the administration of such trust and one or more "U.S. persons" (within the meaning of the Code) have the authority to control all substantial decisions of the trust, or (b) a valid election is in effect to be treated as a U.S. person for U.S. federal income tax purposes.

If a partnership or other entity or arrangement classified as a partnership for U.S. federal income tax purposes holds Common Shares, the U.S. federal income tax treatment of a partner generally will depend on the status of the partner and the activities of the partnership. This summary does not address the tax consequences to any such partner. Such a partner should consult its own tax advisor as to the tax consequences of the partnership purchasing, owning and disposing of Common Shares.

PROSPECTIVE U.S. INVESTORS SHOULD CONSULT THEIR OWN TAX ADVISORS WITH REGARD TO THE APPLICATION OF THE TAX CONSEQUENCES DESCRIBED BELOW TO THEIR PARTICULAR SITUATIONS AS WELL AS THE APPLICATION OF ANY STATE, LOCAL, FOREIGN OR OTHER TAX LAWS, INCLUDING GIFT AND ESTATE TAX LAWS.

Taxation of U.S. Holders of Common Shares

Dividends

Subject to the PFIC rules discussed below, any distributions paid by the Company out of current or accumulated earnings and profits (as determined for U.S. federal income tax purposes), before reduction for any Canadian withholding tax paid with respect thereto, will generally be taxable to a U.S. Holder as foreign source dividend income, and will not be eligible for the dividends received deduction generally allowed to corporations. Distributions in excess of current and accumulated earnings and profits will be treated as a non-taxable return of capital to the extent of the U.S. Holder's adjusted tax basis in the Common Shares and thereafter as capital gain. The Company may not, however, maintain the calculations of its earnings and profits in accordance with US federal income tax principles. Therefore, US Holders should assume (unless advised to the contrary) that any distribution from the Company will be treated for US federal income tax purposes as a dividend. Prospective purchasers should consult their own tax advisors with respect to the appropriate U.S. federal income tax treatment of any distribution received from the Company.

Dividends paid to non-corporate U.S. Holders by the Company in a taxable year in which it is treated as a PFIC, or in the immediately following taxable year, will not be eligible for the special reduced rates normally applicable to long-term capital gains. In all other taxable years, dividends paid by the Company should be taxable to a non-corporate U.S. Holder at the special reduced rates normally applicable to long-term capital gains, provided that certain conditions are satisfied. The Company believes it was not a PFIC for the 2016 taxable year. However, no assurance can be provided that the Company will not be classified as a PFIC for the 2017 or any subsequent taxable year and, therefore, no assurance can be provided that a U.S. Holder will be able to claim a reduced rate for dividends paid in 2017 or any subsequent taxable year (if any). See "Taxation of U.S. Holders of Common Shares – Passive Foreign Investment Company Considerations" below.

Under current law, payments of dividends by the Company to non-Canadian investors are generally subject to a 25% Canadian withholding tax. The rate of withholding tax applicable to U.S. Holders that are eligible for benefits under the Canada-United States Tax Convention (the "Convention") is reduced to a maximum of 15%. This reduced rate of withholding will not apply if the dividends received by a U.S. Holder are effectively connected with a permanent establishment of the U.S. Holder in Canada. For U.S. federal income tax purposes, U.S. Holders will be treated as having received the amount of Canadian taxes withheld by the Company, and as then having paid over the withheld taxes to the Canadian taxing authorities. As a result of this rule, the amount of dividend income included in gross income for U.S. federal income tax purposes by a U.S. Holder with respect to a payment of dividends may be greater than the amount of cash actually received (or receivable) by the U.S. Holder from the Company with respect to the payment.

Table of Contents

Subject to certain limitations, a U.S. Holder will generally be entitled, at the election of the U.S. Holder, to a credit against its U.S. federal income tax liability, or a deduction in computing its U.S. federal taxable income, for Canadian income taxes withheld by the Company. This election is made on a year-by-year basis and applies to all foreign taxes paid (whether directly or through withholding) by a U.S. Holder during a year. For purposes of the foreign tax credit limitation, dividends paid by the Company generally will constitute foreign source income in the "passive category income" basket. The foreign tax credit rules are complex and prospective purchasers should consult their tax advisors concerning the availability of the foreign tax credit in their particular circumstances.

Dividends paid in Canadian dollars will be included in the gross income of a U.S. Holder in a U.S. dollar amount calculated by reference to the exchange rate in effect on the date the U.S. Holder (actually or constructively) receives the dividend, regardless of whether such Canadian dollars are actually converted into U.S. dollars at that time. If the Canadian dollars received are not converted into U.S. dollars on the date of receipt, 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. Gain or loss, if any, realized on a sale or other disposition of the Canadian dollars will generally be U.S. source ordinary income or loss to a U.S. Holder.

The Company generally does not pay any dividends and does not anticipate paying any dividends in the foreseeable future.

Sale, Exchange or Other Taxable Disposition of Common Shares

Subject to the PFIC rules discussed below, upon a sale, exchange or other taxable disposition of Common Shares, a U.S. Holder generally will recognize capital gain or loss for U.S. federal income tax purposes equal to the difference, if any, between the amount realized on the sale, exchange or other taxable disposition and the U.S. Holder's adjusted tax basis in the Common Shares.

