

Aeterna Zentaris Inc.
Form 20-F
March 16, 2017

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

FORM 20-F

Registration Statement Pursuant to Section 12(b) or 12(g) of The Securities Exchange Act of 1934

OR

Annual Report Pursuant to Section 13 or 15(d) of The Securities Exchange Act of 1934 for the fiscal year ended
December 31, 2016

OR

Transition Report Pursuant to Section 13 or 15(d) of The Securities Exchange Act of 1934

OR

Shell Company Report Pursuant to Section 13 or 15(d) of The Securities Exchange Act of 1934

Commission file number 0-30752

AETERNA ZENTARIS INC.

(Exact Name of Registrant as Specified in its Charter)

Not Applicable

(Translation of Registrant's Name into English)

Canada

(Jurisdiction of Incorporation)

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29486

(Address of Principal Executive Offices)

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Summerville, South Carolina

29486

(Name, Telephone, E-mail and Address of Company Contact Person)

Securities registered or to be registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
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Common Shares	NASDAQ Capital Market
---------------	-----------------------

	Toronto Stock Exchange
--	------------------------

Securities registered or to be registered pursuant to Section 12(g) of the Act: NONE

Securities for which there is a reporting obligation pursuant to Section 15(d) of the ACT: NONE

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as at the close of the period covered by the annual report: 12,917,995 Common Shares as at December 31, 2016.

Indicate by check mark whether the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. Yes No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

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Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer or, or a non-accelerated filer. See definitions of "accelerated filer" and "large accelerated filer" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer Accelerated filer Non-accelerated filer

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

US GAAP International Financial Reporting Standards as issued by the Other
International Accounting Standards Board

If "other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow. Item 17 Item 18

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes No

Basis of Presentation

General

Except where the context otherwise requires, all references in this Annual Report on Form 20-F to the "Company", "Aeterna Zentaris Inc.", "we", "us", "our" or similar words or phrases are to Aeterna Zentaris Inc. and its subsidiaries, taken together. In this Annual Report on Form 20-F, references to "\$" and "US\$" are to United States ("US") dollars, references to "CAN\$" are to Canadian dollars and references to "EUR" are to euros. Unless otherwise indicated, the statistical and financial data contained in this Annual Report on Form 20-F are presented as at December 31, 2016. All share, option and share purchase warrant as well as per share, option and share purchase warrant information presented in this Annual Report on Form 20-F have been adjusted, including proportionate adjustments being made to each option and share purchase warrant exercise price, to reflect and to give effect to a share consolidation (or reverse stock split), on November 17, 2015, of our issued and outstanding common shares on a 100-to-1 basis (the "Share Consolidation"). The Share Consolidation affected all shareholders, optionholders and warrantholders uniformly and thus did not materially affect any securityholder's percentage of ownership interest.

This Annual Report on Form 20-F also contains certain information regarding products or product candidates that may potentially compete with our products and product candidates, and such information has been primarily derived from information made publicly available by the companies developing such potentially competing products and product candidates and has not been independently verified by Aeterna Zentaris Inc.

Forward-Looking Statements

This Annual Report on Form 20-F contains forward-looking statements made pursuant to the safe-harbor provision of the US Securities Litigation Reform Act of 1995, which reflect our current expectations regarding future events. Forward-looking statements may include, but are not limited to statements preceded by, followed by, or that include the words "expects," "believes," "intends," "anticipates," and similar terms that relate to future events, performance, or our results. Forward-looking statements involve known risks and uncertainties, which are discussed in this Annual Report on Form 20-F, under the caption "Key Information - Risk Factors" filed with the relevant Canadian securities regulatory authorities in lieu of an annual information form and with the US Securities and Exchange Commission ("SEC"). Such statements include, but are not limited to, statements about the progress of our research, development and clinical trials and the timing of, and prospects for, regulatory approval and commercialization of our product candidates, the timing of expected results of our studies, anticipated results of these studies, statements about the status of our efforts to establish a commercial operation and to obtain the right to promote or sell products that we did not develop and estimates regarding our capital requirements and our needs for, and our ability to obtain, additional financing. Known and unknown risks and uncertainties could cause our actual results to differ materially from those in forward-looking statements. Such risks and uncertainties include, among others, the availability of funds and resources to pursue our research and development projects and clinical trials, the successful and timely completion of clinical studies, the risk that safety and efficacy data from any of our Phase 3 trials may not coincide with the data analyses from previously reported Phase 1 and/or Phase 2 clinical trials, the rejection or non-acceptance of any new drug application by one or more regulatory authorities and, more generally, uncertainties related to the regulatory process (including whether or not the regulatory authorities will accept the Company's conclusions regarding Macrilen™ following its comprehensive review of the Phase 3 study data described elsewhere in this Annual Report on Form 20-F), the ability of the Company to efficiently commercialize one or more of its products or product candidates, the degree of market acceptance once our products are approved for commercialization, our ability to take advantage of business opportunities in the pharmaceutical industry, our ability to protect our intellectual property, the potential of liability arising from shareholder lawsuits and general changes in economic conditions. Investors should consult the Company's quarterly and annual filings with the Canadian and US securities commissions for additional information on risks and uncertainties. Given these uncertainties and risk factors, readers are cautioned not to place undue reliance on these forward-looking statements. We disclaim any obligation to update any such factors or to publicly announce any revisions to any of the forward-looking statements contained herein to reflect future results, events or developments, unless required to do so by a governmental authority or applicable law.

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PART I

Item 1. Identity of Directors, Senior Management and Advisers

A. Directors and senior management

Not applicable.

B. Advisers

Not applicable.

C. Auditors

Not applicable.

Item 2. Offer Statistics and Expected Timetable

A. Offer statistics

Not applicable.

B. Method and expected timetable

Not applicable.

Item 3. Key Information

A. Selected financial data

The consolidated statement of comprehensive (loss) income data set forth in this Item 3.A with respect to the years ended December 31, 2016, 2015 and 2014 and the consolidated statement of financial position data as at December 31, 2016 and 2015 have been derived from the audited consolidated financial statements set forth in Item 18, which have been prepared in accordance with International Financial Reporting Standards ("IFRS"), as issued by the International Accounting Standards Board ("IASB"). The consolidated statement of comprehensive (loss) income information with respect to the years ended December 31, 2013 and 2012 and the consolidated statement of financial position information as at December 31, 2014, 2013 and 2012 set forth in this Item 3.A. have been derived from our previous consolidated financial statements not included herein, and have also been prepared in accordance with IFRS, as issued by the IASB. The selected financial data should be read in conjunction with our audited consolidated financial statements and the related notes included elsewhere in this Annual Report on Form 20-F, as well as "Item 5. – Operating and Financial Review and Prospects" of this Annual Report on Form 20-F.

Consolidated Statements of Comprehensive (Loss) Income Information

(in thousands of US dollars, except share and per share data)

Derived from consolidated financial statements prepared in accordance with IFRS, as issued by the IASB

	December 31,				
	2016	2015	2014	2013	2012
	\$	\$	\$	\$	\$
Revenues					
Sales commission and other	414	297	—	96	834
License fees	497	248	11	6,079	1,219
	911	545	11	6,175	2,053
Operating expenses					
Cost of Sales	—	—	—	51	591
Research and development costs	16,495	17,234	23,716	21,284	20,592
General and administrative expenses	7,147	11,308	9,840	11,091	9,226
Selling expenses	6,745	6,887	3,850	1,225	1,380
	30,387	35,429	37,406	33,651	31,789
Loss from operations	(29,476)	(34,884)	(37,395)	(27,476)	(29,736)
(Loss) gain due to changes in foreign currency exchange rates	(70)	(1,767)	1,879	(1,512)	(382)
Change in fair value of warrant liability	4,437	(10,956)	18,272	1,563	6,746
Warrant exercise inducement fee	—	(2,926)	—	—	—
Other finance income	150	305	168	185	228
Net finance (costs) income	4,517	(15,344)	20,319	236	6,592
Loss before income taxes	(24,959)	(50,228)	(17,076)	(27,240)	(23,144)
Income tax expense	—	—	(111)	—	—
Net loss from continuing operations	(24,959)	(50,228)	(17,187)	(27,240)	(23,144)
Net income from discontinued operations	—	85	623	34,055	2,732
Net (loss) income	(24,959)	(50,143)	(16,564)	6,815	(20,412)
Other comprehensive (loss) income:					
Items that may be reclassified subsequently to profit or loss:					
Foreign currency translation adjustments	569	1,509	(1,158)	1,073	(504)
Items that will not be reclassified to profit or loss:					
Actuarial (loss) gain on defined benefit plans	(1,479)	844	(1,833)	2,346	(3,705)
Comprehensive (loss) income	(25,869)	(47,790)	(19,555)	10,234	(24,621)
Net loss per share (basic and diluted) from continuing operations ¹	(2.41)	(18.17)	(29.12)	(92.41)	(117.04)
Net income per share (basic and diluted) from discontinued operations ¹	—	0.03	1.06	115.53	13.79
Net (loss) income per share (basic and diluted) ¹	(2.41)	(18.14)	(28.06)	23.12	(103.22)
Weighted average number of shares outstanding: ¹					
Basic	10,348,879	2,763,603	590,247	294,765	197,751
Diluted	10,665,149	3,424,336	590,247	294,765	198,067

¹ Adjusted to reflect the November 17, 2015 100-to-1 Share Consolidation

Consolidated Statement of Financial Position Information

(in thousands of US dollars)

Derived from consolidated financial statements prepared in accordance with IFRS, as issued by the IASB

	As at December 31,				
	2016	2015	2014	2013	2012
	\$	\$	\$	\$	\$
Cash and cash equivalents	21,999	41,450	34,931	43,202	39,521
Restricted cash equivalents	496	255	760	865	826
Total assets	31,659	51,498	47,435	59,196	67,665
Warrant liability (current and non-current portion)	6,854	10,891	8,225	18,010	6,176
Share capital	213,980	204,596	150,544	134,101	122,791
Shareholders' equity (deficiency)	6,212	21,615	14,484	17,064	(6,695)

B. Capitalization and indebtedness

Not applicable.

C. Reasons for the offer and use of proceeds

Not applicable.

D. Risk factors

An investment in our securities involves a high degree of risk. You should carefully consider the risks described below, together with all of the other information included in this annual report, before making an investment decision. If any of the following risks actually occurs, our business, prospects, financial condition or results of operations could suffer. In that case, the trading price, if any, of our securities could decline, and you may lose all or part of your investment.

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 or other securities 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 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 or the value of our Common Shares or other securities.

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 or the value of our other securities 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 Annual Report on Form 20-F;
- 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 and/or the value of our other securities 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 or a decline in the value of our other securities.

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 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.

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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 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 and/or a decline in the value of our other securities.

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: (i) of such authorities; (ii) for informed consent; and (iii) 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.

Our financial viability 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 or 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 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 Annual Report on Form 20-F; 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.

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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 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 U.S. Food and Drug Administration ("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 reimportation 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 proposed legislation intended to replace the ACA. 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 ACA 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 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.

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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 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 and/or a decline in the value of our other securities.

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 and/or the value of our other securities 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. Federal 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 patient programs, and reform government program reimbursement methodologies for drugs. 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 an adequate level 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 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.

Some of our patents have recently expired.

The product development timelines for our products is 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 as well as 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 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 of 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 European Medicines Agency ("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);
- 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
- 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 and/or a decline in the value of our other securities.

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.

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.

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 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 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 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 in "Item 10.E - Taxation - Certain Material U.S. Federal Income Tax Considerations" in this annual report on Form 20-F) 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. 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 “Item 10.E - Taxation - Certain Material U.S. Federal Income Tax Considerations” in this annual report on Form 20-F. 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.

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

Our Common Shares may be delisted from the NASDAQ Capital Market ("NASDAQ") or the Toronto Stock Exchange ("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.

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.

As adjusted for and giving effect to the Share Consolidation, between January 1, 2016 and December 31, 2016, the closing price of our Common Shares ranged from \$2.67 to \$4.94 per share on NASDAQ and from C\$3.85 to C\$6.62 per share on TSX. 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. 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 or any of our other securities will appreciate in value or even maintain the price at which shareholders have purchased them.

Future issuances of securities and hedging activities may depress the trading price of our Common Shares. Any additional or future issuance of Common Shares or Convertible Securities, including the issuance of Common Shares upon the exercise of stock options and upon the exercise of warrants, could dilute the interests of our existing shareholders, and could substantially decrease the trading price of our Common Shares. For example, in connection with our At Market Issuance ("ATM") Sales Agreement with H.C. Wainwright & Co., LLC (the "April 2016 ATM Program"), we may, at our discretion, from time to time during the term of the April 2016 ATM Program, sell up to a maximum of 3,000,000 Common Shares through ATM issuances on the NASDAQ Stock Market, up to an aggregate amount of approximately \$10 million at market prices prevailing at the time of the sale of the Common Shares. Under both our April 2016 ATM Program and our shelf registration statement on Form F-3 or any replacement thereof upon its expiration, we may issue and sell additional Common Shares by way of one or more ATM distribution programs. 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 March 15, 2017, there were:

13,473,063	Common Shares issued and outstanding
—	Preferred Shares issued and outstanding
3,779,245	Common Shares issuable upon exercise of outstanding warrants
968,264	Stock Options outstanding
567,665	Additional Common Shares available for future grants under our stock option plan

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.

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 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.

Item 4. Information on the Company

A. History and development of the Company

We are a specialty biopharmaceutical company engaged in developing and commercializing novel treatments in oncology, endocrinology and women's health.

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 located at 1 Place Ville Marie, Suite 2500, Montréal, Quebec, Canada H3B 1R1, c/o Norton Rose Fulbright Canada LLP. Our executive offices are located at 315 Sigma Drive, Suite 302D, Summerville, South Carolina 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 Annual Report on Form 20-F, unless such document is specifically incorporated herein by reference.

On December 30, 2002, we acquired Zentaris AG, a biopharmaceutical company based in Frankfurt, Germany.

Zentaris was a spin-off of Asta Medica GmbH, a former pharmaceutical company affiliated with Degussa AG.

