Aeterna Zentaris Inc.
Form 20-F
March 28, 2008

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 20-F

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

OR

x Annual Report Pursuant to Section 13 or 15(d) of The Securities Exchange Act of 1934 for the fiscal year ended December 31, 2007

OR

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

OR

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

Commission file number 0-30752

ÆTERNA ZENTARIS INC.

(Exact Name of Registrant as Specified in its Charter)

Not Applicable
(Translation of Registrant s Name into English)

Canada
(Jurisdiction of incorporation)

1405, Parc-Technologique Blvd.
Quebec City, Quebec
Canada, G1P 4P5

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**
Common Shares	NASDAQ Global 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 of the close of the period covered by the annual report: 53,187,470 common shares as of December 31, 2007.

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

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 o No x

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 x No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant s knowledge, in a definitive proxy or information statements incorporated by reference in Part III of this Form 20-F or any amendment to this Form 20-F. o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 20-F or any amendment to this Form 20-F. o

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 o	Accelerated filer x	Non-accelerated filer o

Indicate by checkmark which financial statement item the registrant has elected to follow. Item 17 o Item 18 x

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

Basis of Presentation

General

Except where the context otherwise requires, all references in this Annual Report on Form 20-F (Form 20-F) to the Company , Æterna Zentaris Inc. , we , us , our or similar words or phrases are to Æterna Zentaris Inc. and its subsidiaries, taken together. In this Form 20-F, references to $ and US$ are to United States dollars and references to C$ are to Canadian dollars. Unless otherwise indicated, the statistical and financial data contained in this Form 20-F are presented as at December 31, 2007.

Forward-Looking Statements

This annual report contains forward-looking statements made pursuant to the safe harbor provisions of the U.S. Securities Litigation Reform Act of 1995. Forward-looking statements involve known and unknown risks and uncertainties, which could cause the Company s actual results to differ materially from those in the forward-looking statements. Such risks and uncertainties include, among others, the availability of funds and resources to pursue R&D projects, the successful and timely completion of clinical studies, the ability of the Company to take advantage of business opportunities in the pharmaceutical industry, uncertainties related to the regulatory process and general changes in economic conditions. Investors should consult the Company s quarterly and annual filings with the Canadian and U.S. securities commissions for additional information on risks and uncertainties relating to the forward-looking statements. Investors are cautioned not to rely on these forward-looking statements. The Company does not undertake to update these forward-looking statements. We disclaim any obligation to update any such factors or to publicly announce the result of any revisions to any of the forward-looking statements contained herein to reflect future results, events or developments except if we are requested by a governmental authority or applicable law.

TABLE OF CONTENTS

GENERAL INFORMATION

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 selected financial data should be read in conjunction with our audited consolidated financial statements and the related notes included elsewhere in this annual report, and Item 5. Operating and Financial Review and Prospects of this annual report.

Consolidated Statements of Earnings Data:

Amounts under Canadian GAAP

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

	Years Ended December 31,				
	2007	**2006**	**2005**	**2004**	**2003**
	$	**$**	**$**	**$**	**$**
Revenues	42,068	38,799	44,813	42,972	32,897
Operating expenses					
Cost of sales, excluding depreciation and amortization	12,930	11,270	8,250	7,992	4,821
Selling, general and administrative	20,403	16,478	14,403	13,137	11,044
Research and development costs	39,248	27,422	25,544	23,431	31,873
Research and development tax credits and grants	(2,060)	(1,564)	(317)	(845)	(672)
Depreciation and amortization					
Property, plant and equipment	1,562	2,816	1,665	1,958	2,429
Intangible assets	4,004	6,148	4,279	4,178	3,866
Impairment of long-lived asset held for sale	735				
	76,822	62,570	53,824	49,851	53,361
Loss from operations	(34,754)	(23,771)	(9,011)	(6,879)	(20,464)
Other revenues (expenses)					
Interest income	1,904	1,441	1,235	1,286	1,258
Interest expense					
Long-term debt and convertible term loans	(85)	(1,270)	(6,979)	(4,150)	(2,579)
Other		(163)	(31)	(69)	(481)
Foreign exchange (loss) gain	(1,035)	319	(87)	(491)	(103)
Loss on disposal of equipment	(28)				
Gain on disposal of a long-term investment		409			
	756	736	(5,862)	(3,424)	(1,905)
Share in the results of an affiliated company		1,575			
Loss before income taxes	(33,998)	(21,460)	(14,873)	(10,303)	(22,369)
Income tax recovery (expense)	1,961	29,037	(609)	(273)	(823)
Net (loss) earnings from continuing operations	(32,037)	7,577	(15,482)	(10,576)	(23,192)
Net (loss) earnings from discontinued operations	(259)	25,813	26,053	6,151	3,108
Net (loss) earnings	(32,296)	33,390	10,571	(4,425)	(20,084)
Net (loss) earnings per share from continuing operations					
Basic	(0.61)	0.14	(0.34)	(0.23)	(0.54)
Diluted	(0.61)	0.14	(0.34)	(0.23)	(0.54)
Net (loss) earnings per share from discontinued operations					
Basic	(0.00)	0.50	0.57	0.13	0.07

