crystal research associates
Facts Without Fiction

# Æterna Zentaris Inc.

**AEZS-NASDAQ**
**AEZ-TSX**

## Quarterly Update: November 30, 2016

## Company Description

Aeterna Zentaris Inc. ("Aeterna" or "the Company") is a specialty biopharmaceutical company. With a focus on establishing revenues and profitability while optimizing resources to reduce its burn rate, the Company co-promotes two commercial products in multiple U.S. markets: (1) EMD Serono's Saizen® [somatropin (rDNA origin) for injection] for growth hormone deficiencies; and (2) Armune BioScience's APIFINY®, a non-PSA blood test for evaluating prostate cancer risk. Aeterna further holds a pipeline of product candidates in development and is working to acquire or in-license other commercial compounds. One of the Company's wholly owned product candidates, Zoptrex™ [zoptarelin doxorubicin (doxorubicin peptide conjugate targeting LHRH receptor–expressing tumors)], is in a fully enrolled, completed dosing Phase 3 trial in advanced, recurrent, or metastatic endometrial cancer—a disease for which patients typically have a poor prognosis and there is no approved systemic therapy (except in Germany). Aeterna's development program further includes Macrilen™ (macimorelin), which, in October 2016, also completed patient enrollment in a confirmatory Phase 3 trial for the evaluation of Adult Growth Hormone Deficiency (AGHD). Overall, the Company is focused on pursuing strategic initiatives consistent with becoming a commercially operating specialty biopharmaceutical company.

## Key Points

- The Phase 3 trials for both Zoptrex™ and Macrilen™ are nearing completion and are on track to report top-line results in early 2017, potentially followed by the filing of a New Drug Application (NDA) for both Macrilen™ and Zoptrex™ during 2017, pending favorable trial results.
- In October 2016, Aeterna continued to accelerate out-licensing activity for Zoptrex™—further validating market interest in this candidate—with license and supply agreements for Specialised Therapeutics Asia Pty Ltd. for Zoptrex™ in Australia and New Zealand. This represents the fourth global agreement for Zoptrex™ in recent months.
- Commencing June 1, 2016, Aeterna acquired exclusive U.S. marketing rights for the APIFINY® prostate cancer blood test and now holds the sole right to promote APIFINY® to all U.S. medical professionals, receiving a commission on each test sold. Aeterna now promotes APIFINY® in 35 states, with the most recent addition being Florida in August 2016, following the receipt of a clinical laboratory license in the state.
- As of September 30, 2016, Aeterna held cash and cash equivalents of approximately $21.1 million, and subsequently, in November 2016, closed a registered direct offering for $7.56 million in gross proceeds from the sale of common shares, pre-funded warrants, and warrants. For the third quarter 2016, Aeterna reported a net loss of $6.1 million versus a net loss of $15.3 million for the third quarter 2015. Quarter-over-quarter decreases in net loss stemmed from higher comparative net finance income.

Æterna Zentaris

Aeterna Zentaris Inc.
315 Sigma Drive, Suite 302D
Charleston, SC 29483
Phone: (843) 900-3223
Fax: (843) 900-3250
www.aezsinc.com

| Ticker (Exchange) | AEZS (NASDAQ)<br>AEZ (TSX) |
|---|---|
| Recent Price (11/30/16) | $3.40 (NASDAQ) |
| 52-week Range | $2.60 - $10.20* |
| Shares Outstanding | ~12 million |
| Market Capitalization | ~$40.8 million |
| Avg. 3-mo. Daily Volume | 361,379 |
| Insider Ownership + >5% | 5.80% |
| EPS (Qtr. ended 09/30/16) | ($0.61) |
| Employees | 47 |

*100-to-1 share consolidation executed in Nov. 2015.

**AEZS One-Year Chart**

## Recent Events and Financial Results

*All amounts are in U.S. dollars unless otherwise noted.*

Crystal Research Associates continues to have confidence in the potential of the Aeterna story as a result of the accomplished and experienced management team, which has revamped the Company, focusing it across all aspects of the business. The expertise of this management team suggests that, should a product receive approval, the Company possesses the experience to choose the correct course of action to maximize opportunity.

**Recent Events**

- *On November 1, 2016,* Aeterna announced the closing of a previously announced registered direct offering for US$7.56 million in gross proceeds. The offering was to a single healthcare-dedicated institutional investor in the U.S. of 2.1 million units, consisting of either one common share or one-pre-funded warrant to acquire one common share and 0.45 of a warrant to purchase one common share, at a purchase price of US$3.60 per unit. The purchaser acquired units with pre-funded warrants substituted for common shares where the purchase of units with common shares would have resulted in the purchaser beneficially owning more than its beneficial ownership limitation following the consummation of the offering. The warrants have an exercise price of US$4.70 per share and are exercisable six months after their date of issuance and expire three years after their initial exercise date.