In May 2004, we changed our name to Aeterna Zentaris Inc. and on May 11, 2007, Zentaris GmbH was renamed Aeterna Zentaris GmbH ("AEZS GmbH"). AEZS GmbH conducts our drug development efforts. In September 2007, we incorporated Aeterna Zentaris, Inc. under the laws of Delaware. This wholly-owned subsidiary, which is based in the Charleston, South Carolina area, conducts our commercial operations.

On October 1, 2013, we announced the completion of our previously announced agreements with various partners and licensees with respect to the manufacturing rights and obligations for our Cetrotide[®] product. The principal outcome of such agreements was the transfer of all manufacturing rights and the grant of a license to a subsidiary of Merck KGaA of Darmstadt, Germany for the manufacture, testing, assembling, packaging, storage and release of Cetrotide[®] in all territories (the "Cetrotide[®] Business"). Following this transfer and since the year ended December 31, 2013, the Cetrotide[®] Business has been presented in our consolidated financial statements as a discontinued operation. Except for this discontinued operation, we have not made any material divestitures or capital expenditures from 2013 to the present.

On November 17, 2015, we effected a 100-to-1 Share Consolidation (reverse stock split). Our Common Shares commenced trading on a consolidated and adjusted basis on both NASDAQ and TSX on November 20, 2015.

We currently have three wholly-owned direct and indirect subsidiaries, AEZS GmbH, 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 with an office in the Charleston, South Carolina area in

the United States.

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Aeterna
Zentaris
Inc.
(Canada)

100% 100%

Aeterna Zentaris GmbH (Germany)	Aeterna Zentaris, Inc. (Delaware)
--	--

100%

Zentaris
IVF
GmbH
(Germany)

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

Our agent for service of process and SEC matters in the United States is our wholly-owned subsidiary, Aeterna Zentaris, Inc., located at 315 Sigma Drive, Suite 302D, Summerville, South Carolina 29486.

There have been no public takeover offers by third parties with respect to us or by us in respect of other companies' shares during the last or current financial year.

Recent Developments

For a complete description of our recent corporate and pipeline developments, refer to "Item 5. - Operating and Financial Review and Prospects - Key Developments".

B. Business overview

We are engaged in drug development activities and in the promotion of products for others. We have two Phase 3 product candidates in development. The focus of our business development efforts is the acquisition or license of 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 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 and by 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 Business Strategy

Our primary business strategy is to finalize the development and 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™ is subject to receiving positive top-line results, and the registration of Macrilen™ is subject to the outcome of our meeting with the FDA scheduled for the end of March 2017. Our vision is to become a growth-oriented specialty biopharmaceutical company.

Overview of our Drug Development Efforts

Status of Our Drug Pipeline

Pipeline Supporting Long-Term Growth

Outsourcing and Out-Licensing Non-Strategic Activities/Assets

Our drug development efforts are focused currently on two compounds, Zoptrex™ and Macrilen™, which are in Phase 3 clinical development, and 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 following a review of our portfolio, during which we concluded that 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™

Overview

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 advanced 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.

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 ZoptEC under a Special Protocol Assessment (“SPA”) with the FDA. The SPA agreement states that the proposed trial protocol design, clinical endpoints and planned analyzes 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 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.

The illustration above depicts the believed mode of action of our hybrid cytotoxic compound Zoptrex™. The LHRH receptor targeting part of the hybrid is believed to transport doxorubicin to a cancer cell presenting the LHRH receptor, which leads to the death of the cancer cell.

ZoptEC was conducted by Ergomed plc, a contract clinical development organization with which we have entered into a co-development and profit-sharing agreement. Under the terms of the agreement, Ergomed agreed to assume 30% (up to \$10 million) of the clinical and regulatory costs for ZoptEC. Ergomed will receive its return on investment based on an agreed single-digit percentage of any net income or net proceeds from licensing activity we receive for Zoptrex™ in this indication, up to a specified maximum amount.

We are attempting to commercialize Zoptrex™ as a treatment for endometrial cancer because, according to the American Cancer Society, endometrial cancer is the most common invasive gynecologic cancer in women in the United States, with approximately 61,000 new cases and 10,000 deaths annually. This disease primarily affects post-menopausal women at an average age of 60 years at diagnosis. To the best of our knowledge, there is no systemic therapy approved in either the United States or Europe (except in Germany, where doxorubicin is approved for this indication) for treating advanced or recurrent endometrial cancer.

We have licensed the development, commercialization and certain other rights to Zoptrex™ to Sinopharm A-Think for China, Hong Kong and Macau; to an affiliate of Orient EuroPharma Co., Ltd. for Taiwan and southeast Asia; to Rafa Laboratories, Ltd for Israel and the Palestinian territories and to Specialised Therapeutics Asia Pte Ltd for Australia and New Zealand.

Development History

The following is a summary of the history of our development of Zoptrex™ in ovarian and endometrial cancer: In 2007, a Phase 2 open-label, non-comparative, multi-center two-indication trial stratified with two stages Simon Design was prepared. The study was planned to involve up to 82 patients, with up to 41 patients each with a diagnosis of platinum-resistant ovarian cancer (stratum A) or disseminated endometrial cancer (stratum B). Under coordination by Prof. Günter Emons, M.D., Chairman of the Department of Obstetrics & Gynecology at the University of Göttingen, Germany, this open-label, multi-center and multinational Phase 2 study “AGO-GYN 5” was conducted by the German AGO Study Group (Arbeitsgemeinschaft Gynäkologische Onkologie / Gynaecologic Oncology Working Group), in cooperation with clinical sites in Europe. An intravenous infusion of Zoptrex™ (267 mg/m²) was administered on every first day of a 21-day (three-week) cycle. The proposed duration of the study treatment was six cycles. The study was performed with 14 centers of the German Gynaecological Oncology Working Group, in cooperation with three clinical sites in Europe. The primary efficacy endpoint was a response rate with a success criterion at the end of Stage II defined as five or more patients with partial or complete tumor responses according to Response Evaluation Criteria in Solid Tumors (“RECIST”) and/or Gynaecologic Cancer Intergroup (“GCIG”) guidelines. Secondary endpoints included time to progression (“TTP”), survival and toxicity, as well as adverse effects. In October 2008, we announced that we had entered the second stage of patient recruitment for the Phase 2 trial in the platinum-resistant ovarian cancer indication. This decision was taken following the report of two partial responses (“PR”) among patients with ovarian cancer. The second stage of patient recruitment for the endometrial cancer indication was reached in November 2008 and was based on the report of one complete response (“CR”) and two PR among 14 patients with endometrial cancer.

On June 7, 2010, Prof. Emons initially presented positive efficacy and safety data for Zoptrex™ in ovarian cancer at the American Society of Clinical Oncology’s (“ASCO”) Annual Meeting, now published in an article entitled “Phase 2 study of AEZS-108, a targeted cytotoxic LHRH analog, in patients with LHRH receptor-positive platinum resistant ovarian cancer” in the journal *Gynecologic Oncology* (*Gynecol.Oncol.* (2014) 133:427). Efficacy included PR in six patients (14.3%) and stable disease for more than twelve weeks in 16 patients (38%). Based on those data, a clinical benefit rate (“CBR”) of 52% was estimated. Median TTP and OS were evaluated at 2.8 months (12 weeks) and 12.2 months (53 weeks), respectively. Prof. Emons concluded that: (i) Zoptrex™ was efficacious and well tolerated in patients with heavily pre-treated platinum- and taxane-resistant ovarian cancer; (ii) the safety profile confirmed the dose of 267 mg/m²; (iii) hematological toxicity was rapidly reversible; (iv) non-hematological toxicities were usually limited to lower severity; (v) tolerability and CBR compared with topotecan and liposomal doxorubicin; (vi) no cardiotoxic events were observed; and (vii) OS was encouraging as all patients treated with Zoptrex™ had platinum-resistant disease.

On September 14, 2011, Prof. Emons presented positive final Phase 2 efficacy and safety data for Zoptrex™ in advanced endometrial cancer at the European Society of Gynecological Oncology in Milan, Italy. The results of the

study were published in an article by Prof. Emons, et al. in the journal Gynecologic Oncology (Gynecol.Oncol. (2014) 24:260). The study involved 43 patients with LHRH positive advanced or recurrent endometrial cancer. Patients received Zoptrex™ at a dose of 267 mg/m² by intravenous infusion, with retreatment every three weeks, for up to six courses. Response rate per RECIST was defined as the primary endpoint. Secondary endpoints were safety, TTP and OS. The responses, as confirmed by independent review, included two patients with complete response (5%), eight patients with PR (18%) and 20 patients with stable disease (“SD”) (47%). Based on such data, the estimated overall response rate (“ORR”) (ORR=CR+PR) was 23% and the CBR was 70%. Responses were also achieved in patients with prior chemotherapy - two PR and three SD in eight of the patients pre-treated with platinum/taxane regimens. Median TTP and OS were seven months (30 weeks) and 14.9 months (62 weeks), respectively. Prof. Emons concluded as follows: (i) Zoptrex™ was efficacious and well tolerated in patients with advanced endometrial

cancer; (ii) the safety profile confirmed the dose of 267 mg/m²; (iii) hematological toxicity was rapidly reversible; (iv) non-hematological toxicities were usually not severe, causing few deviations from scheduled treatment; (v) no cardiotoxic events were observed; (vi) the ORR of 23% compared well with those of single-agent platinum or taxane treatment; (vii) responders included patients pre-treated with platinum/taxane combination; (viii) in addition, the rate of SD was 47%, resulting in a CBR of 70%; and (ix) the OS after single agent Zoptrex™ was similar to that reported for modern triple combination chemotherapy, but was achieved with lower toxicity.

On April 27, 2015, we announced that the independent Data Safety Monitoring Board (“DSMB”) for the ZoptEC study had completed a pre-specified first interim futility analysis following the deaths of approximately 124 patients in the study and recommended that the Phase 3 study continue as planned.

On October 13, 2015, we announced that the DSMB had completed a pre-specified second interim analysis of the efficacy and safety of Zoptrex™ in the ZoptEC study following the deaths of approximately 192 patients in the study and recommended that the ZoptEC study continue as planned.

On January 30, 2017, we announced the occurrence of the 384th death in the ZoptEC study. We stated in the announcement that we expect to lock the clinical database and to report top-line results in April 2017.

Competition

The following products are among some of the many products currently in clinical trial in endometrial cancer:

Drug	Co-administered drugs & comparator arm	Target	Indication	Clinical Trial/ Approval Status	Innovator	Primary Endpoint	Comments/ Clinical History/ Commercial History/ Previous Phase 2 discontinued by Eisai for combo therapy trials 90-patient trial, still ongoing, but not recruiting patients 56-patient trial, PFS/tumor response data in H2/16, study completed Q1/15
Lenvatinib (E7080)	Paclitaxel	Tyrosine kinase VEGFR2 inhibitor, multi-targeted	Recurrent Endometrial cancer	Phase 1, Interventional	Eisai, OSUCCC	MTD of lenvatinib when given w/ paclitaxel	
MK-2206	Monotherapy	Serine/ threonine kinase Akt inhibitor	Recurrent, advanced endometrial cancer	Phase 2, two-arm, only patients with PIK3CA mutation	US NCI (Astra--Zeneca-Merck partnered drug)	Objective response, PFS	
Buparlisib (BKM120)	Monotherapy	Phosphatidylinositol-3-kinase (PI3K)-Akt-mTOR pathway inhibitor	Second-line endometrial cancer	Phase 2 (ENDOPIK)	Novartis	ORR/PFS out to six months	
GSK 2141795	Mekinist (trametinib, MEK inhibitor)	Akt inhibitor	Recurrent, persistent endometrial cancer	Phase 2, control arm is Mekinist alone	US NCI (is GSK drug, but GSK not identified as sponsor)	PFS, up to five years, impact of Kras status on response	148-patient interim PFS data by H1/17

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Virexxa (Cridanimod Progesterone sodium)		Carboxymethyl-acridinone; elevates PrR expression	Recurrent, persistent endometrial cancer (PrR-negative)	Phase 2	Pharmsynthez (Estonia), AS Kevelt	ORR at one year, PFS at two years	58-patients first enrolled in Jan/15; data in H2/18
Cabozantinib s-malate (Exelixis' Comitriq)	Monotherapy	Multi-kinase inhibitor, already approved in thyroid cancer	Recurrent, metastatic endometrial cancer	Phase 2	US NCI (Exelixis not identified as partner)	ORR/PFS out to three months	72-patient, still recruiting
LY3023414	Monotherapy	PI3K-mTOR dual inhibitor	Recurrent endometrial cancer	Phase 2 (multiple cancer forms)	MSKC, Eli Lilly	Three-month CBR, one-year O/S	25-patient, single-arm, estimated completion Q3/17

The following products are among some of the many products currently in clinical trial in endometrial cancer (continued):

Drug	Co-administered drugs & comparator arm	Target	Indication	Clinical Trial/ Approval Status	Innovator	Primary Endpoint	Comments/ Clinical History/ Commercial History
IMMU-132	Monotherapy	TROP-2-targeted mAb linked to SN38 (metabolite of irinotecan)	Endometrial cancer	Phase 1/2 (multiple epithelial cancers being tested simultaneously)	Immuno medics	Safety, tumor response	250-patient, estimated completion Q2/18
KPT-330 (Selinexor)	Monotherapy	XPO1 (nuclear export protein) antagonist	Advanced gynecologic cancers	Phase 2	Karyopharm Therapeutics	Safety, survival, QoL	105-patient, two-year survival data in H2/17 80-patient, adverse event rate & response rate data in H2/17
HuMax-TF-ADC	Monotherapy	Tissue factor-targeted mAb lined to auristatin	Solid tumors, including endometrial cancer	Phase 1/2	Genmab	Safety, PK, response rate	56 -patient, study completed in H2/11, no Phase 3 listed
Bevacizumab (Genentech's Monotherapy Avastin)		VEGF-A inhibitor	Recurrent, Persistent Endometrial Cancer	Phase 2 Interventional	US NCI (Genentech drug, but Genentech listed as sponsor)	PFS greater than 6 months	56 -patient, study completed in H2/11, no Phase 3 listed

Additional Indications

We believe that Zoptrex™ may be useful in treating other cancers, including breast cancer, bladder cancer and prostate cancer. We terminated early clinical trials of the compound as a treatment for triple-negative breast cancer and bladder cancer as part of our ongoing review of our development activities to ensure the most effective use of our resources.