Diluted	(0.00)	0.48	0.57	0.13	0.07
Net (loss) earnings per share					
Basic	(0.61)	0.64	0.23	(0.10)	(0.47)
Diluted	(0.61)	0.62	0.23	(0.10)	(0.47)
Weighted average number of shares					
Basic	53,182,803	52,099,290	46,139,814	45,569,176	42,993,432
Diluted	53,182,803	52,549,260	46,139,814	45,569,176	42,993,432

Amounts under U.S. GAAP

	2007 $	2006 $	2005 $	2004 $	2003 $
Net earnings (loss) for the year	(37,428)	34,262	15,970	(2,082)	(29,469)
Out of which:					
Net earnings (loss) from:					
continuing operations	(36,415)	8,449	(10,083)	(8,158)	(32,609)
discontinued operations	(1,013)	25,813	26,053	6,076	3,140
Net earnings (loss) per share from continuing operations					
Basic	(0.68)	0.16	(0.22)	(0.18)	(0.76)
Diluted	(0.68)	0.16	(0.22)	(0.18)	(0.76)
Net (loss) earnings per share from discontinued operations					
Basic	(0.02)	0.50	0.56	0.13	0.07
Diluted	(0.02)	0.49	0.56	0.13	0.07
Net (loss) earnings per share					
Basic	(0.70)	0.66	0.34	(0.05)	(0.69)
Diluted	(0.70)	0.65	0.34	(0.05)	(0.69)
Weighted average number of shares					
Basic	53,182,803	52,099,290	46,139,814	45,569,176	42,993,432
Diluted	53,182,803	52,549,260	46,139,814	45,569,176	42,993,432

Consolidated Balance Sheet Data:

Amounts under Canadian GAAP

	2007 $	2006 $	2005 $	2004 $	2003 $
Cash and cash equivalents	10,272	8,939	12,234	13,568	7,454
Short-term investments	31,115	51,550	22,370	22,477	26,253
Working capital	37,325	85,413	99,502	60,291	46,401
Total assets	123,363	223,491	419,785	290,539	187,487
Long-term debt		687	29,866	17,398	14,656
Share capital	30,566	168,466	130,344	127,585	118,915
Shareholder s equity	88,591	178,879	109,531	100,076	79,945

Amounts under U.S. GAAP

	2007 $	2006 $	2005 $	2004 $	2003 $
Cash and cash equivalents	10,272	8,939	12,234	13,568	7,454
Short-term investments	31,115	51,550	22,370	22,477	26,253
Working capital	37,325	85,413	99,502	60,291	46,401

Total assets	109,182	209,143	404,587	271,440	171,399
Long-term debt		687	30,858	19,986	17,876
Share capital	22,589	160,489	129,750	126,991	125,731
Shareholder s equity	74,410	169,704	99,797	86,659	82,128

Note: The 2003 balance sheet data were originally reported in Canadian dollars. These amounts have been translated to U.S. dollars using the exchange rate as of December 31, 2003, which exchange rate was C$1.00 to US$0.6339.

B. Capitalization and indebtedness.

Not applicable.

C. Reasons for the offer and use of proceeds.

Not applicable.

D. Risk factors.

Risks Related to Us and Our Business

Investments in biopharmaceutical companies are generally considered to be speculative.