  The Company announced its intention to use the net proceeds from the offering to fund the preparation and submission of New Drug Applications for Macrilen™ and Zoptrex™ (if the results of its ongoing clinical trials of such products warrant doing so), for general corporate and working capital purposes, and to fund negative cash flow.

- *On October 26, 2016,* the Company announced it had successfully completed patient recruitment for the confirmatory Phase 3 clinical trial of Macrilen™ as a growth hormone stimulation test for the evaluation of growth hormone deficiency in adults (“AGHD”). The Company also confirmed that it expects to file a New Drug Application for Macrilen™ with the FDA during the first half of 2017, if the results of the trial warrant doing so.

- *On October 12, 2016,* Aeterna announced the signing of an exclusive license agreement with Specialised Therapeutics Asia for Zoptrex™ for the territories of Australia and New Zealand. This agreement is detailed on page 7.

**Third Quarter and Year-to-Date 2016 Financial Results**

On November 8, 2016, Aeterna reported its financial and operating results for the third quarter and nine months ended September 30, 2016.

Aeterna reported research and development (R&D) costs of $4.5 million and $11.9 million for the three and nine months ended September 30, 2016, respectively, versus $4.1 million and $13.0 million for the same periods in 2015. The increase in quarter-over-quarter R&D costs resulted from the start of the confirmatory Phase 3 trial for Macrilen™ at the end of 2015, which just completed patient recruitment in October 2016. Year to date, the decrease in R&D costs from the same period in 2015 is largely a result of lower comparative third-party costs attributable to Zoptrex™, for which patient dosing in the ongoing ZoptEC trial ended in February 2016, as well as lower employee compensation, benefits, and other costs related to the Company’s previously enacted ongoing effort to streamline R&D activities.

General and administrative (G&A) expenses for Aeterna were $1.6 million and $5.4 million for the three and nine months ended September 30, 2016, respectively, versus $1.9 million and $7.4 million for the same periods in 2015. The decreases in G&A expenses stems from the impact of recent corporate restructuring as well as the recording, in the prior year period, of certain transaction costs allocated to warrants in connection with the completion of an offering in March 2015.

Aeterna reported relatively flat selling expenses of $1.8 million and $5.2 million for the three and nine months ended September 30, 2016, respectively, versus $1.7 million and $5.1 million for the same periods in 2015. The Company's net loss for the three and nine months ended September 30, 2016, was $6.1 million and $16.7 million, or ($0.61) and ($1.68) per basic and diluted share, versus a net loss of $15.3 million and $40.1 million, or ($6.66) and ($29.12) per basic and diluted share, for the same periods in 2015. The decrease in net loss for the third quarter 2016 was due largely to higher comparative net finance income, while the year-to-date decrease in net loss was due largely to lower operating expenses and higher comparative net finance income.

*Cash Position*

As at September 30, 2016, Aeterna held cash and cash equivalents of approximately $21.1 million versus approximately $26.2 million as at June 30, 2016. During the third quarter 2016 and subsequent to the quarter's end, Aeterna raised approximately $2.3 million in gross proceeds from the sale of 580,912 common shares pursuant to the Company's ATM program. Also subsequent to the quarter's end, Aeterna closed a registered direct offering for $7.56 million in gross proceeds from the sale of common shares, pre-funded warrants, and warrants, and thus believes it is positioned financially to complete both of its pivotal Phase 3 trials and potentially file a New Drug Application for Macrilen™ during 2017.

## Company Background

Aeterna Zentaris Inc. ("Aeterna" or "the Company") is a specialty biopharmaceutical company engaged in developing, commercializing, and promoting novel treatments in oncology and endocrinology via internal development programs as well as expanding its commercial portfolio through co-promotion, in-licensing, and the acquisition of products already on the market. With a focus on establishing revenues and profitability while optimizing resources and reducing its burn rate, the Company has two commercial programs at present: (1) promotion of a growth hormone deficiency product, EMD Serono, Inc.'s Saizen®; and (2) promotion of Armune Bioscience, Inc.'s APIFINY®, the first non-PSA blood test for use in evaluating and managing the risk of prostate cancer. Aeterna routinely pursues opportunities to in-license or acquire products to further complement its portfolio.

Aeterna also holds a pipeline of candidates in varying stages of development, including two product candidates (Zoptrex™ and Macrilen™) in Phase 3 studies. Both Phase 3 trials are nearing completion and are on track to report top-line results in early 2017, potentially followed by the filing of a New Drug Application (NDA) for both Macrilen™ and Zoptrex™ during 2017, pending favorable trial results. This could be a significant milestone for the Company that would mark the completion of two Phase 3 clinical programs.