This capital gain or loss will be long-term capital gain or loss if the U.S. Holder's holding period in the Common Shares exceeds one year. The deductibility of capital losses is subject to limitations. Any gain or loss will generally be U.S. source for U.S. foreign tax credit purposes.

Passive Foreign Investment Company Considerations

A foreign corporation will be classified as a PFIC for any taxable year in which, after taking into account the income and assets of the corporation and certain subsidiaries pursuant to applicable "look-through rules," either (i) at least 75% of its gross income is "passive income" or (ii) at least 50% of the average value of its assets is attributable to assets which produce passive income or are held for the production of passive income. Passive income generally includes dividends, interest, rents and royalties (other than certain rents and royalties derived in the active conduct of a trade or business), annuities and gains from assets that produce passive income. If a non-U.S. corporation owns at least 25% by value of the stock of another corporation, the non-U.S. corporation is treated for purposes of the PFIC tests as owning its proportionate share of the assets of the other corporation and as receiving directly its proportionate share of the other corporation's income.

We believe that we were not a PFIC for the 2016 taxable year and may not be a PFIC for the 2017 taxable year. However, the fair market value of the Company's assets may be determined in large part by the market price of the Common Shares, which is likely to fluctuate, and the composition of the Company's income and assets will be affected by how, and how quickly, the Company spends any cash that is raised in any financing transaction. Thus, no assurance can be provided that the Company will not be classified as a PFIC for the 2017 taxable year or any future taxable year. Prospective purchasers should consult their tax advisors regarding the Company's PFIC status.

If the Company is classified as a PFIC for any taxable year during which a U.S. Holder owns Common Shares, the U.S. Holder, absent certain elections (including the mark-to-market and QEF elections described below), will generally be subject to adverse rules (regardless of whether the Company continues to be classified as a PFIC) with respect to (i) any "excess distributions" (generally, any distributions received by the U.S. Holder on the Common Shares in a taxable year that are greater than 125% of the average annual distributions received by the U.S. Holder in the three preceding taxable years or, if shorter, the U.S. Holder's holding period for the Common Shares) and (ii) any gain realized on the sale or other disposition of the Common Shares.

Table of Contents

Under these adverse rules (a) the excess distribution or gain will be allocated ratably over the U.S. Holder's holding period, (b) the amount allocated to the current taxable year and any taxable year prior to the first taxable year in which the Company is classified as a PFIC will be taxed as ordinary income, and (c) the amount allocated to each of the other taxable years during which the Company was classified as a PFIC will be subject to tax at the highest rate of tax in effect for the applicable category of taxpayer for that year and an interest charge will be imposed with respect to the resulting tax attributable to each such other taxable year. A U.S. Holder that is not a corporation will be required to treat any such interest paid as "personal interest", which is not deductible.

U.S. Holders can avoid the adverse rules described above in part by making a mark-to-market election with respect to the Common Shares, provided that the Common Shares are "marketable". The Common Shares will be marketable if they are "regularly traded" on a "qualified exchange" or other market within the meaning of applicable U.S. Treasury regulations. For this purpose, the Common Shares generally will be considered to be regularly traded during any calendar year during which they are traded, other than in *de minimis* quantities, on at least 15 days during each calendar quarter. The Common Shares are currently listed on NASDAQ, which constitutes a qualified exchange; however, there can be no assurance that the Common Shares will be treated as regularly traded for purposes of the mark-to-market election on a qualified exchange. If the Common Shares were not regularly traded on NASDAQ or were delisted from NASDAQ and were not traded on another qualified exchange for the requisite time period described above, the mark-to-market election would not be available.

A U.S. Holder that makes a mark-to-market election must include in gross income, as ordinary income, for each taxable year an amount equal to the excess, if any, of the fair market value of the U.S. Holder's Common Shares at the close of the taxable year over the U.S. Holder's adjusted tax basis in the Common Shares. An electing U.S. Holder may also claim an ordinary loss deduction for the excess, if any, of the U.S. Holder's adjusted tax basis in the Common Shares over the fair market value of the Common Shares at the close of the taxable year, but this deduction is allowable only to the extent of any net mark-to-market gains previously included in income. A U.S. Holder that makes a mark-to-market election generally will adjust such U.S. Holder's tax basis in the Common Shares to reflect the amount included in gross income or allowed as a deduction because of such mark-to-market election. Gains from an actual sale or other disposition of the Common Shares will be treated as ordinary income, and any losses incurred on a sale or other disposition of the Common Shares will be treated as ordinary losses to the extent of any net mark-to-market gains previously included in income.

If the Company is classified as a PFIC for any taxable year in which a U.S. Holder owns Common Shares but before a mark-to-market election is made, the adverse PFIC rules described above will apply to any mark-to-market gain recognized in the year the election is made. Otherwise, a mark-to-market election will be effective for the taxable year for which the election is made and all subsequent taxable years. The election cannot be revoked without the consent of the IRS unless the Common Shares cease to be marketable, in which case the election is automatically terminated.