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

We have a history of operating losses and we may never achieve or maintain operating profitability.

Our product candidates remain at the development stage and we have incurred substantial expenses in our efforts to develop products. Consequently, we have incurred recurrent operating losses and, as of December 31, 2007, we had an accumulated deficit of approximately $43.0 million. Our operating losses have adversely impacted, and will continue to adversely impact, our working capital, total assets and shareholders equity. We do not expect to reach operating profitability in the immediate future, and our expenses are likely to increase as we continue to expand our research and development (R&D) and clinical study programs and our sales and marketing activities and seek regulatory approval for our product candidates. Even if we succeed in developing new commercial products, we expect to incur additional operating losses for at least the next several years. If we do not ultimately generate sufficient revenue from commercialized products and achieve or maintain operating profitability, an investment in our securities could result in a significant or total loss.

We do not have the required regulatory approvals to market certain of our product candidates, and we do not know if we will ever receive such approvals.

With the exception of Cetrotide® (cetrorelix) for the treatment of infertility, none of our product candidates has to date received regulatory approval for its intended commercial sale. We cannot market a pharmaceutical product in any jurisdiction until it has completed rigorous preclinical testing and clinical trials and passed such jurisdiction s extensive regulatory approval process. In general, significant research and development and clinical studies are required to demonstrate the safety and efficacy of our product candidates before we can submit regulatory applications. Preparing, submitting and advancing applications for regulatory approval is complex, expensive and time-consuming and entails significant uncertainty. Even if a product candidate is approved by the Food and Drug Administration (FDA), the Canadian Therapeutic Products Directorate or any other regulatory authority, we may not obtain approval for an indication whose market is large enough to recoup 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 recoup the R&D and other expenses we incur to develop and test new products.

Our clinical trials may not yield results which 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 our share price.

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 the withdrawal

of marketing approval for approved products or an extension of the review period for developmental products. Clinical trials are inherently lengthy, complex, expensive and uncertain processes. 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.

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.

Clinical trials are subject to continuing oversight by governmental regulatory authorities and institutional review boards and:

- must meet the requirements of these authorities;
- must meet requirements for informed consent; and
- must meet requirements for good clinical practices.

We may not be able to comply with these requirements in respect of one or more of our product candidates.

In addition, we rely on third parties, including contract research organizations (CROs) and outside consultants, to assist us in managing and monitoring clinical trials. Our reliance on these third parties may result in delays in completing, or in failing to complete, these trials if one or more third parties fails to perform with the speed and level of competence we expect.

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 our share price.

If we encounter difficulties enrolling patients in our clinical trials, our trials could be delayed or otherwise adversely affected.

Clinical trials for our product candidates require that we or third parties identify and enroll a specific number of patients. We or such third parties may not be able to enroll a sufficient number of patients to complete our clinical trials in a timely manner. Patient enrollment is a function of many factors including:

- design of the protocol;
- the size of the patient population;
- eligibility criteria for the study in question;
- perceived risks and benefits of the drug under study and of the control drug, if any;
- availability of competing therapies already approved;
- number of competing clinical trials ongoing in the same indication;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- availability of clinical trial sites.

If we or any third party 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.

Even if we obtain regulatory approvals for our product candidates, we will be subject to stringent ongoing government regulation.

Even if regulatory authorities approve any of our product candidates, the manufacture, marketing and sale of such products will be subject to strict and ongoing regulation. 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 products. In addition, as a 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 (cGMP) 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 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.

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 warning 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 which may not accept or utilize our products, our ability to generate significant revenues from our products would be limited and our financial conditions will be materially adversely affected. In addition, if we fail to further penetrate our core markets and existing geographic markets or 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 and therapies 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. We cannot assure you 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 our share price.

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

We set goals and make public statements regarding timing of the accomplishment of objectives material to our success, such as the commencement, enrollment and 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 our clinical trials will be completed, that we will make regulatory submissions 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, our share price would likely decline.