As well, during 2016, Aeterna ramped up out-licensing activity for Zoptrex™, which included agreements for the drug in Taiwan, Southeast Asia, Israel, Palestine, Australia, and New Zealand. In addition, the Company's licensee in China filed an Investigational New Drug (IND) application for Zoptrex™ with the Chinese FDA in June 2016, and anticipates the start of a clinical program in China in the first half of 2017.

Aeterna is also investigating various other compounds as potential treatments in oncology and endocrinology as it pursues strategic initiatives that are consistent with the operations of a commercial specialty biopharmaceutical company.

**Promotional Agreement with Merck's EMD Serono, Inc. for Saizen®**

In May 2015, Aeterna entered into a promotional services agreement with EMD Serono, Inc., the U.S. and Canadian biopharmaceutical businesses of Merck KGaA (MRK-NYSE). Under the agreement, Aeterna is promoting Saizen® [somatropin (rDNA origin) for injection] to designated medical professionals in specified territories in the U.S. Aeterna works within the realm of field promotion of Saizen® by driving awareness of the product among medical professionals, and is compensated on the basis of new, eligible patient starts on Saizen® above an agreed-upon baseline. Aeterna began promoting the product in the U.S. in July 2015. Financial terms of this agreement were not disclosed.

*About Saizen® for Growth Hormone Deficiency*

Saizen® is a recombinant human Growth Hormone (r-hGH) registered in the U.S. for the treatment of growth hormone deficiency (GHD) in both children and adults. A deficiency of growth hormone in the body can cause slow growth in children, and without treatment, few will reach their full height potential as an adult. It is a disorder affecting one in every 4,000 to 10,000 children and up to three in every 10,000 adults. Aeterna believes that Saizen® represents a good fit for the Company's endocrinology portfolio currently in development, which includes Aeterna's in-house product candidate Macrilen™ (profiled on pages 8-9), a novel, orally available peptidomimetic ghrelin receptor agonist that stimulates the secretion of growth hormone and that, if approved, will be used to diagnose adult growth hormone deficiency.

*Please see full prescribing information and important risk information for Saizen® at www.saizenus.com/.

**Co-Marketing Agreement with Armune BioScience, Inc. for APIFINY®**

APIFINY® is a blood test for assessing and managing the risk of prostate cancer that is believed to be the only cancer-specific tool available that does not rely on a PSA reading. Prostate-specific antigen (PSA) is a protein produced in the prostate, a small gland that sits below a man's bladder. A PSA test measures the amount of PSA in the blood in order to help detect the presence of prostate cancer. However, this conventional diagnostic tool is known to significantly over-diagnose prostate cancer risk, resulting in what is believed to be an overuse of prostate biopsies in patients. In an effort to be proactive at detecting prostate cancer, there are approximately 30 million PSA tests conducted annually to screen for prostate cancer. An estimated 1.8 million prostate biopsies are performed based on results of the PSA tests—with 7-8 of every 10 biopsies proving to be benign. Essentially, based on the PSA test, millions of cancer-free patients are sent for unnecessary needle biopsies every year—creating tremendous patient discomfort (including the potential for medical complications resulting in morbidity) along with billions of dollars of needless expenditures. Medical institutions are now recommending more restricted use due to the inability of the PSA test to confidently and noninvasively evaluate the risk that the patient has prostate cancer.

As a modern approach to improve the detection of prostate cancer, APIFINY® is the only cancer-specific, non-PSA blood test designed to aid clinicians in prostate cancer risk assessment. APIFINY® measures eight prostate-cancer-specific autoantibodies in human serum, which have been found to be amplified in response to the presence of prostate cancer cells. To Aeterna's knowledge, APIFINY® is able to detect these stable autoantibodies, particularly in small tumors characteristic of early stage cancers. The autoantibody markers span a range of biological functions integral to prostate cancer progression (including cell cycle, structure, and cellular signaling pathways), thus the use of APIFINY® may help supplement other information about a patient's risk of prostate cancer and may therefore aid clinicians in the detection of prostate cancer.

APIFINY® is intended for use by primary care physicians, urologists, and oncologists as a method of complementing current screening and detection methods in order to give a more complete and accurate picture of a patient's risk of prostate cancer. Aeterna entered into a co-marketing agreement in certain sales territories for APIFINY® with Michigan-based Armune BioScience, Inc. (http://armune.com/) in December 2015. Armune is a medical diagnostics company equipped with a CLIA-certified commercial reference laboratory. Commencing on June 1, 2016, Aeterna acquired exclusive U.S. marketing rights for the APIFINY® prostate cancer blood test and now holds the sole right to promote APIFINY® to all U.S. medical professionals, receiving a commission on each test sold. The most recent new sales territory is Florida, where Armune was granted a clinical laboratory license in summer 2016. The Company now promotes APIFINY® in 35 states. Armune reports that, in less than one year on the market, APIFINY® has been ordered more than 5,000 times as clinicians move beyond PSA-based testing to assess prostate cancer risk.