If the Company is classified as a PFIC, a U.S. Holder of Common Shares will generally be treated as owning stock owned by the Company in any direct or indirect subsidiaries that are also PFICs and will be subject to similar adverse rules with respect to distributions to the Company by, and dispositions by the Company of, the stock of such subsidiaries. A mark-to-market election is not permitted for the shares of any subsidiary of the Company that is also classified as a PFIC. Prospective purchasers should consult their tax advisors regarding the availability of, and procedure for making, a mark-to-market election.

In some cases, a shareholder of a PFIC can avoid the interest charge and the other adverse PFIC consequences described above by making a QEF election to be taxed currently on its share of the PFIC's undistributed income. We will endeavor to satisfy the record keeping requirements that apply to a QEF and to supply requesting U.S. Holders with the information that such U.S. Holders are required to report under the QEF rules with respect to the Company and any subsidiary of the Company that is a PFIC ("PFIC Subsidiary"). However, there can be no assurance that the Company will satisfy the record keeping requirement or provide the information required to be reported by U.S. Holders.

Table of Contents

A U.S. Holder that makes a timely and effective QEF election for the first tax year in which its holding period of its Common Shares begins generally will not be subject to the adverse PFIC consequences described above with respect to its Common Shares. Rather, a U.S. Holder that makes a timely and effective QEF election will be subject to U.S. federal income tax on such U.S. Holder's pro rata share of (a) the Company's net capital gain, which will be taxed as long-term capital gain to such U.S. Holder, and (b) the Company's ordinary earnings, which will be taxed as ordinary income to such U.S. Holder, in each case regardless of which such amounts are actually distributed to the U.S. Holder by the Company. Generally, "net capital gain" is the excess of (a) net long-term capital gain over (b) net short-term capital loss, and "ordinary earnings" are the excess of (a) "earnings and profits" over (b) net capital gain. A U.S. Holder that makes a timely and effective QEF election with respect to the Company generally (a) may receive a tax-free distribution from us to the extent that such distribution represents "earnings and profits" that were previously included in income by the U.S. Holder because of such QEF election and (b) will adjust such U.S. Holder's tax basis in the Common Shares to reflect the amount included in income or allowed as a tax-free distribution because of such QEF election. In addition, a U.S. Holder that makes a QEF election generally will recognize capital gain or loss on the sale or other taxable disposition of Common Shares.

The QEF election is made on a shareholder-by-shareholder basis. Once made, a QEF election will apply to the tax year for which the QEF election is made and to all subsequent tax years, unless the QEF election is invalidated or terminated or the IRS consents to revocation of the QEF election. In addition, if a U.S. Holder makes a QEF election, the QEF election will remain in effect (although it will not be applicable) during those tax years in which the Company is not a PFIC.

A QEF election made with respect to the Company will not apply to any PFIC Subsidiary; a QEF election must be made separately for each PFIC Subsidiary (in which case the treatment described above would apply to such PFIC Subsidiary). If a U.S. Holder makes a timely and effective QEF election with respect to a PFIC Subsidiary, 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 PFIC Subsidiary, but may not receive a distribution of such income.

If the Company is classified as a PFIC and then ceases to be so classified, a U.S. Holder may make an election (a "deemed sale election") to be treated for U.S. federal income tax purposes as having sold such U.S. Holder's Common Shares on the last day of the taxable year of the Company during which it was a PFIC. A U.S. Holder that made a deemed sale election would then cease to be treated as owning stock in a PFIC by reason of ownership of Common Shares in the Company. However, gain recognized as a result of making the deemed sale election would be subject to the adverse rules described above and loss would not be recognized.

If the Company or a subsidiary is a PFIC in any year with respect to a U.S. Holder, the U.S. Holder will be required to file an annual information return on IRS Form 8621 regarding distributions received on Common Shares and any gain realized on the disposition of Common Shares.

In addition, if the Company is a PFIC, U.S. Holders will generally be required to file an annual information return with the IRS (also on IRS Form 8621, which PFIC shareholders are required to file with their U.S. federal income tax or information returns) relating to their ownership of Common Shares. This filing requirement is in addition to the preexisting reporting requirements described above that apply to a U.S. Holder's interest in a PFIC (which this requirement does not affect).

Prospective purchasers should consult their tax advisors regarding the potential application of the PFIC regime and any reporting obligations to which they may be subject under that regime.

Information Reporting and Backup Withholding

Payments made within the U.S., or by a U.S. payor or U.S. middleman, of dividends on, and proceeds arising from sales or other dispositions of Common Shares, generally will be reported to the IRS and to the U.S. Holder as required under applicable regulations. Backup withholding tax may apply to these payments if the U.S. Holder fails to timely provide in the appropriate manner an accurate taxpayer identification number or otherwise fails to comply with, or establish an exemption from, such backup withholding tax requirements. Certain U.S. Holders are not subject to the information reporting or backup withholding tax requirements

Table of Contents

described herein. U.S. Holders should consult their tax advisors as to their qualification for exemption from backup withholding tax and the procedure for establishing an exemption.