We assisted Dr. Jacek Pinski, Associate Professor of Medicine at the Norris Comprehensive Cancer Center of the University of Southern California, to conduct a Phase 1/2 study in refractory prostate cancer with Zoptrex™. Dr. Pinski received a \$1.6 million grant from The National Institutes of Health (“NIH”) to conduct the study. The study, entitled “A Phase I/II Trial of AN-152 [AEZS-108] in Castration-and Taxane-Resistant Prostate Cancer”, was conducted in two portions: an abbreviated dose-escalation study followed by a single arm, Simon Optimum two-stage design Phase 2 study, using the dose selected in the Phase 1 portion.

The following is a summary of Dr. Pinski's study:

On December 14, 2010, we announced the initiation of the Phase 1/2 trial.

On February 3, 2012, we reported updated results for the Phase 1 portion of the study. The results were based on 13 patients who had been previously treated with androgen-deprivation therapy (LHRH agonist) and at least one taxane-based chemotherapy regimen, who were treated on three dose levels of Zoptrex™: three at 160 mg/m², three at 210 mg/m², and seven at 267 mg/m². Overall, Zoptrex™ was well tolerated among this group of heavily pretreated older patients. There were two dose-limiting toxicities, each of which having been a case of asymptomatic Grade 4 neutropenia at the 267 mg/m² dose level and both patients fully recovered. The Grade 3 and 4 toxicities were primarily hematologic. There was minimal non- hematologic toxicity, most frequently fatigue and alopecia. Despite the low doses of Zoptrex™ in the first cohorts, there was some evidence of antitumor activity. One patient received

eight cycles (at 210 mg/m²) due to continued benefit. Among the five evaluable patients with measurable disease, four achieved stable disease. At the time of submission of the abstract, a decrease in PSA was noted in six patients. Six of 13 (46%) treated patients received at least five cycles of therapy with no evidence of disease progression at twelve weeks. Correlative studies on CTC demonstrated the uptake of Zoptrex™ into the targeted tumor.

On November 12, 2012, we announced the initiation of the Phase 2 portion of Dr. Pinski's Phase 1/2 study of Zoptrex™ in prostate cancer. This was a single-arm Simon Optimum design Phase 2 study of Zoptrex™ in 25 patients with CRPC. Patients received Zoptrex™ (210 mg/m²) intravenously over two hours, every three weeks. The primary endpoint was CB, defined as remaining progression-free by RECIST and PSA after treatment for 12+ weeks. Secondary endpoints were progression free survival ("PFS"), best overall response, toxicity, pain and OS.

On June 3, 2013, we announced that final data for the Phase 1 portion of Dr. Pinski's Phase 1/2 trial with Zoptrex™ in prostate cancer demonstrated the compound's promising anti-tumor activity. Results were presented by Dr. Pinski during a poster session at the ASCO Annual Meeting in Chicago. The results of the study were published in an article by Liu et al in the journal *Clinical Cancer Research* (*Clin. Cancer Res.* (2014) 20:6277). Eighteen men were treated at three dose levels: (i) 160 mg/m²; (ii) 210 mg/m²; and (iii) 267 mg/m². Overall, Zoptrex™ was well tolerated among this group of heavily pretreated patients. There were two dose-limiting toxicities (grade four neutropenia and grade three febrile neutropenia), prompting de-escalation to 210 mg/m² and establishing it as the Maximum Tolerated Dose. Among the 15 evaluable patients with measurable disease, ten achieved SD, and a drop in PAS was noted in three patients.

On September 28, 2015, Dr. Pinski announced during a poster session at the 18th ECCO - 40th ESMO European Cancer Congress in Vienna, Austria, that among the 25 patients in the Phase 2 portion of the trial, 11 patients experienced CB as the primary endpoint and 13 patients achieved SD. Maximal PSA response was stable in 20 patients. Pain assessment improved for 11 patients. Zoptrex™ was well tolerated in this heavily pretreated patient population with hematological toxicities, usually limited to grade three, as the most common adverse events. Dr. Pinski concluded that Zoptrex™ was well tolerated and met the primary efficacy endpoint in castration- and taxane-resistant prostate cancer patients.

On February 14, 2017, we announced that Dr. Pinski presented the abstract of his Phase 1/2 trial of Zoptrex™ in castration and taxane-resistant prostate cancer at the ASCO/ASTRO/SVO 2017 Genitourinary Cancer Symposium. We believe that immuno-modulatory and targeted therapies have been key areas of innovation in oncology over the last few years. Zoptrex™ is a targeted cytotoxic therapy using a peptide as the targeting agent and is therefore part of the ongoing innovation in the treatment of cancer. Furthermore, we believe that Zoptrex™ is ahead of many of the immuno-oncology products that are in development. Due to our lack of resources, we intend to pursue the development of Zoptrex™ for indications other than endometrial cancer by seeking development partners to assist with the effort.

Macrilen™

Macrilen™ 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 EMA that Macrilen™ was rejected as proposed invented name for macimorelin because of its similarity to the names of other medicines. We intend to appeal this decision.

Competitors for Macrilen™ as a product for the evaluation of AGHD are principally the diagnostic tests currently performed by endocrinologists, although none of these tests are approved by the FDA for this purpose. The most commonly used diagnostic tests for GHD are:

Measurement of blood levels of Insulin Growth Factor ("IGF")-1, which is typically used as the first test when GHD is suspected. However, this test is not used to definitively diagnose GHD because many growth hormone deficient patients show normal IGF-1 levels.

The Insulin Tolerance Test ("ITT"), which has historically been considered the gold standard for the evaluation of AGHD because of its high sensitivity and specificity. However, the ITT is inconvenient to both patients and physicians, administered intravenously (IV), and contra-indicated in certain patients, such as patients with coronary heart disease or seizure disorder, because it requires the patient to experience hypoglycemia to obtain a result. Some physicians will not induce full hypoglycemia, intentionally compromising accuracy to increase safety and comfort for the patient. Furthermore, administration of the ITT includes additional costs associated with the patient being closely monitored by a physician for the two- to four-hour duration of the test and the test must be administered in a setting where emergency equipment is available and where the patient may be quickly hospitalized. The ITT is not used for patients with co-morbidities, such as cardiovascular disease, seizure disorder or a history of brain cancer or for patients who are elderly and frail, due to safety concerns.

The Glucagon Stimulation Test (“GST”) is considered relatively safe by endocrinologists. The mechanism of action for this test is unclear. Also, this test takes up to three to four hours. It produces side effects in up to one-third of the patients with the most common being nausea during and after the test. This test is administered intramuscularly (IM). The GHRH + ARG test (growth hormone releasing hormone-arginine stimulation) which is an easier test to perform in an office setting and has a good safety profile but is considered to be costly to administer compared to the ITT and the GST. GHRH + ARG is approved in the EU and has been proposed to be the best alternative to ITT, but GHRH is no longer available in the United States. This test is administered intravenously (IV).

Oral administration of Macrilen™ offers convenience and simplicity over the current GHD tests used, all of which require either intravenous or intramuscular administration. Additionally, Macrilen™ may demonstrate a more favorable safety profile than existing diagnostic tests, some of which may be inappropriate for certain patient populations, e.g. diabetes mellitus or coronary heart disease, and have demonstrated a variety of side effects, which Macrilen™ has not thus far. These factors may be limiting the use of GHD testing and may potentially enable Macrilen™ to become the product of choice in evaluating AGHD. We believe that Macrilen™, if it is approved, is likely to rapidly displace the ITT as the preferred means of evaluating AGHD for the following reasons:

- it is safer and more convenient than the ITT because it does not require the patient to become hypoglycemic;
- Macrilen™ is administered orally, while the ITT requires an intravenous injection of insulin;
- Macrilen™ is a more robust test than the ITT leading to evaluable test results;
- Macrilen™ results are highly reproducible;
- the evaluation of AGHD using Macrilen™ is less time-consuming and labor-intensive than the ITT ; and
- the evaluation can be conducted in the physician's office rather than in a hospital-like setting.

We believe that approximately 40,000 AGHD tests will be conducted annually, in the U.S, after the introduction of Macrilen™. In addition, based on published information from the U.S. Centers for Disease Control and Prevention, different scientific publications and Navigant Research, we estimate that the total potential US market for AGHD evaluation is approximately 150,000 tests per year, including the evaluation of patients who have suffered traumatic brain injury (“TBI”). In patients with TBI, GHD is frequent and may contribute to cognitive sequelae and reduction in quality of life. GHD may develop in approximately 19% of both severe and moderate hospitalized TBI victims.

Development History

The following is a summary of the history of our development of Macrilen™ :

We out-licensed the development compound macimorelin acetate to Ardana Bioscience in 2004. Ardana Bioscience subsequently initiated the clinical development program of macimorelin acetate as an orally active compound intended to be used in the diagnosis of adult growth hormone deficiency. Following agreement with the FDA on the study design, Ardana Bioscience initiated a pivotal Phase 3 study in 2007, which tested the compound compared to a test of growth hormone- releasing hormone (“GHRH”) + L-Arginine (“ARG”), using a competitor's compound. The study was discontinued in 2008 due to Ardana Bioscience's bankruptcy. We terminated Ardana Bioscience's license to the compound due to its bankruptcy.

On October 19, 2009, we announced that we had initiated activities intended to complete the clinical development of Macrilen™ for use in evaluating AGHD. We had already assumed the sponsorship of the IND from Ardana Bioscience and discussed with the FDA the best way to complete the ongoing Phase 3 clinical trial and subsequently to file an NDA for approval of Macrilen™ for use in evaluating AGHD. The pivotal Phase 3 trial was designed to investigate the safety and efficacy of the oral administration of Macrilen™ as a growth hormone stimulator for use in evaluating AGHD. It was accepted by the FDA that for the ongoing part of the study, Macrilen™ would not be compared to the GHRH + ARG test because the competitor's compound had been removed from the market.

On December 20, 2010, we announced we had reached agreement with the FDA on a SPA for Macrilen™, enabling us to complete the ongoing registration study required to gain approval for use in evaluating AGHD. The first part of the study, conducted by our former licensee, Ardana, was a two-way cross-over study and included 42 patients with confirmed AGHD or multiple pituitary hormone deficiencies and a low IGF-1. A control group of ten subjects without AGHD was matched to patients for age, gender, body mass index and (for females) estrogen status.

On July 26, 2011, we announced the completion of the Phase 3 study of Macrilen™ as a first oral product for use in evaluating AGHD and the decision to meet with the FDA for the future filing of an NDA for the registration of Macrilen™ in the United States.

On June 26, 2012, we announced that the final results from a Phase 3 trial for Macrilen™ showed that the drug is safe and effective in evaluating AGHD. Jose M. Garcia, MD, PhD, then of the Baylor College of Medicine and the Michael E. DeBakey VA Medical Center, disclosed these data during an oral presentation at the 94th ENDO Annual Meeting and Expo in Houston, Texas. The study had originally been designed as a cross-over trial of Macrilen™ compared to the GHRH + ARG test in AGHD patients and in controls matched for body mass index (“BMI”), estrogen status, gender and age. After 43 AGHD patients and ten controls had been tested, the GHRH + ARG test became

unavailable because the competitor's compound was withdrawn from the market. The study was completed by testing ten more AGHD patients and 38 controls with Macrilen™ alone. Of the 53 AGHD subjects enrolled, 52 received Macrilen™, and 50 who had confirmed AGHD prior to study entry

were included in this analysis, along with 48 controls. Two AGHD subjects could not be matched due to the combination of young age, high BMI and estrogen use. The objective of this clinical trial was to determine the efficacy and safety of Macrilen™ in the evaluation of AGHD. Mean peak growth hormone ("GH") levels in AGHD patients and controls following Macrilen™ administration were 2.36ng/mL (range 0.03-33) and 17.71ng/mL (range 10.5-94), respectively. The ROC plot analysis yielded an optimal GH cut-point of 2.7ng/mL, with 82% sensitivity, 92% specificity and a 13% misclassification rate. Obesity (BMI>30) was present in 58% of cases and controls, and peak GH levels were inversely associated with BMI in controls. Adverse events ("AE") were seen in 37% of AGHD patients and in 21% of controls following Macrilen™. In contrast, 61% of AGHD subjects and 30% of controls experienced AEs with L ARG+GHRH. The most common AEs after Macrilen™ were unpleasant taste (19.2%) and diarrhea (3.8%) for the AGHD patients and unpleasant taste (4.2%) and diarrhea (4.2%) for the matched controls. No clinically meaningful changes from baseline in ECG results during the study for AGHD patients were observed; however, one control subject had an ECG change (T wave abnormality and QTc interval prolongation) one hour after treatment with Macrilen™ that was considered a serious treatment-related adverse event and resolved spontaneously within 24 hours. The subject had been pre-treated with citalopram, a drug that was later reported by the FDA to be associated with QT prolongation, although the patient had stopped this medication seven days prior to dosing. In an expert statement of January 9, 2015, Prof. Dr. W. Haverkamp, Centrum Herz-, Kreislauf- und Gefäßmedizin, Charité, Berlin, considered the observed QT prolongation to be not related to Macrilen™. Overall, this study demonstrated that Macrilen™ is safe and effective for use in evaluating AGHD.

In November 2013, we filed an NDA for Macrilen™ for the evaluation of AGHD by evaluating the pituitary gland secretion of growth hormone in response to an oral dose of the product. The FDA accepted the NDA for substantive review in January 2014. On November 6, 2014, the FDA informed us, by issuing a Complete Response Letter ("CRL"), that it had determined that our NDA could not be approved in its then present form. The CRL stated that the planned analysis of our pivotal trial did not meet its stated primary efficacy objective as agreed to in the SPA. The CRL further mentioned issues related to the lack of complete and verifiable source data for determining whether patients were accurately diagnosed with AGHD. The FDA concluded that, "in light of the failed primary analysis and data deficiencies noted, the clinical trial does not by itself support the indication." To address the deficiencies identified above, the CRL stated that we needed to demonstrate the efficacy of Macrilen™ as a diagnostic test for GHD in a new, confirmatory clinical study. The CRL also stated that a serious event of electrocardiogram QT interval prolongation occurred for which attribution to drug could not be excluded. Therefore, a dedicated thorough QT study to evaluate the effect of macimorelin on the QT interval would be necessary.