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

The ability for us and/or our partners 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 government 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. Our products may not be considered cost-effective, and reimbursement to the patient may not be available or sufficient to allow us or our partners to sell our products on a competitive basis. It may not be possible to negotiate favorable reimbursement rates for 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 control to continue. 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.A., 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 biomedical 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 biopharmaceutical and pharmaceutical companies and academic research institutions 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 Æterna Zentaris, are uncertain and involve complex questions of law and fact for which important legal issues remain unresolved. Applications for patents and trademarks in Canada, the U.S.A. and in other foreign territories have been filed and are being actively pursued by us. 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. Even if issued, patents to us or our licensors 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 United States 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 and 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 also may 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 opposition or nullity proceedings in certain countries outside the U.S.A. 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 such conflict could reduce the scope of patent protection which we could otherwise obtain. Because patent applications in the United States 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, neither we nor our licensors can be certain that we or they were the first to make the inventions claimed in our or their issued patents or pending patent applications, or that we or they were the first to file for protection of the inventions set forth in these patent applications. If a third party has also filed a U.S. patent application covering our product candidates or a similar invention, we may have to participate in an adversarial proceeding, known as an interference, declared by the U.S. Patent Office to determine priority of invention in the United States. 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.

In addition to patents, we 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 which 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 technology under license agreements with third parties. Our failure to comply with the requirements of material 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.

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.

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 methods are found to infringe. Moreover, there may be published pending applications that do not currently include a claim covering our products or methods but which nonetheless provide support for a later drafted claim that, if issued, our products or methods 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 issue 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 United States 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, 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.

Our involvement in any patent litigation, interference, opposition or other administrative proceedings will likely cause us to incur substantial expenses, 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.

We have filed applications for trademark registrations in connection with our product candidates in various jurisdictions, including the U.S.A. We intend to file further applications for other possible trademarks for our product candidates. No assurance can be given that any of our trademark applications will be registered in the U.S.A. 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. 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 may require significant additional financing, and we may not have access to sufficient capital.

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

We may attempt to raise additional funds through public or private financings, collaborations with other pharmaceutical companies or financing from other sources. Additional funding may not be available on terms which are acceptable to us. If adequate funding is not available 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 for equity securities, the issuance of those securities could result in dilution to our shareholders. Moreover, the incurrence of debt financing 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 and could impose restrictions on our operations. This could render us more vulnerable to competitive pressures and economic downturns.

We anticipate that our existing working capital, including anticipated revenues, will be sufficient to fund our development programs, clinical trials and other operating expenses for the foreseeable future. However, our future capital requirements are substantial and may increase beyond our current expectations depending on many factors including:

- the duration and results of our clinical trials for cetrorelix, ozarelix and perifosine, as well as other product candidates going forward;
- unexpected delays or developments in seeking regulatory approvals;
- the time and cost in preparing, filing, prosecuting, maintaining and enforcing patent claims;
- other unexpected developments encountered in implementing our business development and commercialization strategies;
- the outcome of litigation, if any; and

- further arrangements, if any, with collaborators.

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 our share price.

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

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

- the timing of regulatory submissions and approvals;

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

- the revenue available from royalties derived from our strategic partners;

- licensing fees revenues;

- tax credits and grants (R&D);

- the outcome of litigation, if any;

- changes in foreign currency fluctuations;

- the timing of 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 indicative of our future performance. It is possible that in some future quarter or quarters, our revenues and expenses will be above or below the expectations of securities analysts or investors. In this case, our share price could fluctuate significantly or decline.

We will not be able to successfully commercialize our product candidates if we are unable to make adequate arrangements with third parties for such purposes.

We currently have a lean sales and marketing staff. In order to commercialize our product candidates successfully, we need to make arrangements with third parties to perform some or all of these services in certain territories.

We contract with third parties for the sales and marketing of our products. Our revenues will depend upon the efforts of these third parties, whose efforts may not be successful. If we fail to establish successful marketing and sales capabilities or to make arrangements with third parties for such purposes, our business, financial condition and results of operations will be materially adversely affected.

If we had to resort to developing a sales force internally, the cost of establishing and maintaining a sales force would be substantial and may exceed its cost effectiveness. In addition, in marketing our products, we would likely compete with many companies that currently have extensive and well-funded marketing and sales operations. Despite our marketing and sales efforts, we may be unable to compete successfully against these companies.