Backup withholding tax is not an additional tax. U.S. Holders generally will be allowed a refund or credit against their U.S. federal income tax liability for amounts withheld, provided the required information is timely furnished to the IRS. Certain U.S. Holders are required to file IRS Form 926 and certain U.S. Holders may be required to file Form 5471 reporting transfers of cash or other property to the Company and information relating to the U.S. Holder and the Company. In addition, certain U.S. Holders are required to report information on IRS Form 8938 with respect to their investments in certain "foreign financial assets," which would include an investment in our Common Shares. Substantial penalties may be imposed upon a U.S. Holder that fails to comply. U.S. Holders should consult their tax advisors regarding the information reporting obligations that may arise from their acquisition, ownership or disposition of Common Shares.

Canadian Federal Income Tax Considerations for U.S. Shareholders

The following is a general summary, as of the date hereof, of the principal Canadian federal income tax considerations generally applicable to the holding and disposition of Common Shares acquired pursuant to this prospectus supplement by a holder who, at all relevant times, (a) for the purposes of the *Income Tax Act* (Canada) (the "Tax Act"), (i) is not resident, or deemed to be resident, in Canada, (ii) deals at arm's length with, and is not affiliated with, the Company, (iii) beneficially owns Common Shares as capital property, (iv) does not use or hold the Common Shares in the course of carrying on, or otherwise in connection with, a business or a part of a business carried on or deemed to be carried on in Canada and (v) is not a "registered non-resident insurer" or "authorized foreign bank" within the meaning of the Tax Act, and (b) for the purposes of the Convention, is a resident of the U.S., has never been a resident of Canada, does not have and has not had, at any time, a permanent establishment or fixed base in Canada, and is a qualifying person or otherwise qualifies for the full benefits of the Convention. Common Shares will generally be considered to be capital property to a holder unless such Common Shares are held in the course of carrying on a business of buying or selling securities, or an adventure or concern in the nature of trade. Our shares will generally not be capital property to holders that are "financial institutions" (as defined in subsection 142.2(1) of the Tax Act). Holders who meet all the criteria in clauses (a) and (b) are referred to herein as a "U.S. Shareholder" or "U.S. Shareholders". This summary does not deal with special situations, such as the particular circumstances of traders or dealers, holders an interest in which is a "tax shelter investment" as defined in the Tax Act, tax exempt entities, insurers, financial institutions, holders who have made a "functional currency" reporting election under section 261 of the Tax Act or holders who have entered or will enter into a "derivative forward agreement" (as defined in the Tax Act) in respect of Common Shares. Such holders and other holders who do not meet the criteria in clauses (a) and (b) should consult their own tax advisors.

This summary is based upon the current provisions of the Tax Act and the regulations thereunder (the "Regulations") and the Company's understanding of the current administrative policies and assessing practices of the Canada Revenue Agency ("CRA") made publicly available prior to the date hereof. It also takes into account all proposed amendments to the Tax Act and the Regulations publicly released by the Minister of Finance (Canada) ("Tax Proposals") prior to the date hereof, and assumes that all such Tax Proposals will be enacted as currently proposed. No assurance can be given that the Tax Proposals will be enacted in the form proposed or at all. This summary does not otherwise take into account or anticipate any changes in law, whether by way of legislative, judicial or administrative action or interpretation, nor does it take into account tax laws of any province or territory of Canada or of any other jurisdiction outside Canada.

For purposes of the Tax Act, all amounts, including dividends, adjusted cost base and proceeds of disposition, must generally be determined in Canadian dollars. Amounts denominated in U.S. dollars must be converted to Canadian currency using the "Relevant Spot Rate" (as defined in the Tax Act). The amount of any capital gain or any capital loss to a U.S. Shareholder with respect to the Common Shares may be affected by fluctuations in Canadian dollar exchange rates.

This summary is of a general nature only and is not intended to be, nor should it be construed to be, legal or tax advice to any particular U.S. Shareholder and no representation with respect to the federal income tax consequences to any particular U.S. Shareholder or prospective U.S. Shareholder is made. The tax consequences

Table of Contents

to a U.S. Shareholder will depend on the holder's particular circumstances. Accordingly, U.S. Shareholders should consult with their own tax advisors for advice with respect to their own particular circumstances.

The cost for Canadian tax purposes to a U.S. Shareholder of a Common Share must be averaged at the time such Common Share is acquired with the adjusted cost base of all other Common Shares held by such U.S. Shareholder as capital property at that time for purposes of calculating the adjusted cost base of such Common Shares.

Dividends

Amounts paid or credited or deemed to be paid or credited as, on account or in lieu of payment, or in satisfaction of, dividends on our Common Shares to a U.S. Shareholder will be subject to Canadian withholding tax. Under the Convention, the rate of Canadian withholding tax on dividends paid or credited by us to a U.S. Shareholder that beneficially owns such dividends is generally 15% unless the beneficial owner is a company that owns at least 10% of our voting stock at that time, in which case the rate of Canadian withholding tax is reduced to 5%.