The transaction with Armune enhances Aeterna's focus on the oncology market, especially for the diagnosis, monitoring, and treatment of prostate cancer, which is also a relevant medical indication for the Company's Zoptrex™ product candidate in development.

*Prostate Cancer*

As the second leading cancer in men, prostate cancer is also the leading cause of cancer death among men of all races and populations. In 2015, approximately 221,000 men in the U.S. were diagnosed with prostate cancer and approximately 28,000 men died from the disease.

**Zoptrex™ [Zoptarelin Doxorubicin (Doxorubicin Peptide Conjugate)]**

Zoptrex™ (zoptarelin doxorubicin), an investigational new drug, represents a new concept in oncology using a hybrid molecule composed of a synthetic peptide carrier and a well-known chemotherapy agent, doxorubicin. As the first intravenous drug in a clinical study to direct a chemotherapy agent specifically to luteinizing hormone-releasing hormone (LHRH)-receptor expressing tumors, Zoptrex™ is believed to lead to a more targeted treatment with less damage to healthy tissue and reduced side effects. The Company's most advanced indication is for advanced, recurrent, or metastatic endometrial cancer (noting that endometrial cancer is the most common of the gynecologic malignancies and was estimated to affect 1 in 37 women during 2015). If Zoptrex™ is approved for its first indication, Aeterna intends to develop the compound for other tumors also expressing the LHRH-receptor, such as ovarian, prostate, and possibly additional cancer indications as part of the product's lifecycle management program. A Phase 2 trial in ovarian cancer has been successfully completed and published, while an investigator-initiated Phase 2 trial in prostate cancer was recently reported to have successfully met its primary endpoint.

Patients with advanced and recurrent endometrial cancer typical have a poor prognosis. There is no known or approved systemic therapy (except in Germany) for advanced (Stages III or IV) and recurrent metastatic endometrial cancer. Moreover, while response rates of up to 50% have been seen in patients receiving combination chemotherapy, the duration of the responses are short and the medications carry high toxicity. Due to the difficulty in treating women with late-stage endometrial cancer, new therapies are being developed to try and help better target and kill cancerous cells. As such, Aeterna is developing Zoptrex™ for an advanced form of endometrial cancer.

*Phase 3 Zoptrex™ Study in Endometrial Cancer*

The ZoptEC Phase 3 study in women with advanced, recurrent, or metastatic endometrial cancer who have progressed and have received one chemotherapeutic regimen with platinum and taxane (either as adjuvant or first-line treatment) has completed enrollment of 500 patients. The first patient was dosed in July 2013, and the trial is being conducted at over 120 sites across North America, Europe, and Israel. The primary efficacy endpoint of this study is improvement in median overall survival as compared to standard therapy with doxorubicin.

In October 2015, the Zoptrex™ trial's independent Data and Safety Monitoring Board (DSMB) recommended that the Company continue its Phase 3 clinical study as planned to full completion. The DSMB's decision came after the completion of a pre-specified second interim analysis on efficacy and safety for the Zoptrex™ Phase 3 trial at approximately 192 events. In April 2015, the DSMB made the same recommendation following its first pre-specified analysis on safety and futility at approximately 128 events. A final analysis of the data is expected at approximately 384 events.

The Company expects top-line results in the first quarter 2017, which may be followed by the filing of an NDA and Marketing Authorization Application (MAA) for Zoptrex™ in 2017, and a potential commercial launch in late 2018. If approved, Zoptrex™ could become the first FDA-approved medical therapy for treating recurrent endometrial cancer. Medical therapies used in treating recurrent endometrial cancer account for approximately $300 million to $500 million in the U.S. When considering additional indications in the U.S., the annual market opportunity could exceed $1 billion in Aeterna's opinion.

Sinopharm A-Think License

In China, Hong Kong, and Macau, rights to Zoptrex™ have been out-licensed to Sinopharm A-Think (a subsidiary of China National Pharmaceutical Group Corp., the largest medical and healthcare group in China and on *Fortune's* Global 500 list). Sinopharm submitted an IND for Zoptrex™ in China in mid-2016, and is poised to commence clinical development of the product candidate during 2017. The licensee has also already implemented local manufacturing processes for Zoptrex™ for clinical trials. Aeterna provided Sinopharm with the information regarding the chemistry, manufacturing, and controls related to the manufacture of Zoptrex™, which was used for the IND application.