Following receipt of the CRL, we assembled a panel of experts in the field of growth-hormone deficiency, including experts in the field from both the United States of America and the EU. The panel met on January 8, 2015, during which we discussed our conclusions from the CRL, as well as the potential design of a new pivotal study. The panel advised us to continue to seek approval for Macrilen™ because of their confidence in its efficacy and because there currently is no FDA-approved diagnostic test for AGHD. In parallel, we collected information on timelines and costs for such a study.

During an end-of-review meeting with the FDA on March 6, 2015, we agreed with the FDA on the general design of the confirmatory Phase 3 study of Macrilen™ for the evaluation of AGHD, as well as evaluation criteria. We agreed with the FDA that the confirmatory study will be conducted as a two-way crossover with the ITT as the benchmark comparator.

On April 13, 2015, we announced plans to conduct a new, confirmatory Phase 3 clinical study to demonstrate the efficacy of Macrilen™ for the evaluation of AGHD, as well as a dedicated thorough QT study to evaluate the effect of Macrilen™ on myocardial repolarization. The confirmatory Phase 3 clinical study of Macrilen™, entitled "Confirmatory validation of oral macimorelin as a growth hormone (GH) stimulation test (ST) for the diagnosis of adult growth hormone deficiency (AGHD) in comparison with the insulin tolerance test (ITT)", was designed as a two-way crossover study with the ITT as the benchmark comparator and involved 31 sites in the United States and Europe. The study population was planned to include at least 110 subjects (at least 55 ITT-positive and 55 ITT-negative) with a medical history documenting risk factors for AGHD, and was planned to include a spectrum of subjects from those with a low risk of having AGHD to those with a high risk of having the condition.

On May 26, 2015, we announced that we had received written scientific advice from the European Medicines Agency (“EMA”) regarding the further development plan, including the study design, for the new confirmatory Phase 3 clinical study of Macrilen™ for use in evaluating AGHD. As a result of the advice, we believe that the confirmatory Phase 3 study that was agreed with the FDA meets the EMA’s study-design expectations as well, allowing for US and European approval, if the study is successful.

On November 19, 2015, we announced the enrollment of the first patient in the confirmatory Phase 3 clinical study of Macrilen™.

On October 26, 2016, we announced completion of patient recruitment for the confirmatory Phase 3 clinical trial of Macrilen™ as a growth hormone stimulation test for the evaluation of AGHD.

The dedicated thorough QT study to evaluate the effect of macimorelin on the QT interval, as requested by the FDA in the CRL, was conducted and completed in 2016.

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 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 had 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. The Company will meet with the FDA at the end of March 2017 to discuss this position.

On March 7, 2017, we announced that the Pediatric Committee (“PDCO”) EMA agreed to the Company’s Pediatric Investigation Plan (“PIP”) for Macrilen™ and agreed that the Company may defer conducting the PIP until after it files a Marketing Authorization Application (“MAA”) seeking marketing authorization for the use of Macrilen™ for the evaluation of AGHD. The decision will permit the Company to file an MAA substantially earlier than if it were required to complete the PIP before filing.

LHRH-Disorazol Z (AEZS-138)

In search of new antitumor agents, we found that disorazol Z, a compound that was isolated from the myxobacterium *Sorangium cellulosum*, possesses cytotoxic activity in the picomolar range in a panel of different tumor cell lines. Inhibition of tubulin polymerization, cell cycle arrest and efficient induction of apoptosis have been identified as modes of action. AEZS-138 is a cytotoxic conjugate of disorazol Z and a synthetic peptide carrier that targets the LHRH receptor. It is, therefore, an outgrowth of our research that lead to our formulation of Zoptrex™. The following is a summary of our development efforts with respect to AEZS-138:

On March 24, 2011, we were awarded a \$1.5 million grant from the German Ministry of Education and Research to develop, up to the clinical stage, cytotoxic conjugates of the proprietary cytotoxic compound disorazol Z and peptides targeting G- protein coupled receptors, including the LHRH receptors. The compounds combine the targeting principle being studied in the ZoptEC study with the novel cytotoxic disorazol Z. The grant was payable as a partial reimbursement of qualifying expenditures over a three-year period, until January 31, 2014. The qualified project was performed with Morphisto GmbH and the Helmholtz Institute in Saarbrücken, Germany, which received additional funding of approximately \$0.7 million. Researchers from the departments of Gynecology and Obstetrics at both the University of Göttingen and the University of Würzburg, Germany, were also part of the collaboration.

On November 16, 2011, we announced the presentation of a poster at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics on encouraging preclinical data for disorazol Z. The data showed that disorazol Z possesses cytotoxicity in a highly diverse panel of 60 different tumor cell lines, and also underlined the identification of important aspects of this novel natural compound's mechanism of action. Disorazol Z has been identified as a tubulin binding agent with highly potent antitumor properties. Cell cycle analysis revealed that disorazol Z arrested cells in the G2/M cell cycle phase and subsequently induced apoptosis with remarkable potency, as shown by sub-nanomolar EC50 values. To expand our zoptarelin doxorubicin technology platform, we aim to evaluate the utility of disorazol Z as a cytotoxic component in a drug-targeting approach utilizing GPCR ligands as the targeting moieties for the treatment of GPCR over-expressing cancers.

On April 10, 2013, we announced at the American Association for Cancer Research's ("AACR") annual meeting encouraging updated proof-of-concept results for disorazol Z cytotoxic conjugates, such as AEZS-138, in human ovarian and endometrial cancer xenograft models. Data demonstrated that conjugates of D-Lys6-LHRH and disorazol Z retained strong binding to the LHRH receptor and showed potent inhibition of tubulin polymerization. Cellular cytotoxicity of the conjugates was in the low nanomolar EC50 range. Increased cytotoxicity in cells over-expressing the LHRH receptor, support receptor targeting as a mechanism of action. The LHRH receptor-dependent efficacies of

disorazol Z-D-Lys6-LHRH conjugates in vitro and in mouse xenograft models that were presented support the principle of tumor targeting by the LHRH receptor as considered to be employed by zoptarelin doxorubicin. On February 11, 2014, at the 11th International Symposium on GnRH in Salzburg, Austria, we presented further data on the mechanism of action and proof of concept of the disorazol Z cytotoxic conjugate, AEZS-138, which led to the initiation of its preclinical development during the second quarter of 2013.

Overview of our 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 inVentiv Commercial Services, LLC, an affiliate of inVentiv Health, Inc. (“inVentiv”), 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 agreement with inVentiv provides that the inVentiv personnel who provide services to us are independent contractors and not our employees. Furthermore, inVentiv is solely responsible for the human-resources and performance-management functions of all such personnel. It is also responsible for paying the compensation, benefits, payroll-related or withholding taxes and any governmental charges or benefits, including unemployment and disability insurance contributions or benefits and workers compensation contributions with respect to such personnel and for reimbursing them for their expenses. We pay a fixed monthly fee to inVentiv for the services of the sales representatives it provides for us, which is subject to adjustment if the assumptions regarding the annual salaries paid to the sales representatives prove to be too high or too low, and we also reimburse inVentiv for certain expenses that it incurs as a result of providing sales representatives to us.

Our agreement with inVentiv had a two-year term that started in November 2014. The term was recently extended for one year. The term may be extended for additional periods of one year, if we reach a written agreement with inVentiv regarding the terms of the extension not less than 60 days before the end of the expiring term. The agreement is subject to customary termination provisions for non-payment of amounts due, material breach and bankruptcy or insolvency. In addition, we may terminate the agreement without cause by giving inVentiv at least 45 days' prior written notice.

Effective September 1, 2016, we terminated our agreement with ASCEND Therapeutics US LLC to co-promote a non-patch transdermal hormone replacement therapy product because of we were dissatisfied with the financial results of our efforts.

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. A description of the principal geographic areas in which we compete, including a geographical and categorical breakdown of our revenues in the past three years is presented in note 22 (Segment information) to our consolidated financial statements included in this Annual Report on Form 20-F at Item 18.

Raw Materials

Raw materials and supplies are generally available in quantities adequate to meet the needs of our business. We will be dependent on third-party manufacturers for the pharmaceutical products that we will market. An interruption in the

availability of certain raw materials or ingredients, or significant increases in the prices paid by us for them, could have a material adverse effect on our business, financial condition, liquidity and operating results.

Regulation of Drug Development

Generally, governmental authorities in the United States, Canada, Europe and other countries extensively regulate the preclinical and clinical testing, manufacturing, labeling, storage, record keeping, advertising, promotion, export, marketing and distribution, among other things, of pharmaceuticals. Under the laws of the United States, the countries of the EU, and other countries, we are subject to obligations to ensure that our clinical trials are conducted in accordance with Good Clinical Practices ("GCP") guidelines and the investigational plan and protocols contained in an Investigational New Drug ("IND") application, or comparable foreign regulatory submission. Set forth below is a brief summary of the material governmental regulations affecting us in the major markets in which we intend to market our products and/or promote products that we acquire or in-license or to which we obtain promotional rights. The United States. In the United States, the FDA's Center for Drug Evaluation and Research (CDER) under the Federal Food, Drug and Cosmetic Act of 1938, as amended (the "FDCA"), the Public Health Service Act and other federal statutes and regulations, subjects pharmaceutical products to rigorous review. In order to market and sell a new drug product in the United States, we must first test it and send CDER evidence from these tests to prove that the drug is safe and effective for its intended use. In most cases, these tests include extensive preclinical, clinical, and laboratory tests. A team of CDER physicians, statisticians, chemists, pharmacologists, and other scientists reviews the company's data and proposed labeling. If this independent and unbiased review establishes that a drug's health benefits outweigh its known risks, the drug is approved for sale. CDER does not test the drug itself but it does conduct limited research in the areas of drug quality, safety, and effectiveness standards. Before approving a new drug or marketing application, the FDA may conduct pre-approval inspections of the developer of the drug (the "sponsor"), its CROs and/or its clinical trial sites to ensure that clinical, safety, quality control, and other regulated activities are compliant with GCP, or Good Laboratory Practices ("GLP"), for specific non-clinical toxicology studies. Manufacturing facilities used to produce a product are also subject to ongoing inspection by the FDA. The FDA may also require confirmatory trials, post-marketing testing, and/or extra surveillance to monitor the effects of approved products, or place conditions on any approvals that could restrict the commercial applications of a product. Once approved, the labeling, advertising, promotion, marketing, and distribution of a drug or biologic product must be in compliance with FDA regulatory requirements.

The first stage required for ultimate FDA approval of a new biologic or drug involves completion of preclinical studies whereby a sponsor must test new drugs on animals for toxicity. Multiple species are used to gather basic information on the safety and efficacy of the compound being investigated and/or researched. The FDA regulates preclinical studies under a series of regulations called the current GLP regulations as well as regulatory requirements found in Part 21 subchapter D of the Code of Federal Regulations. If the sponsor violates these regulations, the FDA may require that the sponsor replicate those studies or can subject the sponsor to enforcement actions or penalties as described further below. The sponsor then submits to the FDA an IND application based on the results from initial testing that include the drug's composition and manufacturing, along with a plan for testing the drug on humans. The FDA reviews the IND to ensure that the proposed studies (clinical trials) do not place human subjects at unreasonable risk of harm. FDA also verifies that there are adequate informed consent and human subject protections in place. After a sponsor submits an IND application, it must wait 30 days before starting a clinical trial to allow FDA time to review the prospective study. If FDA finds a problem, it can order a clinical hold to delay an investigation, or interrupt a clinical trial if problems occur during the study. After the IND application is in effect, a sponsor may commence human clinical trials. The sponsor typically conducts human clinical trials in three sequential phases, but the phases may overlap. In Phase 1 trials, the sponsor tests the product in a small number of patients or healthy volunteers (typically 20-80 healthy volunteers), primarily for safety at one or more doses. The goal in this phase is to determine what the drug's most frequent side effects are and, often, how the drug is metabolized and excreted. Phase 2 studies begin if Phase 1 studies do not reveal unacceptable toxicity. In Phase 2, in addition to safety, the sponsor evaluates the efficacy of the product in a patient population somewhat larger than Phase 1 trials. The number of subjects in Phase 2 studies typically ranges from a few dozen to about 300. This phase aims to obtain preliminary data on whether a drug works in people who have a certain disease or condition. At the end of Phase 2, the FDA and sponsor try to come to an agreement on how large-scale studies in Phase 3 should be done.

Phase 3 studies begin if evidence of effectiveness is shown in Phase 2. Phase 3 trials typically involve additional testing for safety and clinical efficacy in an expanded population at geographically dispersed test sites. The sponsor must submit to the FDA a clinical plan, or "protocol", accompanied by the approval of the institutions participating in the trials, prior to commencement of each clinical trial. The FDA may order the temporary or permanent discontinuation of a clinical trial at any time. In the case of product candidates for cancer, the initial human testing may be done in patients with the disease rather than in healthy volunteers. Because these patients are already afflicted with the target disease, such studies may provide results traditionally obtained in Phase 2 studies. Accordingly, these studies are often referred to as "Phase 1/2" studies as they combine two phases. Even if patients participate in initial human testing and a Phase 1/2 study is carried out, the sponsor is still responsible for obtaining all the data usually obtained in both Phase 1 and Phase 2 studies.

The sponsor must submit to the FDA the results of the preclinical and clinical testing, together with, among other things, detailed information on the manufacture and composition of the product, in the form of a New Drug Application ("NDA") or, in the case of a biologic, a Biologics License Applications ("BLA"). In a process that can take a year or more, the FDA reviews this application and, when and if it decides that adequate data are available to show that the new compound is both safe and effective for a particular indication and that other applicable requirements have been met, approves the drug or biologic for marketing. The amount of time taken for this approval process is a function of a number of variables, including the quality of the submission and studies presented and the potential contribution that the compound will make in improving the treatment of the disease in question.