Dispositions

A U.S. Shareholder will generally not be subject to tax under the Tax Act on any capital gain realized on a disposition or deemed disposition of our Common Shares, unless the Common Shares constitute "taxable Canadian property" to the U.S. Shareholder at the time of disposition and the U.S. Shareholder is not entitled to relief under the Convention. Generally, our Common Shares will not constitute taxable Canadian property to a U.S. Shareholder provided our Common Shares are listed on a designated stock exchange (which currently includes NASDAQ and TSX) at the time of the disposition, unless (1) at any time during the 60-month period immediately preceding the disposition, (a) one or any combination of (A) the U.S. Shareholder, (B) persons with whom the U.S. Shareholder did not deal at arm's length, and (C) partnerships in which the U.S. Shareholder or a person described in (B) holds a membership interest directly or indirectly through one or more partnerships, owned 25% or more of the issued shares of any series or class of our capital stock and (b) more than 50% of the fair market value of our Common Shares was derived directly or indirectly from one or any combination of (i) real or immovable property situated in Canada, (ii) "Canadian resource properties" (as defined in the Tax Act), (iii) "timber resource properties" (as defined in the Tax Act), and (iv) options in respect of, or interests in, or for civil law rights in property described in (i) to (iii), whether or not the property exists, or (2) our Common Shares are otherwise deemed to be taxable Canadian property to the U.S. Shareholder.

If our Common Shares constitute taxable Canadian property to a particular U.S. Shareholder, any capital gain arising on their disposition may be exempt from Canadian tax under the Convention if, at the time of disposition, our Common Shares do not derive their value principally from real property situated in Canada as defined in the Convention.

As long as our Common Shares are listed at the time of their disposition on NASDAQ, TSX or another "recognized stock exchange" (as defined in the Tax Act), a U.S. Shareholder who disposes of our Common Shares that are taxable Canadian property will not be required to apply for and obtain a certificate of compliance and will not be subject to withholding by a purchaser under Section 116 of the Tax Act. An exemption from such obligations may also be available in respect of such a disposition if the Common Shares are "treaty-protected property" (as defined in the Tax Act) of the disposing U.S. Shareholder.

LEGAL MATTERS

Certain legal matters relating to the offering will be passed upon for us by Norton Rose Fulbright Canada LLP with respect to matters of Canadian law and by Norton Rose Fulbright US LLP with respect to matters of U.S. law. Wainwright is being represented in connection with this offering by Ellenoff Grossman & Schole LLP with respect to certain matters of U.S. law. At the date of this prospectus supplement, the partners and associates of Norton Rose Fulbright Canada LLP as a group and the partners and associates of Norton Rose Fulbright US LLP as a group, beneficially own, directly or indirectly, less than 1% of the outstanding securities of any class of securities issued by us.

Table of Contents

EXPERTS

The consolidated financial statements incorporated into this prospectus supplement and the accompanying prospectus by reference to our Annual Report on Form 20-F for the financial year ended December 31, 2016, have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, independent auditors, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual reports on Form 20-F with the SEC, and we furnish other documents, such as quarterly and current reports, proxy statements and other information and documents that we file with the Canadian securities regulatory authorities, to the SEC, as required. You may read and copy any materials we file with or furnish to the SEC at the public reference room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the public reference room by calling the SEC at 1-800-SEC-0330. In addition, the SEC maintains an Internet site (www.sec.gov) that contains reports, proxy and information statements and other information regarding registrants who file electronically with the SEC. As we are a Canadian issuer, we also file continuous disclosure documents with the Canadian securities regulatory authorities, which documents are available on the System for Electronic Document Analysis and Retrieval ("SEDAR") website maintained by the Canadian Securities administrators at www.sedar.com.

This prospectus supplement and the accompanying prospectus form part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus regarding us and our Common Shares, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC at the address listed above or electronically at www.sec.gov/edgar.shtml.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

This prospectus supplement and the accompanying prospectus are part of a registration statement on Form F-3 filed by us with the SEC. This prospectus supplement and the accompanying prospectus do not contain all of the information set forth in the registration statement, certain parts of which are omitted in accordance with the rules and regulations of the SEC. Statements contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference into this prospectus supplement or the accompanying prospectus as to the contents of any contract or other document referred to are not necessarily complete and in each instance reference is made to the copy of that contract or other document filed with or furnished to the SEC. For further information about us and the securities offered by this prospectus supplement, we refer you to the registration statement and its exhibits and schedules which may be obtained as described herein.

The SEC allows us to "incorporate by reference" the information contained in documents that we file with or furnish to it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, and information in documents that we subsequently file with or furnish to the SEC and the Canadian securities regulatory authorities will automatically update and supersede information in this prospectus supplement and the accompanying prospectus. We incorporate by reference the documents listed below into this prospectus supplement, and any future filings made by us with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act until the offering of all the securities by this prospectus supplement is completed, including all filings made after the date of this prospectus supplement. We hereby incorporate by reference the documents listed below:

our Annual Report on Form 20-F for the financial year ended December 31, 2016, which includes (i) our consolidated statements of financial position as at December 31, 2016 and December 31, 2015 and our consolidated statements of changes in shareholders' equity, comprehensive loss and cash flows for the years ended December 31, 2016, 2015 and 2014 and the auditors' report dated March 15, 2017 on such consolidated financial statements as Item 18, (ii) management's annual report on internal control over financial reporting included in Item 15, and (iii) our Management's Discussion and Analysis as "Item 5. Operating and Financial Review and Prospects";

Edgar Filing: Aeterna Zentaris Inc. - Form 424B5

Table of Contents

our management information circular dated March 20, 2017 in connection with our annual meeting of shareholders to be held on May 9, 2017, included as Exhibit 99.1 to our Report on Form 6-K furnished to the SEC on March 20, 2017;

our material change report dated January 5, 2017 in connection with the publication of the top-line results of the confirmatory Phase 3 trial of Macrilen , included as Exhibit 99.2 to our Report on Form 6-K furnished to the SEC on January 5, 2017; and

to the extent permitted by applicable securities law, any other documents which we elect to incorporate by reference into this prospectus supplement.