Ergomed Agreement

In April 2013, Aeterna announced that it had signed a co-development and profit-sharing agreement with UK-based Ergomed plc for zoptarelin doxorubicin in endometrial cancer. Ergomed was selected as the contract clinical development organization to conduct the Zoptrex™ Phase 3 trial. Under the terms of the agreement, Ergomed has agreed to assume 30% (up to $10 million) of the out-of-pocket clinical and regulatory costs for the trial, estimated at approximately $32.5 million. As well, Ergomed is to receive its return on investment based on an agreed percentage of any net income received by Aeterna for zoptarelin doxorubicin in this indication (up to a maximum amount specified in the agreement).

In June 2015, Aeterna executed another agreement with Ergomed for the management of the Company's confirmatory Phase 3 clinical study of Macrilen™ as well.

Orient EuroPharma Co., Ltd.

On July 1, 2016, Aeterna entered into an exclusive license agreement and a manufacturing tech transfer agreement with an affiliate of Orient EuroPharma, called Cyntec Co., Ltd., for Zoptrex™. Orient EuroPharma is a multinational pharmaceutical company able to integrate pharmaceutical R&D, clinical trials, manufacturing, and marketing in Taiwan. In particular, Orient offers a comprehensive Southeast Asian sales and operations network. Under the license agreement, Cyntec is granted the right to commercialize Zoptrex™ for endometrial cancer in Taiwan and nine countries of Southeast Asia, in exchange for a non-refundable upfront payment, future milestone payments, and royalties on potential sales. Cyntec is further responsible for the development, registration, reimbursement, and commercialization of Zoptrex™ in Taiwan and Southeast Asia.

License to Rafa Laboratories, Ltd.

In July 2016, Aeterna licensed the rights to commercialize Zoptrex™ in endometrial cancer to Israeli pharmaceutical company Rafa Laboratories, Ltd. for distribution in Israel and Palestine. Rafa compensated Aeterna with a non-refundable upfront payment in consideration for the license and the related intellectual property as well as anticipated milestone payments upon the completion of certain regulatory and commercial milestones and double-digit royalties on future net sales of Zoptrex™. Rafa must further be responsible for the development, registration, reimbursement, and commercialization of the oncology candidate in the Israel and Palestinian territories. The supply of Zoptrex™ for this agreement is expected to come from Aeterna.

Specialised Therapeutics Asia Pte Ltd.

On October 12, 2016, Aeterna and international biopharmaceutical company Specialised Therapeutics entered into an exclusive license agreement for Zoptrex™ in Australia and New Zealand. Under the terms of the agreement, Aeterna is entitled to receive a non-refundable upfront payment in exchange for granting Specialised Therapeutics the right to commercialize Zoptrex™ and associated intellectual property in Australia and New Zealand. Specialised Therapeutics agreed to make additional payments to the Company as well, upon achieving certain pre-established regulatory and commercial milestones, and royalties on future net sales of Zoptrex™. Specialised Therapeutics is responsible for the development, registration, reimbursement, and commercialization of Zoptrex™ in Australia and New Zealand. Aeterna has agreed to supply Specialised Therapeutics with Zoptrex™ for the duration of the license agreement.

Patent Applications for Zoptrex™

Aeterna has recently filed patent applications to protect the method of manufacturing Zoptrex™ in a number of global jurisdictions, including the U.S., China, Taiwan, Japan, India, and the European Union. This proprietary manufacturing method is anticipated to lead to a significant cost reduction in the production of Zoptrex™ and a possibly stronger competitive position for Aeterna in the future as it seeks to commercialize this product candidate.

*Additional Potential Indications for Zoptrex™*

Aeterna is continuing to develop its commercialization plans regarding Zoptrex™ in endometrial cancer, including establishing partnerships in territories that the Company does not intend to pursue. In addition, contingent on the success of the current clinical program, the Company may have additional areas of interest for further therapeutic development, including ovarian, prostate, triple negative breast cancer, and potentially bladder cancer.

By and large, recurrent ovarian cancer is considered incurable, with therapies at this stage mainly seeking palliative treatment of symptoms, maintaining or improving quality of life, and increasing survival. Aeterna has completed a successful Phase 2 trial with zoptarelin doxorubicin in women with platinum-resistant ovarian cancer, a late-stage form of the disease during which refractory tumor growth is observed despite use of primary therapy. The compound has been granted orphan drug designation by the FDA and orphan medicinal product designation from the European Medicines Agency (EMA) in treating ovarian cancer.

Zoptrex™ was also evaluated as a treatment for prostate cancer by an independent investigator. An article on final data for the Phase 1 portion of a Phase 1/2 trial in prostate cancer with zoptarelin doxorubicin was published in the December 2014 issue of *Clinical Cancer Research*. The article outlines data previously disclosed in June 2013 at the ASCO Annual Meeting, which demonstrated the compound's safety profile and potential anti-tumor activity in men with castration- and taxane-resistant prostate cancer (CRPC) who have been heavily pre-treated. Results from the Phase 2 portion of this investigator-driven trial were released in late 2015 and are overviewed below.