Orphan-drug designation is granted by the FDA Office of Orphan Drug Products to novel drugs or biologics that are intended for the safe and effective treatment, diagnosis or prevention of rare diseases or disorders that affect fewer than 200,000 people in the U.S., or that affect more than 200,000 people but are not expected to recover the costs of developing and marketing a treatment drug. The designation provides the sponsor with a seven-year period of U.S. marketing exclusivity if the drug is the first of its type approved for the specified indication or if it demonstrates superior safety, efficacy or a major contribution to patient care versus another drug of its type previously granted the designation for the same indication. We have been granted orphan drug designations for Zoptrex™ for the treatment of advanced ovarian cancer and for Macrilen™ for the evaluation of growth hormone deficiency.

Under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act"), newly-approved drugs and indications may benefit from a statutory period of non-patent data exclusivity. The Hatch-Waxman Act provides five-year data exclusivity to the first applicant to gain approval of an NDA for a new chemical entity, or NCE, meaning that the FDA has not previously approved any other drug containing the same active pharmaceutical ingredient, or active moiety. Although protection under the Hatch-Waxman Act will not prevent the submission or approval of another full NDA, such an NDA applicant would be required to conduct its own preclinical and adequate, well-controlled clinical trials to demonstrate safety and effectiveness.

The Hatch-Waxman Act also provides three years of data exclusivity for the approval of new and supplemental NDAs, including Section 505(b)(2) applications, for, among other things, new indications, dosage forms, routes of administration, or strengths of an existing drug, or for a new use, if new clinical investigations that were conducted or sponsored by the sponsor are determined by the FDA to be essential to the approval of the application. This exclusivity, which is sometimes referred to as clinical investigation exclusivity, would not prevent the approval of another application if the sponsor has conducted its own adequate, well-controlled clinical trials demonstrating safety and efficacy, nor would it prevent approval of a generic product that did not incorporate the exclusivity-protected changes of the approved drug product.

The labeling, advertising, promotion, marketing, and distribution of a drug or biologic product must be in compliance with FDA regulatory requirements. Failure to comply with applicable requirements can lead to the FDA demanding that production and shipment cease and, in some cases, that the manufacturer recall products, or to enforcement actions that can include seizures, injunctions, and criminal prosecution. These failures can also lead to FDA withdrawal of approval to market a product.

Canada. In Canada, the Therapeutic Products Directorate of Health Canada is the Canadian federal authority that regulates pharmaceutical drugs and medical devices for human use. Prior to being given market authorization, a sponsor must present substantive scientific evidence of a product's safety, efficacy and quality as required by the Food and Drugs Act and other legislation and regulations. The requirements for the development and sale of pharmaceutical drugs in Canada are substantially similar to those in the United States, which are described above.

The European Union. Medicines can be authorized in the EU by using either the centralized authorization procedure or national authorization procedures. The EU has implemented a centralized procedure coordinated by the EMA for the approval of human medicines, which results in a single marketing authorization issued by the European Commission that is valid across the EU, as well as Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for human medicines that are derived from biotechnology processes, such as genetic engineering, that contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions, and designated orphan medicines. For medicines that do not fall within these categories, an applicant has the option of submitting an

application for a centralized marketing authorization to the EMA, as long as the medicine concerned is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health.

There are also two other possible routes to authorize medicinal products in several EU countries, which are available for investigational drug products that fall outside the scope of the centralized procedure:

- Decentralized procedure. Using the decentralized procedure, a sponsor may apply for simultaneous authorization in more than one EU country of medicinal products that have not yet been authorized in any EU country and that do not fall within the mandatory scope of the centralized procedure. The application will be reviewed by a selected Reference Member State ("RMS"). The Marketing Authorization granted by the RMS will then be recognized by the other Member States involved in this procedure.

•Mutual recognition procedure. In the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other EU countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

Regulation of Commercial Operations

The marketing, promotional, and pricing practices of human pharmaceutical manufacturers, as well as the manner in which manufacturers interact with purchasers and prescribers, are subject to various U.S. federal and state laws, including the federal anti-kickback statute and the False Claims Act and state laws governing kickbacks, false claims, unfair trade practices, and consumer protection, and to similar laws in other countries. In the U.S., these laws are administered by, among others, the Department of Justice ("DOJ"), the Office of Inspector General of the Department of Health and Human Services, the Federal Trade Commission, the Office of Personnel Management, and state attorneys general. Over the past several years, the FDA, the DOJ, and many other agencies have increased their enforcement activities with respect to pharmaceutical companies and increased the inter-agency coordination of enforcement activities.

In the United States, biopharmaceutical and medical device manufacturers are required to record any transfers of value made to licensed physicians and teaching hospitals and to disclose such data to the Department of Health and Human Services ("HHS"). In addition to civil penalties for failure to report transfers of value to physicians or teaching hospitals, there will be criminal penalties if a manufacturer intentionally makes false statements or excludes information in such reports. The payment data across biopharmaceutical and medical device companies is posted by HHS on a publicly available website. Increased access to such data by fraud and abuse investigators, industry critics and media will draw attention to our collaborations with reported entities and will importantly provide opportunities to underscore the critical nature of our collaborations for developing new medicines and exchanging scientific information. This national payment transparency effort coupled with industry commitment to uphold voluntary codes of conduct (such as the PhRMA Code on Interactions with Healthcare Professionals and PhRMA Guiding Principles Direct to Consumer Advertisements About Prescription Medicines) and rigorous internal training and compliance efforts will complement existing laws and regulations to help ensure ethical collaboration and truthful product communications. The Canadian association of Research-Based Pharmaceutical Companies ("Rx & D") has adopted "Guidelines for Transparency in Stakeholder Funding" that require member companies to regularly disclose, by means of the web sites and annual reports, a list of all stakeholders to which they provide direct funding. The term "stakeholder" is defined in Rx & D's Code of Ethical Practices to include "Health Care Professionals". In the EU, the disclosure code of transfers of value to healthcare professionals and organizations adopted by the European Federation of Pharmaceutical Industries and Associations ("EFPIA") requires all members of EFPIA to disclose transfers of value to healthcare professionals and healthcare organizations beginning in 2016, covering the relevant transfers in 2015. Each member company will be required to document and disclose: (i) the names of healthcare professionals and associations that have received payments or other transfers of value and (ii) the amounts or value transferred, and the type of relationship.

For more information about the regulatory risks associated with our business operations, see "Item 3D. Risk Factors".

Intellectual Property - Patents

We seek to protect our compounds, manufacturing processes, compositions and methods of medical use for our lead drugs and drug candidates through a combination of patents, trade secrets and know-how. Our patent portfolio consists of approximately 13 owned and in-licensed patent families (issued, granted or pending in the United States, Europe and other jurisdictions). The patent positions of companies in the biotechnology and pharmaceutical industries are highly uncertain and involve complex legal and factual questions. Therefore, we cannot predict the breadth of claims, if any, that may be allowed under any of our patent applications, or the enforceability of any of our allowed patents. See "Item 3D. Risk Factors - We may not obtain adequate protection for our products through our intellectual property."

Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country. In the United States, the patent term of a patent that covers an FDA-approved drug may also be eligible

for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent, in which the patentee may file an application for yearly interim extensions within five years if the patent will expire and the FDA has not yet approved the NDA. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended.

Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In these jurisdictions, however, no interim extensions exist and the marketing approval must be granted before the patent expires. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. While we anticipate that any such applications for patent term extensions will likely be granted, we cannot predict the precise length of time for which such patent terms would be extended in the United States, Europe or other jurisdictions. If we are not able to secure patent term extensions on patents covering our products for meaningful periods of additional time, we may not achieve or sustain profitability, which would adversely affect our business.

In addition to patent protection, our products may benefit from the market-exclusivity provisions contained in the orphan-drug regulations or the pediatric-exclusivity provisions or other provisions of the FDA Act, such as new chemical entity exclusivity or new formulation exclusivity. Orphan drug regulations provide incentives to pharmaceutical and biotechnology companies to develop and manufacture drugs for the treatment of rare diseases, currently defined as diseases that exist in fewer than 200,000 individuals in the U.S., or diseases that affect more than 200,000 individuals in the U.S. but that the sponsor does not realistically anticipate will generate a net profit. Under these provisions, a manufacturer of a designated orphan drug can seek tax benefits, and the holder of the first FDA approval of a designated orphan product will be granted a seven-year period of marketing exclusivity for such FDA-approved orphan product. In the U.S., the FDA has the authority to grant additional data protection for approved drugs where the sponsor conducts specified testing in pediatric or adolescent populations. If granted, this pediatric exclusivity provides an additional six months which are added to the term of data protection as well as to the term of any relevant patents, to the extent these protections have not already expired. We may also seek to utilize market exclusivities in other territories, such as in the EU. There can be no assurance that any of our drug candidates will obtain such orphan drug designation, pediatric exclusivity, new chemical entity exclusivity or any other market exclusivity in the U.S., the EU or any other territory, or that we will be the first to receive the regulatory approval in a given country or territory for such drugs so as to be eligible for any market exclusivity protection.

Our drug development efforts are currently focused on two compounds, Zoptrex™ and Macrilen™, which recently completed clinical development, and on an LHRH-disorazol Z conjugate (AEZS-138), which is in pre-clinical development. The following is a description of our intellectual property rights with respect to these compounds.

Zoptrex™:

We have licensed the intellectual property and associated rights relating to LHRH agonists and LH-RH antagonists carrying various cytotoxic radicals (including zoptarelin doxorubicin) from the Administrators of the Tulane Educational Fund ("Tulane") pursuant to a License Agreement dated September 17, 2002 between Tulane, as licensor, and AEZS GmbH, as licensee (the "Tulane Agreement"). The Tulane Agreement grants to us an exclusive worldwide license for all therapeutic uses of LH-RH agonists and LH-RH antagonists carrying various cytotoxic radicals, to the extent covered by one of the patents listed below. The term of the Tulane Agreement continues for ten years after the first commercial sale of a product based on the licensed intellectual property (a "Licensed Product") or until the expiration of the last to expire of the patents listed below, whichever is longer, on a country-by-country basis.

Pursuant to the Tulane Agreement, we are required to pay Tulane the following amounts: (i) \$400,000 upon the first grant of regulatory approval for a Licensed Product in the U.S., Canada, the EU or Japan; (ii) 10% of all consideration received by us from a sublicensee for authorization to use the licensed intellectual property to develop, manufacture, market, distribute and sell a Licensed Product; (iii) 2.5% of our net sales of Licensed Products; and (iv) 50% of any royalties that we receive from a sublicensee with respect to its net sales of Licensed Products; provided, however, that the payment with respect to royalties received from a sublicensee shall not be less than 1.75% nor more than 2.5% of the sublicensee's net sales of the Licensed Product.

The following patents are covered by the Tulane Agreement:

U.S. patent 5,843,903 covers zoptarelin doxorubicin and other related targeted cytotoxic anthracycline analogs, pharmaceutical compositions comprising the compounds as well as their medical use for the treatment of tumors. This patent expired in November 2015.

European patent 0 863 917 B1 covers zoptarelin doxorubicin and other related targeted cytotoxic anthracycline analogs, pharmaceutical compositions comprising the compounds as well as their medical use for the treatment of

tumors. This patent expired in November 2016.

Japanese patent 3 987 575 covers zoptarelin doxorubicin and other related targeted cytotoxic anthracycline analogs, pharmaceutical compositions comprising the compounds as well as their medical use for the treatment of tumors. This patent expired in November 2016.

Chinese patent ZL96198605.0 covers zoptarelin doxorubicin and other related targeted cytotoxic anthracycline analogs, pharmaceutical compositions comprising the compounds as well as their medical use for the treatment of tumors. This patent expired in November 2016.

Hong Kong patent 1017363 covers zoptarelin doxorubicin and other related targeted cytotoxic anthracycline analogs, pharmaceutical compositions comprising the compounds as well as their medical use for the treatment of tumors. This patent expired in November 2016.

In early 2015, we filed a European patent application directed to a novel method of manufacturing Zoptrex™. Within the 12 months priority period, we also filed an international patent application for the manufacturing process, as well as national patent applications in selected countries, including the U.S., China, and Taiwan, Japan and India. We decided to file patent applications in additional territories after the European Patent Office issued a search report for the European patent application that we consider to be favorable. The claimed manufacturing process is expected to result in a significant reduction in our cost of manufacturing Zoptrex™, providing us with what should be a stronger competitive position and discouraging competition from generic manufacturers after our five-year period of data exclusivity expires.

Macrilen™:

We hold the worldwide rights to macimorelin pursuant to an exclusive license agreement with the French Centre National de la Recherche Scientifique, as licensor, and AEZS GmbH, as licensee.

The following patents relate to Macrilen™:

U.S. patent 6,861,409 covers Macrilen™ and U.S. patent 7,297,681 covers other related growth hormone secretagogue compounds, each also covering pharmaceutical compositions comprising the compounds as well as their medical use for elevating the plasma level of growth hormone. U.S. patent 6,861,409 and U.S. patent 7,297,681 both expire in August 2022.

European patent 1 289 951 covers Macrilen™ and European patent 1 344 773 covers other related growth hormone secretagogue compounds, pharmaceutical compositions comprising the compounds as well as their medical use for elevating the plasma level of growth hormone. EP patent 1 289 951 and EP patent 1 344 773 both expire in June 2021.

Japanese patent 3 522 265 covers Macrilen™ and pharmaceutical compositions comprising the compounds as well as their medical use for elevating the plasma level of growth hormone. This patent expires in June 2021.

Canadian patent 2,407,659 covers Macrilen™ and pharmaceutical compositions comprising the compounds as well as their medical use for elevating the plasma level of growth hormone. This patent expires in June 2021.

U.S. patent 8,192,719 covers a method of assessing pituitary-related growth hormone deficiency in a human or animal subject comprising an oral administration of the compound Macrilen™ and determination of the level of growth hormone in the sample and assessing whether the level of growth hormone in the sample is indicative of growth hormone deficiency. This patent expires in October 2027.