All subsequent annual reports on Form 20-F filed by us and all subsequent reports on Form 6-K filed by us that are identified by us as being incorporated by reference shall be deemed to be incorporated by reference into this prospectus supplement and deemed to be a part hereof after the date of this prospectus supplement but before the termination of the offering by this prospectus supplement.

We will provide each person to whom this prospectus supplement is delivered a copy of all of the information that has been incorporated by reference into this prospectus supplement or the accompanying prospectus but not delivered with this prospectus supplement and the accompanying prospectus. You may obtain copies of these filings, at no cost, by writing or telephoning us at:

Aeterna Zentaris Inc.
Attention: Investor Relations
315 Sigma Drive, Suite 302D
Charleston, South Carolina
USA, 29486
Tel. (843) 900-3223

S-43

Table of Contents

PROSPECTUS

US\$50,000,000

Common Shares

Aeterna Zentaris Inc. ("Aeterna Zentaris", "we", "us" or the "Company") may from time to time during the period that this prospectus (the "Prospectus"), including any amendments hereto, remains valid, offer, sell, and issue under this Prospectus common shares (the "Common Shares") having an aggregate initial offering price of US\$50,000,000 in one or more at-the-market transactions in such amounts and, if applicable, with such terms, as we may determine in light of prevailing market conditions at the time of sale.

The specific terms of any offering of Common Shares will be set out in the applicable supplement to this Prospectus (each, a "Prospectus Supplement"), including, where applicable, the number of Common Shares offered, the manner of determination of the public offering price, the currency in which the Common Shares will be issued and any other specific terms applicable thereto.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR PASSED UPON THE ACCURACY OF THIS PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

Investing in the Common Shares involves a high degree of risk. See "Risk Factors".

Our Common Shares are listed on the NASDAQ Capital Market ("NASDAQ") under the symbol "AEZS" and on the Toronto Stock Exchange ("TSX") under the symbol "AEZ". On March 12, 2014, the last reported sales price of our Common Shares on NASDAQ was \$1.38 per share and on TSX was C\$1.54 per share.

The Common Shares will be sold through agents designated by us from time to time in transactions only in the U.S. that are "at-the-market" offerings. The Common Shares will be offered at prevailing market prices at the time of sale. The Prospectus Supplement will set out the names of any agents involved in the sale of our Common Shares and the plan of distribution for such Common Shares, including the manner of determination of the public offering price and the compensation of any such agents. See "Plan of Distribution".

The date of this Prospectus is March 28, 2014

Table of Contents

TABLE OF CONTENTS

	Page
<u>ABOUT THIS PROSPECTUS</u>	<u>2</u>
<u>OUR BUSINESS</u>	<u>2</u>
<u>RISK FACTORS</u>	<u>3</u>
<u>SPECIAL NOTE ON FORWARD-LOOKING STATEMENTS</u>	<u>3</u>
<u>DESCRIPTION OF SHARE CAPITAL</u>	<u>3</u>
<u>USE OF PROCEEDS</u>	<u>4</u>
<u>PLAN OF DISTRIBUTION</u>	<u>4</u>
<u>CERTAIN INCOME TAX CONSIDERATIONS</u>	<u>5</u>
<u>LEGAL MATTERS</u>	<u>5</u>
<u>EXPERTS</u>	<u>5</u>
<u>ENFORCEABILITY OF CIVIL LIABILITIES</u>	<u>6</u>
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	<u>6</u>
<u>DOCUMENTS INCORPORATED BY REFERENCE</u>	<u>6</u>

Table of Contents

ABOUT THIS PROSPECTUS

This Prospectus is a part of a registration statement that we have filed with the Securities and Exchange Commission ("SEC") utilizing a "shelf" registration process. Under this shelf registration process, we may sell Common Shares in one or more at-the-market offerings for a maximum aggregate offering price of \$50,000,000. This Prospectus provides you with a general description of the Common Shares that we may offer. Each time we sell Common Shares, we will provide a Prospectus Supplement that will contain specific information about the terms of that offering. The Prospectus Supplement may also add, update or change information contained in this Prospectus. If there is any inconsistency between the information in this Prospectus and the applicable Prospectus Supplement, you should rely on the information in the Prospectus Supplement. Before investing in our Common Shares, you should read both this Prospectus and any applicable Prospectus Supplement together with the additional information described under the heading "Where You Can Find More Information".