Achieved Primary Endpoint in Men with Heavily Pre-treated, Castration- and Taxane-Resistant Prostate Cancer

In September 2015, zoptarelin doxorubicin met its primary endpoint in an investigator-driven and sponsored Phase 2 clinical trial in CRPC and demonstrated good tolerability. The primary endpoint was clinical benefit (CB), defined as remaining progression-free by RECIST and Prostate-Specific Antigen (PSA) after treatment for over 12 weeks. The trial enrolled 25 patients with CRPC. Data show that 11 patients in the trial experienced a clinical benefit; 13 with stable disease. The median progression-free survival and overall survival timelines were 4.4 months (95% confidence interval [CI]: 3.6, 5.5) and 6 months (95% CI: 4.2, 10.7), respectively. In addition, 44% of patients reported an improvement in pain score at 12 weeks, and maximal PSA response was stable in 20 patients. Zoptarelin doxorubicin demonstrated good tolerability with grade 3-4 hematologic (n=7) and grade 3 blood and lymphatic system disorders (n=5) adverse events as the most common events. Results were presented by the study's lead investigator, Jacek Pinski, M.D., Ph.D., of the USC Norris Comprehensive Cancer Center, during a poster session at the 18$^{th}$ ECCO – 40$^{th}$ ESMO European Cancer Congress in Vienna, Austria.

**Macrilen™ (Macimorelin)**

Macrilen™, an investigational new drug, is an orally active ghrelin agonist for use in evaluating AGHD. On April 13, 2015, the Company announced plans to conduct a new, confirmatory clinical study to demonstrate the efficacy of Macrilen™ for use in the evaluation of AGHD, as well as a dedicated thorough QT study to evaluate the effect of Macrilen™ on myocardial repolarization. Aeterna has stated that this decision followed a positive and constructive meeting with the FDA regarding the NDA for Macrilen™. The Company requested the meeting to gain clarity on the approval deficiencies described in a Complete Response Letter (CRL) that Aeterna had received on November 6, 2014. Following receipt of the CRL, the Company convened a panel of U.S. and EU endocrinology experts to advise it regarding the options for Macrilen™. According to Aeterna, the panel advised the Company to continue to seek approval for the compound because of their confidence in its efficacy and because there is not currently an FDA-approved diagnostic test for AGHD.

Following an end-of-review meeting with the FDA on March 6, 2015, the Company and the FDA agreed on the general design of the confirmatory study as well as evaluation criteria. The study is a two-way crossover with the insulin tolerance test as the benchmark comparator. The study population consists of patients with a medical history documenting risk factors for AGHD and includes a spectrum of patients, ranging from those who have a low risk of AGHD to those with a high risk of the condition. Additionally, Aeterna received written scientific advice from the EMA in May 2015 suggesting that the Company's plan for a new Phase 3 trial of Macrilen™, as discussed with the FDA, would also be acceptable to the EMA (Source: Aeterna's May 26, 2015, press release). The EMA did

propose that Aeterna consider additional aspects regarding the demonstration of reproducibility of a diagnosis made using Macrilen™, which would further enhance the profile of the compound.

With continued development and the initiation of a confirmatory Phase 3 trial in November 2015, Aeterna was able to reach a key milestone in its Phase 3 development of Macrilen™ in early 2016, when the Company met with clinical investigators for its Phase 3 trial. This January 2016 meeting included 77 investigators and site personnel who reviewed Macrilen™ and the clinical trial protocol for the compound's multicenter Phase 3 trial. The Phase 3 trial completed patient enrollment in October 2016, and is on track to report top-line data in early 2017, which could be followed by an NDA submission in the first half of 2017, pending the outcome of trial results. This trial is examining Macrilen™ in comparison to the insulin tolerance test (ITT) at approximately 30 trial sites across the U.S. and Europe, and in over 110 patients who have a medical history documenting risk factors for AGHD (a spectrum of low- and high-risk patients).

Aeterna estimates that approximately 40,000 confirmatory tests for AGHD could be conducted annually in the U.S. after the market introduction of Macrilen™, if it is approved by the FDA, with physician and patient adoption likely driven by the following factors:

- Increased patient safety due to avoiding the insulin injection procedure and potential complications;
- Oral administration instead of intravenous insulin injection;
- Improvements in speed of the diagnostic procedure while also being less labor intensive and less expensive than ITT; and
- Appropriateness for administration in a physician's office versus a hospital.