European patent 1 984 744 covers a method of assessing pituitary-related growth hormone deficiency by oral administration of Macrilen™. This patent expires in February 2027.

Japanese patent 4 852 728 covers a method of assessing pituitary-related growth hormone deficiency by oral administration of Macrilen™. This patent expires in February 2027.

Disorazol Z - LHRH conjugates (AEZS-138):

We own a number of patents that relate to our Disorazol Z - LHRH conjugates, as follows:

U.S. patent 7,741,277 covers AEZS-138 (disorazol Z - LHRH conjugate). This patent expires in January 2028 (including PTA).

U.S. patent 8,470,776 covers methods of treatment for compound AEZS-138 (disorazol Z - LHRH conjugate). This patent expires in February 2029 (including PTA).

European patent application 2,066,679 covers AEZS-138 (disorazol Z - LHRH conjugate) as well as methods of treatment for this compound. If granted, this patent will expire in September 2027.

Japanese patent 5,340,155 covers AEZS-138 (disorazol Z - LHRH conjugate) as well as methods of treatment for this compound. This patent expires in September 2027.

C. Organizational structure

Our corporate structure, the jurisdiction of incorporation of our direct and indirect subsidiaries and the percentage of shares that we held in those subsidiaries as at December 31, 2016 is depicted in the chart set forth under the caption "Item 4.A. History and development of the Company".

D. Property, plants and equipment

Our registered address is located in Montreal, Canada. Our corporate head office is located in Summerville, South Carolina, which is a suburb of Charleston, South Carolina. The following table sets forth information with respect to our main facilities as at December 31, 2016.

Location	Use of space	Square Footage	Type of interest
315 Sigma Drive, Suite 302D, Summerville SC 29486	Partially occupied for management, administration, commercial operations and business development	4,623	Leasehold
Weismüllerstr. 50 D-60314 Frankfurt-am-Main, Germany	Occupied for management, R&D, business development and administration	36,168	Leasehold

Item 4A Unresolved Staff Comments

None.

Item 5. Operating and Financial Review and Prospects

Key Developments

Zoptrex™

Zoptrex™ is a complex molecule that combines a synthetic peptide carrier with doxorubicin, a well-known chemotherapy agent. The synthetic peptide carrier is a luteinizing hormone-releasing hormone ("LHRH") agonist, a modified natural hormone with affinity for the LHRH receptor. The design of the compound allows for the specific binding and selective uptake of the cytotoxic conjugate by LHRH receptor-positive tumors. Potential benefits of this targeted approach include a better efficacy and a more favorable safety profile with lower incidence and severity of side effects as compared to doxorubicin alone. Zoptrex™ is our proposed trade name for zoptarelin doxorubicin. The proposed trade name is subject to approval by the FDA.

We believe that Zoptrex™ has the potential to become the first FDA-approved medical therapy for advanced, recurrent endometrial cancer, potentially resulting in the compound's rapid adoption as a novel core therapy for patient treatment and management, representing a significant potential market opportunity for us. Moving forward, we will continue to develop our commercialization plans regarding Zoptrex™ in this indication. In addition, contingent on the success of the ZoptEC (Zoptarelin Doxorubicin in Endometrial Cancer) pivotal Phase 3 clinical trial in women with advanced, recurrent or metastatic endometrial cancer, we have additional areas of interest for further therapeutic development for Zoptrex™, including ovarian, prostate, breast and potentially, bladder cancer.

The following paragraphs describe recent key developments with respect to Zoptrex™ :

On October 13, 2015, we announced that an independent data and safety monitoring board ("DSMB") had recommended that the pivotal Phase 3 ZoptEC study continue as planned. The DSMB's decision followed completion of its pre-specified second interim analysis on efficacy and safety at approximately 192 events.

On June 14, 2016, we announced that our licensee, Sinopharm A-Think Pharmaceuticals Co., Ltd. ("Sinopharm"), which is affiliated with the largest state-owned pharmaceutical company in the People's Republic of China, submitted an Investigational New Drug application ("IND") for Zoptrex™ to the Chinese State Food and Drug Administration ("CFDA"), remaining on track to commence its clinical program in 2017.

- On July 1, 2016, we announced that we had entered into an exclusive License Agreement with Cyntec Co., Ltd. ("Cyntec"), an affiliate of Orient EuroPharma Co., Ltd. ("OEP") for Zoptrex™ for the initial indication of endometrial cancer. Under the terms of the License Agreement, we were paid a non-refundable upfront cash payment in consideration for the license to Cyntec of our intellectual property related to Zoptrex™ and the grant to Cyntec of the right to commercialize Zoptrex™ in a territory consisting of Taiwan and nine countries in southeast Asia (the "OEP Territory"). Cyntec has also agreed to make additional payments to us upon achieving certain pre-established regulatory and commercial milestones. Furthermore, we will receive royalties based on future net sales of Zoptrex™ in the OEP Territory. Cyntec will be responsible for the development, registration, reimbursement and commercialization of the product in the OEP Territory. We entered into related Technology Transfer and Supply Agreements with another affiliate of OEP, pursuant to which we will transfer to such affiliate the technology necessary to permit the affiliate to manufacture

finished Zoptrex™ using quantities of the active pharmaceutical ingredient purchased from us pursuant to the Supply Agreement.

On July 31, 2016, we announced that we had entered into an exclusive License Agreement with Rafa Laboratories Ltd ("Rafa") for Zoptrex™ for the initial indication of endometrial cancer. Under the terms of the License Agreement, we were paid a non-refundable upfront cash payment in consideration for the license to Rafa of our intellectual property related to Zoptrex™ and the grant to Rafa of the right to commercialize Zoptrex™ in a territory consisting of Israel and the Palestinian territories (the "Rafa Territory"). Rafa has also agreed to make additional payments to us upon achieving certain pre-established regulatory and commercial milestones. Furthermore, we will receive royalties based on future net sales of Zoptrex™ in the Rafa Territory. Rafa will be responsible for the development, registration, reimbursement and commercialization of the product in the Rafa Territory. We entered into a related Supply Agreement with Rafa pursuant to which we will sell finished Zoptrex™ to Rafa.

On October 12, 2016, we announced that we had entered into an exclusive License Agreement with Specialised Therapeutics Asia Pte Ltd ("STA") for Zoptrex™ for the initial indication of endometrial cancer. Under the terms of the License Agreement, we were paid a non-refundable upfront cash payment in consideration for the license to STA of our intellectual property related to Zoptrex™ and the grant to STA of the right to commercialize Zoptrex™ in a territory consisting of Australia and New Zealand (the "STA Territory"). STA has also agreed to make additional payments to us upon achieving certain pre-established regulatory and commercial milestones. Furthermore, we will receive royalties based on future net sales of Zoptrex™ in the STA Territory. STA will be responsible for the development, registration, reimbursement and commercialization of the product in the STA Territory. We entered into a related Supply Agreement with STA pursuant to which we will sell finished Zoptrex™ to STA.

On January 30, 2017, we announced the completion of the clinical phase of the pivotal Phase 3 ZoptEC study with the occurrence of the 384th death. We currently expect to lock the clinical database and to report top-line results in April 2017. With the completion of the clinical portion of this trial, we will now focus on analyzing the data and, if warranted by the results, submitting a new drug application later this year.

Macrilen™

Macrilen™, a ghrelin receptor agonist, is a novel orally-active small molecule that stimulates the secretion of growth hormone. Macrilen™ has been granted orphan drug designation by the FDA for the evaluation of growth hormone deficiency. We own the worldwide rights to this novel patented compound. Macrilen™ is our proposed trade name for macimorelin. The proposed trade name is subject to approval by the FDA. On December 16, 2016 we were advised by the EMA that Macrilen™ was rejected as the proposed invented name for macimorelin because of its similarity to the names of other medicines. We intend to appeal this decision.

We recently concluded a confirmatory Phase 3 clinical trial of Macrilen™ for the evaluation of growth hormone deficiency in adults ("AGHD"). The confirmatory trial was an open-label, randomized, two-way crossover study that compared the results of the evaluation of AGHD using Macrilen™ to the results of the evaluation of AGHD using a procedure known as the "Insulin Tolerance Test" (the "ITT") on the same patient. The trial involved patients, each of whom was evaluated for AGHD using both Macrilen™ and the ITT. Thirty of the patients were evaluated using Macrilen™ a second time to measure the repeatability of the result obtained using Macrilen™ as the evaluation method. The study population consisted of more than 110 patients who were suspected of having AGHD as a result of the presence of one or more symptoms. This segment of the population included a range of patients from those considered at low risk of having AGHD to those considered at high risk. The study population also included 25 healthy subjects, who had no risk of having AGHD.

On January 4, 2017, we announced that the confirmatory Phase 3 clinical trial of Macrilen™ failed to achieve its objective of validating a single oral dose of macimorelin for the evaluation of AGHD, using the ITT as a comparator. Based on an analysis of top-line data, macimorelin did not achieve equivalence to the ITT as a means of diagnosing AGHD. Under the study protocol, the evaluation of AGHD with Macrilen™ would have been 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 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, following a comprehensive review of the data obtained from the confirmatory Phase 3 clinical trial of Macrilen™ for the evaluation of AGHD using the ITT as a comparator, we concluded that Macrilen™ demonstrated performance supportive of FDA registration consideration. The press release in which we made such announcement set forth the facts on which our conclusion was based. We will meet with the FDA at the end of March 2017 to discuss this position.

Pre-clinical developments

On January 13, 2016, we announced that, in addition to our focus on Zoptrex,TM we are also focusing on AEZS-138/Disorazol Z, because we believe that it is an ideal compound for the formation of cytotoxic conjugates with peptides, proteins and antibodies to selectively target cancer cells. AEZS-138 is a cytotoxic conjugate in preclinical development. It is a conjugate based on Disorazol Z and the LHRH receptor agonist that is utilized in Zoptrex.TM We believe that the peptide directs the compound specifically to the LHRH receptor expressing tumor cells, and mediates binding and uptake via endocytosis. Within the cancer cell, the conjugates are cleaved and Disorazol Z can deploy its potent anti-proliferative activity. We have patented the cytotoxic agent Disorazol Z in 35 countries, including the US, Japan, Europe, China, Russia, Korea and Taiwan. This patent protection expires in 2026. The conjugate of Disorazol Z and the LHRH receptor agonist as a targeted cytotoxic agent is patented in 15 countries, including the US, Japan, China, Russia, Korea and Taiwan. This patent protection expires in 2027. We expect the European patent to be granted in the near future.

Commercial Operations

Our commercial operations consist of 13 full-time sales representatives and a three person sales-management staff in the US. The sales representatives are employed by a contract sales organization and provide services to us pursuant to our contract with the contract sales organization while we employ the sales-management staff. Maintaining a sales force is an essential part of our strategy to transform the Company into a commercially operating specialty biopharmaceutical company. We do not believe that it is practical for a company of our size to sustain itself solely on a portfolio of internally derived products: development takes too long, costs too much money and entails too much risk. Therefore, we are seeking to acquire or to in-license products that fit our areas of therapeutic interest and capabilities and that are available on what we consider to be reasonable commercial terms.

Our sales force currently co-promotes two products that are owned by others: Saizen[®] and APIFINY[®]. Until September 1, 2016, we co-promoted a third product, EstroGel[®].

Saizen[®]

On May 8, 2015, we announced that we had entered into a promotional services agreement with EMD Serono, allowing us to promote Saizen[®] [somatropin (rDNA origin) for injection] to designated medical professionals in specified US territories. Saizen[®] is a recombinant human growth hormone registered in the US for the treatment of pediatric growth hormone deficiency and AGHD. Under this agreement, we were promoting Saizen[®] to designated pediatric endocrinologists and we were receiving commissions based on new, eligible patient starts on Saizen[®] above an agreed-upon base line. This agreement was amended in December 2016. The EMD Serono agreement, as amended, provides that we will promote Saizen[®] in specific agreed-upon US territories to both adult and pediatric endocrinologists in consideration for a sales commission that is based upon new, eligible patient starts, without any baseline.

APIFINY[®]

During the fourth quarter of 2015, we signed a co-marketing agreement with Armune BioScience, Inc. ("Armune") giving us the right to promote this product to specified targets in the United States. APIFINY[®] is the only cancer-specific, non-PSA based blood test for the evaluation of the risk of prostate cancer. As such, it is an important adjunct to the traditional PSA test.

On April 27, 2016, we announced that we had entered into a new co-marketing agreement with Armune that gives us the exclusive right to promote APIFINY[®] throughout the entire United States. Under the terms of the new co-marketing agreement, we receive a commission for every APIFINY[®] test ordered. The amount of the commission varies depending upon the payer. For commercial insurance tests, we receive an upfront payment when the test is performed and, within 30 to 90 days, an additional percentage of the reimbursement, minus the amount of the upfront payment. For all other tests, we receive a flat fee at the time the test is performed.

Corporate Activities

Public offerings and related events

On December 30, 2015, we announced that we had filed a preliminary short-form base shelf prospectus (the "Shelf Prospectus") with the securities regulatory authorities in each of the provinces of Canada, and a corresponding shelf registration statement on Form F-10 with the SEC under the US/Canada Multijurisdictional Disclosure System. The

Shelf Prospectus and corresponding shelf registration statement, which became effective on January 13, 2016, allow us to offer up to \$150 million of common shares, preferred shares, debt securities, subscription receipts, warrants or units comprised of one or more of such securities during the 25-month period that the shelf prospectus is effective.

On April 1, 2016, we entered into an "At-the-Market" ("ATM") sales agreement under which we are able, at our discretion and from time to time, to sell up to 3 million of our common shares through ATM issuances on the NASDAQ for aggregate gross proceeds of up to approximately \$10 million (the "ATM Program"). The ATM Program provides that common shares are to be sold at market prices prevailing at the time of sale and, as a result, prices may vary. Between April 1, 2016 and March 15, 2017, we issued approximately 1.4 million common shares at an average issuance sales price of \$3.62 per share pursuant to our ATM Program. The shelf registration statement pursuant to which this ATM Program was established expires on March 28, 2017.

