Aeterna Zentaris Inc.
Form 424B5
March 29, 2017

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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.

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.

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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.

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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.

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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 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.

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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".

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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.

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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;

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;

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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;

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.

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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

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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

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

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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.

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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, 2107, 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.

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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

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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

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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

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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

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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