**Other Preclinical Compounds**

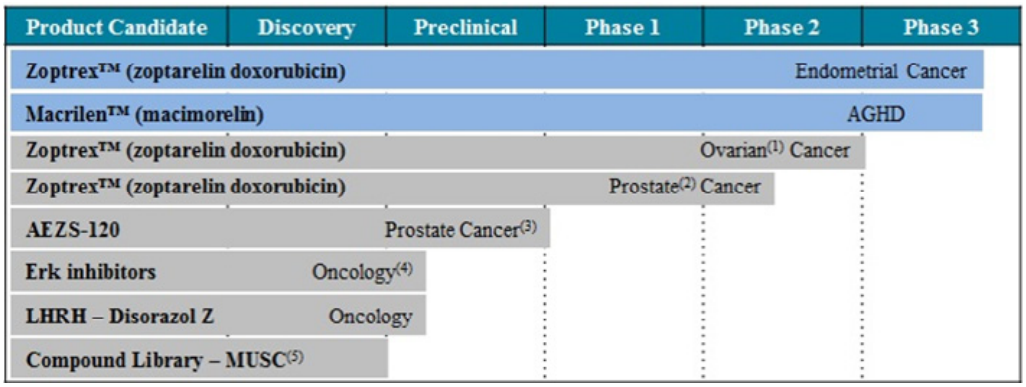
Aeterna also has in its pipeline LHRH disorazol Z, a next-generation zoptarelin doxorubicin, which is a cytotoxic conjugate of disorazol Z and a synthetic peptide carrier that targets the LHRH receptor (and may also have potential in solid tumors). Aeterna believes disorazol Z is a beneficial compound for the formation of cytotoxic conjugates with peptides, proteins, and antibodies to selectively target cancer cells. The Company has patented disorazol Z in 35 countries, including the U.S., Japan, Europe, China, Russia, Korea, and Taiwan. This patent protection expires in 2026. As well, a conjugate of disorazol Z and the LHRH receptor agonist as a targeted cytotoxic agent is patented in 15 countries, including the U.S., Japan, China, Russia, Korea, and Taiwan. This patent protection expires in 2027. Aeterna expects a European patent to be granted in the near future.

**Pipeline and Development Summary**

Figure 1 (page 10) summarizes the Company's current product pipeline, which is described in greater detail on pages 16-30 of Crystal Research Associates' base Executive Informational Overview® (EIO) published on Aeterna and available at http://www.crystalra.com/research-library/aeterna-zentaris.

Figure 1

PRODUCT PIPELINE




(1) Phase 2 in ovarian cancer completed.

(2) Investigator-driven and sponsored Phase 2 trial in castration- and taxane-resistant prostate cancer completed.

(3) Potential oral prostate cancer vaccine available for co-development/out-licensing, subject to an option granted to a third party.

(4) Available for co-development/out-licensing.

(5) Compound library transferred to Medical University of South Carolina (MUSC). Aeterna Zentaris has access to future potential development candidates.

*Source: Aeterna Zentaris Inc.*

**Key Corporation Information**

The Company was incorporated on September 12, 1990, under the Canada Business Corporations Act (CBCA) and continues to be governed by the CBCA. On December 30, 2002, it 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, the Company's name was changed to Aeterna Zentaris Inc. and on May 11, 2007, Zentaris GmbH was renamed Aeterna Zentaris GmbH. On October 2, 2012, Aeterna effected a 6-to-1 reverse stock split and on October 5, 2012, the common shares began trading on a consolidated and adjusted basis on both the NASDAQ and TSX. In November 2015, the Company performed another share consolidation at a ratio of 100-to-1.

The Company's operational base is in Charleston, South Carolina, with offices also in Frankfurt, Germany. Aeterna trades on the NASDAQ under the ticker symbol AEZS and on the TSX under AEZ. Its three wholly owned direct and indirect subsidiaries include Aeterna Zentaris GmbH (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.

## Key Points to Consider

- **Aeterna is a specialty biopharmaceutical company in oncology and endocrinology, focused on establishing revenues and profitability while optimizing resources and reducing burn rate.** The Company is working to achieve a commercial presence and growth via licensing and acquisition opportunities, and currently co-promotes two marketed products: (1) Saizen®, a growth hormone deficiency therapy, and (2) APIFINY®, a non-PSA blood test for use in evaluating the risk of prostate cancer. Aeterna also holds a pipeline of candidates in varying stages of development, including Zoptrex™ (doxorubicin peptide conjugate), a Phase 3 therapy for advanced, recurrent, or metastatic endometrial cancer; and Macrilen™ (macimorelin), an orally available, Phase 3, peptidomimetic ghrelin receptor agonist that stimulates the secretion of growth hormone and may diagnose AGHD. Other indications for zoptarelin doxorubicin may include tumors expressing the LHRH receptor, such as prostate cancer, bladder cancer, breast cancer, or ovarian cancer.