On September 12, 2016, all 8,064 remaining Series B Warrants that had been issued in connection with a financing in March 2015 expired without having been exercised.

On November 1, 2016, we completed a registered direct offering of 2,100,000 units (the "Units"), with each Unit consisting of one common share or one pre-funded warrant to purchase one common share and 0.45 of a warrant to purchase one common share (the "November 2016 Offering"). Total gross cash proceeds raised through the November 2016 Offering amounted to approximately \$7.6 million, less cash transaction costs of approximately \$1.0 million, including the placement agent's fee and expenses. The warrants are exercisable six months after their date of issuance and for a period of three years thereafter at an exercise price of \$4.70 per share. The warrants contain a call provision which provides that, in the event our common shares trade at or above \$10.00 on the principal trading market for our common shares during a specified measurement period and subject to a minimum volume of trading during such measurement period, then, subject to certain conditions, we have the right to call for cancellation all or any portion of the warrants which are not exercised by holders within 10 trading days following receipt of a call notice from us. Upon complete exercise for cash, these warrants would result in the issuance of an aggregate of 945,000 common shares that would generate additional proceeds of approximately \$4.4 million, although these warrants may be exercised on a "net" or "cashless" basis.

Class action lawsuit

The Company and certain of its current and former officers are defendants in a putative class-action lawsuit brought on behalf of shareholders of the Company. The pending lawsuit is the result of the consolidation of several lawsuits, the first of which was filed on November 11, 2014. The plaintiffs filed their amended consolidated complaint on April 10, 2015. The amended complaint alleged violations of the Securities Exchange Act of 1934 in connection with allegedly false and misleading statements made by the defendants between August 30, 2011 and November 6, 2014 (the "Class Period"), regarding the safety and efficacy of Macrilen™ and the prospects for the approval of the Company's new drug application for the product by the FDA. The plaintiffs seek to represent a class comprised of purchasers of the Company's common shares during the Class Period and seek unspecified damages, costs and expenses and such other relief as determined by the court.

On September 14, 2015, the Court dismissed the lawsuit, but granted the plaintiffs leave to amend. In dismissing the lawsuit, the court affirmed that the plaintiffs had failed to state a claim. On October 14, 2015, the plaintiffs filed a second amended complaint. 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.

We filed a motion for reconsideration of the Court's March 2, 2016 order on March 16, 2016 and filed an answer to the second amended complaint on April 6, 2016. 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. During the second quarter of 2016, we exceeded the deductible amount applicable to this claim.

Therefore, we believe that most of the costs for our defense in future periods will be borne by the insurers who provide directors' and officers' liability insurance to us, subject to our policy limits.

While we believe that we have meritorious defenses and intend to defend this lawsuit vigorously, management cannot currently predict the outcome of this suit or reasonably estimate any potential loss that may result from this suit.

Accordingly, we have not recorded any liability related to the lawsuit. No assurance can be given with respect to the ultimate outcome of such proceedings, and we could incur substantial unreimbursed legal fees, damages, settlements, judgments, and other expenses in connection with these proceedings that may not qualify for coverage under, or may exceed the limits of, our applicable D&O Insurance and could have a material adverse impact on our financial condition, results of operations, liquidity and cash flows.

A. Operating Results

Consolidated Statements of Comprehensive Loss Information

(in thousands, except share and per share data)	Three months ended December 31,		Years ended December 31,		
	2016	2015	2016	2015	2014
	\$	\$	\$	\$	\$
Revenues					
Sales commission and other	94	41	414	297	—
License fees	210	61	497	248	11
	304	102	911	545	11
Operating expenses					
Research and development costs	4,619	4,243	16,495	17,234	23,716
General and administrative expenses	1,757	3,953	7,147	11,308	9,840
Selling expenses	1,526	1,764	6,745	6,887	3,850
	7,902	9,960	30,387	35,429	37,406
Loss from operations	(7,598)	(9,858)	(29,476)	(34,884)	(37,395)
(Loss) gain due to changes in foreign currency exchange rates	(396)	(315)	(70)	(1,767)	1,879
Change in fair value of warrant liability	(245)	3,030	4,437	(10,956)	18,272
Warrant exercise inducement fee	—	(2,926)	—	(2,926)	—
Other finance income	19	26	150	305	168
Net finance (costs) income	(622)	(185)	4,517	(15,344)	20,319
Loss before income taxes	(8,220)	(10,043)	(24,959)	(50,228)	(17,076)
Income tax expense	—	—	—	—	(111)
Net loss from continuing operations	(8,220)	(10,043)	(24,959)	(50,228)	(17,187)
Net income from discontinued operations	—	25	—	85	623
Net loss	(8,220)	(10,018)	(24,959)	(50,143)	(16,564)
Other comprehensive loss:					
Items that may be reclassified subsequently to profit or loss:					
Foreign currency translation adjustments	870	249	569	1,509	(1,158)
Items that will not be reclassified to profit or loss:					
Actuarial gain (loss) on defined benefit plans	1,143	(116)	(1,479)	844	(1,833)
Comprehensive loss	(6,207)	(9,885)	(25,869)	(47,790)	(19,555)
Net loss per share (basic and diluted) from continuing operations ¹	(0.71)	(1.46)	(2.41)	(18.17)	(29.12)
Net income per share (basic and diluted) from discontinued operations ¹	—	—	—	0.03	1.06
Net loss per share (basic and diluted) ¹	(0.71)	(1.46)	(2.41)	(18.14)	(28.06)
Weighted average number of shares outstanding: ¹					
Basic	11,565,210	6,874,460	10,348,879	2,763,603	590,247
Diluted	11,614,234	7,302,816	10,665,149	3,424,336	590,247

¹ Adjusted to reflect the November 17, 2015 100-to-1 Share Consolidation

Our operating and financial review and prospects should be read in conjunction with our consolidated financial statements, accompanying notes and other information appearing in this Annual Report.

2016 compared to 2015

Revenues

Sales commission and other were \$0.1 million and \$0.4 million for the three and twelve months ended December 31, 2016 and \$41,000 and \$0.3 million for the same periods in 2015, respectively, and thus increased in 2016 as compared to 2015. In 2016, those revenues mainly resulted from our sales team exceeding pre-established unit sales baseline thresholds under our co-promotion agreement to sell Saizen®. We also generated sales commission in connection with our promotion of APIFINY®. In the corresponding periods in 2015, sales commission and other revenues were mainly related to EstroGel®.

After a good first quarter, the results of our co-promotion of Saizen® during the second, third and fourth quarters of 2016 were disappointing. The demand for Saizen® appears to be more seasonal than we previously realized. Additionally, the non-commercial and self-pay business slowed in part due to competitive price pressures. Further, a recent decision by a large commercial health insurance provider to exclude Saizen® from its formulary was recently announced, taking effect in 2017. Therefore, in December 2016, we negotiated an amended agreement with EMD Serono in order to receive commission on each new patient start, without any baseline, as well as being able to promote to adult endocrinologists. As described in the "Key Developments" section above, the original agreement included a baseline that we needed to exceed before receiving commissions.

License fees were \$0.2 million and \$0.5 million for the three and twelve months ended December 31, 2016, respectively, as compared to \$0.1 million and \$0.2 million for the same periods in 2015. The increase is explained by the out-licensing agreements that we entered into in 2016 for Zoptrex™, as described in the "Key Developments" section above.

Operating Expenses

Research and Development ("R&D") costs were \$4.6 million and \$16.5 million for the three and twelve months ended December 31, 2016, respectively, compared to \$4.2 million and \$17.2 million for the same periods in 2015.

The increase in our R&D costs for the three months ended December 31, 2016, as compared to the same period in 2015, is mainly attributable to higher comparative third-party costs, as described below.

The decrease in our R&D costs for the twelve months ended December 31, 2016, as compared to the same period in 2015, is attributable to lower employee compensation and benefits costs, lower facilities rent and maintenance costs as well as lower other costs. A substantial portion of this decrease is due to the realization of cost savings in connection with our ongoing efforts to streamline our R&D activities and to increase our commercial operations and flexibility by reducing our R&D staff, which was started in 2014 (the "Resource Optimization Program"). The R&D costs for the year ended December 31, 2016 were lower than anticipated mainly because we were able to negotiate reductions to a change order received from our principal R&D third-party service provider.

The following table summarizes our net R&D costs by nature of expense:

(in thousands)	Three months ended December 31,		Years ended December 31,		
	2016	2015	2016	2015	2014
	\$	\$	\$	\$	\$
Third-party costs	3,233	2,899	11,829	11,891	11,356
Employee compensation and benefits	845	905	3,216	3,699	8,430 *
Facilities rent and maintenance	232	224	873	940	2,160
Other costs**	309	231	579	727	1,901
Gain on disposal of equipment	—	(16)	(2)	(23)	(131)
	4,619	4,243	16,495	17,234	23,716

* Includes a provision for restructuring in the amount of \$2.2 million.

**Includes mainly depreciation, amortization, impairment and operating foreign exchange losses.

The following table summarizes third-party R&D costs, by product candidate, incurred by the Company during the three-month periods ended December 31, 2016 and 2015.

(in thousands, except percentages)	Three months ended			
	December 31,			
Product Candidate	2016		2015	
	\$	%	\$	%
Zoptrex™	1,453	44.9	1,488	51.3
Macrilen™	1,568	48.5	977	33.7
LHRH - Disorazol Z	86	2.7	73	2.5
Erk inhibitors	16	0.5	71	2.5
Other	110	3.4	290	10.0
	3,233	100.0	2,899	100.0

The following table summarizes third-party R&D costs, by product candidate, incurred by the Company during the years ended December 31, 2016, 2015 and 2014.

(in thousands, except percentages)	Years ended December 31,					
	2016		2015		2014	
Product Candidate	\$	%	\$	%	\$	%
	Zoptrex™	6,742	57.0	8,635	72.6	9,668
Macrilen™	4,326	36.6	1,555	13.1	404	3.6
LHRH - Disorazol Z	294	2.5	212	1.8	257	2.3
Erk Inhibitors	130	1.1	1,081	9.1	488	4.3
Other	337	2.8	408	3.4	539	4.7
	11,829	100.0	11,891	100.0	11,356	100.0

As shown above, a substantial portion of the quarter-to-date and year-to-date R&D costs relate to development initiatives associated with Zoptrex™, and in particular with our pivotal Phase 3 ZoptEC clinical trial initiated in 2013 with Ergomed. Third-party costs attributable to Zoptrex™ decreased considerably during the twelve months ended December 31, 2016, as compared to the same period in 2015, mainly due to the fact that dosing of patients in the ZoptEC trial was completed in February 2016. This is consistent with our expectations, as we completed the study during the first quarter of 2017 and we expect to report top-line results in April 2017.

In addition, during 2015, we initiated the new confirmatory Phase 3 clinical trial of Macrilen™, which explains the increase in costs for this product candidate. The first patient was enrolled in the fourth quarter of 2015, we announced completion of patient recruitment in the fourth quarter of 2016 and we announced top-line results of the trial on January 4, 2017. Finally, in 2015, we also decided to suspend our efforts on internally developing Erk inhibitor, a molecule for potential cancer therapies, to conserve our resources for other projects.

Excluding the impact of foreign exchange rate fluctuations, we expect that we will incur overall R&D costs of between \$19.0 million and \$20.0 million for the year ended December 31, 2017. Although we expect a decrease in costs related to the contract research organization following the end of the clinical trials, this will be offset by the costs associated with the NDA preparation for both products, the FDA submission fee for Zoptrex™, if the results of the clinical trial warrant submitting a new drug application, as well as by the investments needed in inventory prior to the potential commercial launch of both Macrilen™ and Zoptrex™ and by the costs related to the validation of a second supplier for both products to be able to fulfill the expected demand.

General and administrative ("G&A") expenses were \$1.8 million and \$7.1 million for the three and twelve months ended December 31, 2016, respectively, as compared to \$4.0 million and \$11.3 million for the same periods in 2015. The decrease in our G&A costs for the three months and twelve months ended December 31, 2016, as compared to the same periods in 2015, is due to the recording of a provision, in the fourth quarter of 2015, related to a corporate restructuring that we announced on October 12, 2015 (the "Corporate Restructuring"). The Corporate Restructuring included the restructuring of our finance and accounting staff and the closure of our office in Quebec City. As a result of the Corporate Restructuring, recurring G&A expenses also decreased

in 2016, as compared to 2015. Finally, the comparative decrease for the three-month and twelve-month periods is also explained by certain transaction costs allocated to warrants in connection with the completion of share issuances in March and December 2015.

Excluding the impact of foreign exchange rate fluctuations and the recording of transaction costs related to potential financing activities (not currently known or estimable), we expect G&A expenses to slightly increase in 2017, as compared to 2016, because we expect to hire additional employees in connection with the potential commercialization of our products. We expect that G&A expenses will range between \$7.5 million and \$8.5 million in 2017.

Selling expenses were \$1.5 million and \$6.7 million for the three and twelve months ended December 31, 2016, respectively, as compared to \$1.8 million and \$6.9 million for the same periods in 2015. The selling expenses for the three and twelve months ended December 31, 2016 and 2015 represent mainly the costs of our contracted sales force related to the co-promotion activities as well as our internal sales management team. The selling expenses remained relatively stable during 2016 and are slightly below what we anticipated because we postponed some expenses related to the potential commercial launch of Zoptrex™ and Macrilen™ mainly because the related clinical trials took more time than expected.

Based on currently available information, we expect selling expenses to range between \$7.0 million and \$8.0 million in 2017. The expected increase in 2017 as compared to 2016 is mainly due to the fact that we are starting to prepare for the expected commercial launch of Zoptrex™ and Macrilen™.