The financial statements included in or incorporated by reference into this Prospectus have been prepared in accordance with International Financial Reporting Standards ("IFRS") as issued by the International Accounting Standards Board. Our consolidated financial statements are subject to Canadian generally accepted auditing standards and auditor independence standards, in addition to the standards of the Public Company Accounting Oversight Board (United States) and the SEC independence standards, and thus may not be comparable to financial statements of United States ("U.S.") companies.

You should rely only on the information contained in this Prospectus. We have not authorized anyone to provide you with information different from that contained in this Prospectus. The information contained in this Prospectus is accurate only as of the date of this Prospectus, regardless of the time of delivery of this Prospectus or of any sale of our Common Shares.

Unless otherwise stated, currency amounts in this Prospectus are stated in United States dollars, or "\$" or "US\$".

In this Prospectus and in any Prospectus Supplement, unless otherwise indicated, references to "we", "us", "our", "Aeterna Zentaris" or the "Company" are to Aeterna Zentaris Inc., a Canadian corporation, and its consolidated subsidiaries, unless it is clear that such terms refer only to Aeterna Zentaris Inc. excluding its subsidiaries.

OUR BUSINESS

We are a specialty biopharmaceutical company engaged in developing novel treatments in oncology and endocrinology. Our pipeline encompasses compounds at various stages of development.

In oncology, we have an ongoing Phase 3 "ZoptEC" (**Zoptarelin** doxorubicin in **Endometrial Cancer**) trial in endometrial cancer under a Special Protocol Assessment ("SPA") with the U.S. Food and Drug Administration (the "FDA") with zoptarelin doxorubicin (previously referred to by us as AEZS-108), a doxorubicin luteinizing hormone releasing hormone-targeted conjugate compound for which we have successfully completed a Phase 2 trial in advanced endometrial and advanced ovarian cancer. We are also advancing a Phase 2 investigator-driven trial with zoptarelin doxorubicin in castration- and taxane-resistant prostate cancer. Our oncology pipeline also encompasses earlier-stage programs, including AEZS-120, a targeted, live recombinant oral tumor vaccine candidate, and our Erk/PI3K inhibitors, such as AEZS-129 and AEZS-136. We are also investigating various additional compounds as potential treatments for a host of unmet medical needs.

In endocrinology, we filed a New Drug Application ("NDA") in the U.S. for the registration of MACRILEN (previously referred to by us as macimorelin acetate and AEZS-130), for our orally available peptidomimetic ghrelin receptor agonist with growth hormone secretagogue activity in adult growth hormone deficiency ("AGHD"). On January 6, 2014, we announced that the FDA had accepted for substantive review our NDA for MACRILEN in AGHD. The acceptance for filing of the NDA indicates the FDA has determined that the application is sufficiently complete to permit a substantive review. The NDA, submitted on November 5, 2013, seeks approval for the commercialization of MACRILEN, which, if approved, will be the first orally administered drug indicated for the diagnosis of AGHD by evaluating the pituitary gland secretion of growth hormone in response to an oral dose of the product. The application is subject to a standard review and will have

Table of Contents

a Prescription Drug User Fee Act ("PDUFA") date of November 5, 2014. The PDUFA date is the goal date for the FDA to complete its review of the NDA.

Corporate Information

Aeterna Zentaris Inc. was incorporated on September 12, 1990 under the laws of Canada. Our registered address and head office is located at 1405 du Parc-Technologique Boulevard, Quebec City, Quebec, Canada, G1P 4P5, our telephone number is (418) 652-8525 and our website is www.aezsinc.com. None of the documents or information found on our website shall be deemed to be included in or incorporated into this Prospectus, unless such document is specifically incorporated herein by reference.

We currently have three wholly-owned direct and indirect subsidiaries, Aeterna Zentaris GmbH ("AEZS Germany"), based in Frankfurt, Germany, Zentaris IVF GmbH, a direct wholly-owned subsidiary of AEZS Germany, based in Frankfurt, Germany, and Aeterna Zentaris, Inc., an entity incorporated in the State of Delaware based in Basking Ridge, New Jersey in the U.S.

RISK FACTORS

Investing in our Common Shares involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described in the applicable Prospectus Supplement, together with all of the other information incorporated by reference into this Prospectus, including those described in our most recent Annual Report on Form 20-F and subsequent consolidated financial statements and corresponding management's discussion and analysis filed with the Canadian securities regulatory authorities and our Reports on Form 6-K furnished to the SEC including our unaudited interim consolidated financial statements and corresponding management's discussion and analysis.

SPECIAL NOTE ON FORWARD-LOOKING STATEMENTS

This Prospectus and the documents incorporated herein by reference contain forward-looking statements concerning the business, operations, financial performance and condition of the Company. When used in this Prospectus and the documents incorporated herein by reference, words such as "may", "will", "should", "could", "expects", "plans", "seeks", "anticipates", "intends", "believes", "estimates", "predicts", "potential" or "continue" or the negative of these terms and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain such words. These forward-looking statements are based on current expectations and are naturally subject to uncertainty and changes in circumstances that may cause actual results to differ materially from those expressed or implied by such forward-looking statements. Such statements, based as they are on the current expectations of management, inherently involve numerous risks and uncertainties, known and unknown, many of which are beyond our control.