- **Aeterna has promotion services agreements with Merck's EMD Serono, Inc. for Saizen® [somatropin (rDNA origin) for injection] and with Armune BioScience, Inc. for APIFINY®—enabling Aeterna to transition beyond the development stage and into a commercial entity.** Aeterna's contractual sales force promotes Saizen® in 21 U.S. sales territories on a commission basis and APIFINY® across the entire U.S. exclusively (also on a commission basis).

- **Zoptrex™ (zoptarelin doxorubicin) is a new concept in oncology.** This hybrid molecule, which is delivered intravenously, is composed of a synthetic peptide carrier and doxorubicin, which directs the chemotherapy agent specifically to LHRH-receptor-expressing tumors. There is an indication from Phase 2 studies that the compound results in a targeted treatment with less damage to healthy tissue and fewer side effects than doxorubicin, which does not represent any form of targeted therapy.

- **As an ongoing Phase 3 trial for endometrial cancer, the ZoptEC (zoptarelin doxorubicin in endometrial cancer) study has enrolled 500 patients at over 120 sites in North America, Europe, and Israel.** The Company is working under a Special Protocol Assessment (SPA) with UK-based Ergomed plc where the two entities have a cost-sharing agreement in place. The trial is expected to be completed by the end of 2016, followed by an NDA submission to the FDA in 2017. If approved, Zoptrex™ could become the first FDA-approved therapy for treating recurrent endometrial cancer.

- **The Company is also near to the completion of a confirmatory Phase 3 clinical study to demonstrate the efficacy of Macrilen™ for use in evaluating AGHD.** This decision followed positive meetings with the U.S. FDA and the European Medicines Agency (EMA) regarding Macrilen™. The Phase 3 trial completed enrollment in October 2016 with patients who have a medical history documenting risk factors for AGHD (including low-, medium-, and high-risk patients). Aeterna believes it will likely release top-line results in early 2017. Submission of the NDA for Macrilen™ is anticipated in the first half of 2017, pending trial results.

- **Aeterna has assembled a strong leadership team with experience and demonstrated ability in building significant value in the pharmaceutical industry.** The Company is listed on both the NASDAQ and the TSX exchanges. As of September 30, 2016, Aeterna held cash and cash equivalents of approximately $21.1 million and subsequently raised $7.56 million in gross proceeds from a registered direct offering and an additional $1.7 million through use of an ATM.

## Risks and Disclosures

This Quarterly Update has been prepared by Crystal Research Associates, LLC (CRA) based upon information provided by Aeterna. CRA has not independently verified such information. Some of the information in this Update relates to future events or future business and financial performance. Such statements constitute forward-looking information within the meaning of the Private Securities Litigation Act of 1995. Such statements can only be predictions and the actual events or results may differ from those discussed due to the risks described in Aeterna's statements in its public and investor materials as well as regulatory forms filed from time to time.

The content of this report with respect to Aeterna has been compiled primarily from information available to the public released by the Company through news releases, investor presentations, and other materials released from time to time. Aeterna is solely responsible for the accuracy of this information. Information as to other companies and information as to the prevalence of certain disease and of the use of certain treatment modalities has been prepared from publicly available information and has not been independently verified by Aeterna or CRA. Certain summaries of activities and outcomes have been condensed to aid the reader in gaining a general understanding. CRA assumes no responsibility to update the information contained in this report. In addition, CRA has been compensated by the Company in cash of thirty-nine thousand U.S. dollars for its services in creating the base report and updates. Investors should carefully consider the risks and information about Aeterna's business, as described in Crystal Research Associates' Executive Informational Overview® (EIO) published on April 21, 2015, and Aeterna's regulatory filings. Investors should not interpret the order in which considerations are presented in filings as an indication of their relative importance. The risks and uncertainties overviewed in the EIO are not the only risks that the Company faces. Additional risks and uncertainties not presently known to Aeterna or that it currently believes to be immaterial may also adversely affect the Company's business. If any of such risks and uncertainties develops into an actual event, Aeterna's business, financial condition, and results of operations could be materially and adversely affected, and the trading price of the Company's shares could decline. This report is published solely for information purposes and is not to be construed as an offer to sell or the solicitation of an offer to buy any security in any state. Past performance does not guarantee future performance. Additional information about Aeterna, as well as copies of this report, can be obtained by calling (843) 900-3223.

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## QUARTERLY UPDATE: November 30, 2016

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Crystal Research Associates is led by Wall Street veterans, Jeffrey Kraws and Karen Goldfarb. Together, Kraws and Goldfarb have built a unique business model, capitalizing on decades of experience as an award-winning sell-side analyst team to produce institutional-quality industry and market research in a manner that is easily understood by investors and consumers. Our firm's approach has been proven successful over the years as our products are published and available on Bloomberg, Thomson Reuters/First Call, Capital IQ, FactSet, Yahoo! Finance, and scores of other popular forums.

880 Third Avenue, 6th Floor, New York, NY 10022 Office: (212) 851-6685