Net finance (costs) income were (\$0.6) million and \$4.5 million for the three and twelve months ended December 31, 2016, as compared to (\$0.2) million and (\$15.3) million, for the same periods in 2015. These increases in finance income or decreases in finance costs are mainly attributable to the change in fair value recorded in connection with our warrant liability. Such change in fair value results from the periodic "mark-to-market" revaluation, via the application of option pricing models, of outstanding share purchase warrants. During 2016, the "mark-to-market" warrant valuation was impacted by the expiration of the remaining Series B Warrants. During 2015, the change in assumptions that were applied to determine the fair value of the alternate cashless exercise feature included in the Series B Warrants significantly impacted the "mark-to-market" valuation. Furthermore, the closing price of our common shares, which, on the NASDAQ, fluctuated from \$3.25 to \$4.94 during the three-month period and \$2.67 to \$4.94 during the twelve-month period ended December 31, 2016, respectively, compared to \$4.00 to \$11.43 and \$4.00 to \$84.20 during the same periods in 2015, also had a direct impact on the change in fair value of warrant liability. In addition, with specific reference to 2015, finance costs were also impacted by the warrant exercise inducement fee paid to certain holders of the Series B Warrants.

Net loss for the three and twelve months ended December 31, 2016 was (\$8.2) million and \$(25.0) million, or (\$0.71) and (\$2.41) per basic and diluted share, as compared to a net loss of \$(10.0) million and \$(50.1) million, or (\$1.46) and (\$18.14) per basic and diluted share, for the same periods in 2015. The decrease in net loss for the three months ended December 31, 2016, as compared to the same period in 2015, is due largely to lower G&A expenses, as presented above. The decrease in net loss for the twelve months ended December 31, 2016, as compared to the same period in 2015, is due largely to lower operating expenses and higher comparative net finance income, as presented above.

2015 compared to 2014

Revenues

Revenues were \$0.5 million for the year ended December 31, 2015 compared to \$0.01 million for the same period in 2014. The revenues recorded during the year ended December 31, 2015 resulted primarily from the amortization of a one-time, non-refundable payment made to us in December 2014 in connection with a master collaboration agreement, a technology transfer and technical assistance agreement and a license agreement that we entered into with Sinopharm related to Zoptrex™. We deferred this non-refundable payment and we amortize it on a straightline basis over a four-year period. In addition, we generated sales commission in connection with our co-promotion efforts related to EstroGel®, which we no longer promote.

Operating Expenses

R&D costs were \$17.2 million for the year ended December 31, 2015 compared to \$23.7 million for the same period in 2014.

The decrease for the year ended December 31, 2015, as compared to the same period in 2014, is mainly attributable to lower comparative employee compensation and benefits costs, facilities rent and maintenance costs as well as other costs. A substantial portion of this decrease is due to the realization of cost savings in connection with our Resource Optimization Program rolled out in the third quarter of 2014, as well as to the weakening, in 2015, of the EUR against the US dollar, which appreciated on average by approximately 16.5% from the year ended December 31, 2014 to the same period in 2015. The decrease for the year ended December 31, 2015 was partly offset by higher third-party costs.

A substantial portion of third-party R&D costs in 2015 related to development initiatives associated with Zoptrex™, and in particular with our pivotal Phase 3 ZoptEC clinical trial initiated in 2013 with Ergomed. Excluding the impact of the foreign exchange rate fluctuations, third-party costs attributable to Zoptrex™ increased slightly during the year ended December 31, 2015, as compared to the same period in 2014, mainly due to a higher comparative number of patients enrolled in the clinical trial. In addition, during the year 2015, we started the new confirmatory Phase 3 clinical trial of Macrilen™, which explains the increase in costs for this product candidate.

General and administrative ("G&A") expenses were \$11.3 million for the year ended December 31, 2015, as compared to \$9.8 million for the same period in 2014. The increase is mainly attributable to the recording of a provision related to our Corporate Restructuring in the fourth quarter of 2015, as well as to the recording of certain transaction costs associated with the completion of share issuances in March and December 2015.

Selling expenses were \$6.9 million for the year ended December 31, 2015, as compared to \$3.9 million for the same period in 2014. The increase in selling expenses for the year ended December 31, 2015 as compared to the same period in 2014 is attributable to the fact that 2014 was not a full year of sales activity.

Net finance (costs) income were \$(15.3) million for the year ended December 31, 2015, as compared to \$20.3 million for the same period in 2014 and are comprised predominantly of the change in fair value of warrant liability and of gains and losses recorded due to changes in foreign currency exchange rates.

The change in fair value of our warrant liability results from the periodic "mark-to-market" revaluation, via the application of the option pricing models, of share purchase warrants that were outstanding during the relevant period. The "mark-to-market" warrant valuation was most notably impacted by the issuance of 3.1 million additional share purchase warrants in 2015 and by the closing price of our common shares, which, on the NASDAQ, fluctuated from \$4.00 to \$84.20 during the year ended December 31, 2015 and from \$52.00 to \$150.00 during the year ended December 31, 2014.

With specific reference to 2014, we recorded substantial fair value gains on our warrant liability, resulting from the significant reduction in our share price following our announcement, in November 2014, that the FDA had issued a complete response letter ("CRL") in connection with our new drug application ("NDA") for Macrilen™. The lower closing price of our shares following our announcement of the CRL resulted in a lower Black-Scholes valuation of our share purchase warrants that were outstanding during the fourth quarter of 2014. In 2015, the change in fair value of warrant liability was significantly impacted by the issuance of the Series B Warrants.

In addition, with specific reference to 2015, finance costs were also impacted by the warrant exercise inducement fee paid to certain holders of the Series B Warrants.

Net loss for the year ended December 31, 2015 was \$(50.1) million, or \$(18.14) per basic and diluted share compared to \$(16.6) million, or \$(28.06) per basic and diluted share for the same period in 2014. The increase in our net loss from continuing operations for the year ended December 31, 2015, as compared to the same period in 2014, is due to the higher comparative G&A and selling expenses and net finance costs, partly offset by lower comparative R&D costs, as presented above.

Quarterly Consolidated Results of Operations Information

(in thousands, except for per share data)	Three months ended			
	December 31, 2016	September 30, 2016	June 30, 2016	March 31, 2016
	\$	\$	\$	\$
Revenues	304	269	96	242
Loss from operations	(7,598)	(7,703)	(7,184)	(6,991)
Net loss	(8,220)	(6,055)	(7,008)	(3,676)
Net loss per share (basic and diluted)*	(0.71)	(0.61)	(0.71)	(0.37)
(in thousands, except for per share data)	Three months ended			
	December 31, 2015	September 30, 2015	June 30, 2015	March 31, 2015
	\$	\$	\$	\$
Revenues	102	173	197	73
Loss from operations	(9,858)	(7,501)	(7,989)	(9,536)
Net (loss)	(10,018)	(15,290)	(15,099)	(9,736)
Net (loss) income per share (basic and diluted)*	(1.46)	(6.66)	(13.65)	(13.59)

Net loss per share is based on the weighted average number of shares outstanding during each reporting period, *which may differ on a quarter-to-quarter basis. As such, the sum of the quarterly net loss per share amounts may not equal full-year net loss per share.

Historical quarterly results of operations and net loss cannot be taken as reflective of recurring revenue or expenditure patterns or of predictable trends, largely given the non-recurring nature of certain components of our historical revenues due most notably to unpredictable quarterly variations attributable to our net finance income (costs), which in turn are comprised mainly of the impact of the periodic "mark-to-market" revaluation of our warrant liability and of foreign exchange gains and losses. Additionally, our net R&D costs have historically varied on a quarter-over-quarter basis due to the ramping up or winding down of potential product candidate activities, which in turn are dependent upon a number of factors that often do not occur on a linear or predictable basis.

Condensed Consolidated Statement of Financial Position Information

(in thousands)	As at	
	December 31, 2016	December 31, 2015
	\$	\$
Cash and cash equivalents ¹	21,999	41,450
Trade and other receivables and other current assets	744	944
Restricted cash equivalents	496	255
Property, plant and equipment	204	256
Other non-current assets	8,216	8,593
Total assets	31,659	51,498
Payables and other current liabilities ²	3,778	4,770
Current portion of deferred revenues	426	244
Warrant liability	6,854	10,891
Non-financial non-current liabilities ³	14,389	13,978
Total liabilities	25,447	29,883
Shareholders' equity	6,212	21,615
Total liabilities and shareholders' equity	31,659	51,498

1. Approximately \$1.5 million was denominated in EUR as at December 31, 2016 and December 31, 2015, and approximately \$3.7 and \$4.4 million were denominated in Canadian dollars as at December 31, 2016 and December

- 31, 2015, respectively.
2. Approximately \$0.6 million was related to our provision for restructuring as at December 31, 2016.
3. Comprised mainly of employee future benefits, provisions for onerous contracts and non-current portion of deferred revenues.

The decrease in cash and cash equivalents as at December 31, 2016, as compared to December 31, 2015, is due to the net cash used in operating activities and variations in components of our working capital and by the increase in restricted cash equivalents. The decrease was partially offset by the net proceeds generated by the sale and issuance of common shares under our ATM Program and as part of the November 2016 Offering as well as the upfront cash payments received in consideration for the licenses to Cyntec, Rafa and STA.

The increase in restricted cash equivalents is mainly explained by the fact that we launched a corporate credit card program, which requires us to set aside a reserve of a certain sum of funds.

The increase in the current portion of deferred revenues is explained by the out-licensing agreement signed with Cyntec during the third quarter of 2016.

The decrease in our warrant liability from December 31, 2015 to December 31, 2016 is due to a net fair value revaluation gain of \$4.4 million, which was recorded pursuant to our periodic "mark-to-market" revaluation of the underlying outstanding warrants. The revaluation gain is mainly explained by the decrease of the price of our common shares during the period as well as the impact of the expiration of the Series B Warrants. This was partially offset by the fair value attributable to the warrants issued in the November 2016 Offering.

The increase in non-financial non-current liabilities from December 31, 2015 to December 31, 2016 is mainly due to a decrease in the discount rate used to estimate our employee future benefits obligation.

The decrease in shareholders' equity as at December 31, 2016, as compared to December 31, 2015, is attributable primarily to the recording of a net loss for the twelve-month period and an actuarial loss on our pension-related employee benefit obligation for the same period. This was partly offset by the increase in our share capital following the issuance of common shares and warrants in the November 2016 Offering.

Outstanding Share Data

As at March 15, 2017, we had 13.5 million common shares issued and outstanding, as well as 968,264 stock options outstanding. Share purchase warrants outstanding as at March 15, 2017 represented a total of 3,779,245 equivalent common shares.

Recent Accounting Pronouncements

The IASB continues to issue new and revised IFRS. A listing of the recent accounting pronouncements promulgated by the IASB and not yet adopted by the Company is included in note 4 to the Company's December 31, 2016 consolidated financial statements which are included in Item 18 of this Annual Report on Form 20-F.

B. Liquidity, Cash Flows and Capital Resources

Our operations and capital expenditures have been financed through certain transactions impacting our cash flows from operating activities, public equity offerings, as well as from drawdowns under various ATM programs.

While the Company had \$22.0 million of cash and cash equivalents as at December 31, 2016, we believe that our cash and cash resources will not be sufficient to fund operations for the next twelve months unless our expenditures are reduced or further financing is obtained. See the section below titled "Summary of key expectations for revenues, operating expenses and cash flows". Our ability to continue as a going concern is dependent upon raising additional financing through equity, debt and/or other non-dilutive funding and partnerships. There can be no assurance that we will have sufficient capital to fund our ongoing operations or the development or commercialization of our products without future financings. There can be no assurance that additional financing will be available on acceptable terms or at all. We are currently pursuing financing alternatives that may include equity, debt, and non-dilutive financing alternatives, including co-development through potential collaborations, strategic partnerships or other transactions with third parties. If we are unable to obtain additional financing when required, we may have to substantially reduce or eliminate planned expenditures or we may be unable to continue our operations. These uncertainties cast substantial doubt as to the ability of the Company to meet its obligations as they come due and, accordingly, the appropriateness of the use of accounting principles applicable to a going concern. The Company's ultimate success, its ability to raise additional financing, whether through equity, debt or other sources of funding and, consequently, to continue as a going concern, is also dependent upon at least one of the two internally developed compounds obtaining positive results in their currently ongoing Phase 3 studies.

On April 1, 2016, we entered into an ATM sales agreement under which we are able, at our discretion and from time to time, to sell up to 3 million of our common shares through ATM issuances on the NASDAQ for aggregate gross proceeds of up to approximately \$10 million. The ATM program provides that common shares are to be sold at market prices prevailing at the time of sale and, as a result, prices may vary. Subsequent to December 31, 2016, the Company issued an additional 555,068 common shares under the April 2016 ATM Program at an average price of approximately \$3.20 per share for gross proceeds of approximately \$1.8 million. The shelf registration statement pursuant to which this program was established expires on March 28, 2017.

On November 1, 2016, we completed a registered direct offering of 2,100,000 units (the "Units"), with each Unit consisting of one common share or one pre-funded warrant to purchase one common share and 0.45 of a warrant to purchase one common share (the "November 2016 Offering"). Total gross cash proceeds raised through the November 2016 Offering amounted to approximately \$7.6 million, less cash transaction costs of approximately \$1.0 million, including the placement agent's fee and expenses. The warrants are exercisable six months after their date of issuance and for a period of three years thereafter at an exercise price of \$4.70 per share. The warrants contain a call provision which provides that, in the event our common shares trade at or above \$10.00 on the principal trading market of our common shares during a specified measurement period and subject to a minimum volume of trading during such measurement period, then, subject to certain conditions, we have the right to call for cancellation all or any portion of the warrants which are not exercised by holders within 10 trading days following receipt of a call notice from us. Upon complete exercise for cash, these warrants would result in the issuance of an aggregate of 945,000 common shares that would generate additional proceeds of approximately \$4.4 million, although these warrants may be exercised on a "net" or "cashless" basis.

The variations in our liquidity by activity are explained below.

(in thousands)	Three months ended December 31, 2016				
	2016		Years ended December 31, 2015		
	2016	2015	2016	2015	2014
Cash and cash equivalents - Beginning of period	21,052	38,345	41,450	34,931	43,202
Cash flows from operating activities:					
Cash used in operating activities from continuing operations	(8,131)	(8,419)	(29,010)	(33,929)	(30,787)
Cash provided by (used in) operating activities from discontinued operations	—	25	—	85	(295)