More detailed information about these and other factors is referenced under "Risk Factors" in this Prospectus as well as in other documents incorporated herein by reference. Many of these factors are beyond our control. Future events may vary substantially from what we currently foresee. You should not place undue reliance, if any, on such forward-looking statements. The Company disavows and is under no obligation to update or alter such forward-looking statements whether as a result of new information, future events or otherwise, other than as required by applicable securities legislation.

DESCRIPTION OF SHARE CAPITAL

Our authorized share capital structure consists of an unlimited number of shares of the following classes (all classes are without nominal or par value): Common Shares; and first preferred shares (the "First Preferred Shares") and second preferred shares (the "Second Preferred Shares") and, together with the First Preferred Shares, the "Preferred Shares"), each issuable in series. As of the date of this Prospectus, there are 56,513,969 Common Shares issued and outstanding. No Preferred Shares have been issued to date.

Table of Contents

Common Shares

The holders of the Common Shares are entitled to one vote for each Common Share held by them at all meetings of shareholders, except meetings at which only shareholders of a specified class of shares are entitled to vote. In addition, the holders are entitled to receive dividends if, as and when declared by the Company's Board of Directors on the Common Shares. Finally, the holders of the Common Shares are entitled to receive the remaining property of the Company upon any liquidation, dissolution or winding-up of the affairs of the Company, whether voluntary or involuntary. Shareholders have no liability to further capital calls as all issued and outstanding shares are fully paid and non-assessable.

Preferred Shares

The Preferred Shares are issuable in series with rights and privileges specific to each class. The holders of Preferred Shares are not entitled to receive notice of or to attend or vote at meetings of shareholders. The holders of First Preferred Shares are entitled to preference and priority to any participation of holders of Second Preferred Shares, Common Shares or shares of any other class of shares of the share capital of the Company ranking junior to the First Preferred Shares with respect to dividends and, in the event of the liquidation of the Company, the distribution of its property upon its dissolution or winding-up, or the distribution of all or part of its assets among the shareholders, to an amount equal to the value of the consideration paid in respect of such shares outstanding, as credited to the issued and paid-up share capital of the Company, on an equal basis, in proportion to the amount of their respective claims in regard to such shares held by them. The holders of Second Preferred Shares are entitled to preference and priority to any participation of holders of Common Shares or shares of any other class of shares of the share capital of the Company ranking junior to the Second Preferred Shares with respect to dividends and, in the event of the liquidation of the Company, the distribution of its property upon its dissolution or winding-up, or the distribution of all or part of its assets among the shareholders, to an amount equal to the value of the consideration paid in respect of such shares outstanding, as credited to the issued and paid-up share capital of the Company, on an equal basis, in proportion to the amount of their respective claims in regard to such shares held by them.

Our Board of Directors may, from time to time, provide for additional series of Preferred Shares to be created and issued, but the issuance of any Preferred Shares is subject to the general duties of the directors under the *Canada Business Corporations Act* to act honestly and in good faith with a view to the best interests of the Company and to exercise the care, diligence and skill that a reasonably prudent person would exercise in comparable circumstances.

USE OF PROCEEDS

Unless otherwise specified in a Prospectus Supplement, the net proceeds resulting from the issuance of Common Shares will be used for the general corporate purposes of Aeterna Zentaris, which may include the continued funding of the Company's ongoing drug development activities, which, as of the date of this Prospectus, primarily includes the advancement of its zoptarelin doxorubicin program, the marketing and commercialization of MACRILEN (assuming the FDA issues final approval in the expected timeframe), the potential in-licensing or acquisition of new commercial products or other corporate and business development activities, and the potential expansion of existing product candidates into other indications. All expenses relating to an offering of Common Shares and any compensation paid to underwriters, dealers or agents, as the case may be, will be paid out of our general funds or from the proceeds of any offering under this Prospectus or a Prospectus Supplement. The use of proceeds will be specified in the Prospectus Supplement relating to a particular offering of Common Shares, as required by applicable securities legislation.

PLAN OF DISTRIBUTION

The Common Shares will be sold to one or more purchasers through an agent pursuant to one or more sales agreements to be entered into between us and any such agent. The sales, if any, of Common Shares under the applicable sales agreement and Prospectus Supplement will be made in the U.S. only and will only be made by way of "at-the-market" offerings. The Common Shares may be sold from time to time in one or more transactions at prevailing market prices at the time of sale. The prices at which the Common Shares may be

Table of Contents

offered may vary as between purchasers and during the period of distribution. Any agent's overall compensation will vary depending on the gross proceeds from the sale of such Common Shares.

A Prospectus Supplement will identify each agent engaged by us in connection with the offering and sale of a particular issue of Common Shares, and will also set forth the terms of the offering, including the manner of determination of the public offering price, the proceeds to us and any compensation payable to the agents.

Under the sales agreements which may be entered into by Aeterna Zentaris, agents who participate in the distribution of the Common Shares may be entitled to indemnification by us against certain liabilities, including liabilities arising out of any misrepresentation in this Prospectus and the documents incorporated by reference herein, other than liabilities arising out of any misrepresentation made by agents who participate in the offering of the Common Shares.

CERTAIN INCO