We are currently dependent on strategic partners and may enter into future collaborations for the research, development and commercialization of our product candidates. Our arrangements with these strategic partners 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, strategic partners to perform various functions related to our business, including, but not limited to, the research, development and commercialization 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 issue our equity securities to corporate partners, licensees and others. Any license or sublicense of our commercial rights may reduce our product revenue.

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

- not all of our strategic partners 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 strategic partnership agreements that do contain such contractual prohibitions or restrictions, prohibitions or restrictions do not always apply to our partners affiliates 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;

- our strategic partners may under-fund or fail to commit sufficient resources to marketing, distribution or other development of our products;

- we may not be able to renew such agreements;

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

- our strategic partners 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 our strategic partners 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 our strategic partners to act in their own self-interest and not in our interest or those of our shareholders or other stakeholders.

In addition, our strategic partners 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 partner or abandon this product candidate which would likely cause a drop in our share price.

We have entered into important strategic partnership agreements relating to cetrorelix, ozarelix, perifosine and AEZS-130. Detailed information on our research and collaboration agreements is available in Note 24 of our annual audited consolidated financial statements as of and for the year ended December 31, 2007, included elsewhere in this annual report.

We have also entered into a variety of collaborative licensing agreements with various universities and institutes under which we are obligated to support some of the research expenses incurred by the university laboratories and pay royalties on future sales of the products. In turn, we have retained exclusive rights for the worldwide exploitation of results generated during the collaborations.

In particular, we have entered into an agreement with Tulane University (Tulane), which provides for the payment by us of single-digit royalties on future worldwide net sales for all indications, except in the BPH indication, where it provides the payment of low single-digit royalties. Tulane is also entitled to receive a low double-digit royalty on any lump sum, periodic or other cash payments received by us from sub-licensees.

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 cGCP guidelines and the investigational plan and protocols contained in an Investigational New Drug application (IND), or 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 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 partners, 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 paid by us for them, could have a material adverse effect on our business, financial condition, liquidity and operating results.

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. Competition for skilled personnel is intense, and our ability to attract and retain qualified personnel may be affected by such competition.

Our strategic partners manufacturing capabilities may not be adequate to effectively commercialize our product candidates.

Our manufacturing experience to date with respect to our product candidates consists of producing drug substance for clinical studies. To be successful, these product candidates have to be manufactured in commercial quantities in compliance with regulatory requirements and at acceptable costs. Our strategic partners current manufacturing facilities have the capacity to produce projected product requirements for the foreseeable future, but we will need to increase capacity if sales continue to grow. Our strategic partners may not be able to expand capacity or to produce additional product requirements on favorable terms. Moreover, delays associated with securing additional manufacturing capacity may reduce our revenues and adversely affect our business and financial position. There can be no assurance that we will be able to meet increased demand over time.

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

The sale and use of our products, in particular our biopharmaceutical products, involve the risk of product liability claims and associated adverse publicity. Our risks relate to human participants in our clinical trials, who may suffer unintended consequences, as well as products on the market whereby claims might be made directly by patients, healthcare providers or pharmaceutical companies or others selling, buying or using our products. We manage our liability risks by means of insurance. We maintain liability insurance covering our liability for our preclinical and clinical studies and for our pharmaceutical products already marketed. 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.

Our business involves the use of hazardous materials which requires us 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 and radioactive 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.

Legislative actions, new accounting pronouncements and higher insurance costs are likely to 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.

We may incur losses associated with foreign currency fluctuations.

Our operations are in many instances conducted in currencies other than the U.S. dollar (principally Euros) and we hold a significant portion of our cash, cash equivalents and debt in other currencies (principally Canadian dollars), and fluctuations in the value of foreign currencies relative to the Canadian dollar could cause us to incur currency exchange losses.

We may not be able to successfully integrate acquired businesses.

Future acquisitions may not be successfully integrated. The failure to successfully integrate the personnel and operations of businesses which we may acquire in the future with ours could have a material adverse effect on our operations and results.

Risks Related to Our Shares

Our share price is volatile, which may result from factors outside of our control. If we experience low trading volume or if our securities are delisted from the TSX or NASDAQ, you may have difficulty selling your shares.

During 2007, the closing price of our shares ranged from C$1.47 to C$5.10 per share on the Toronto Stock Exchange (TSX), and from $1.46 to $4.36 on the NASDAQ Global Market (NASDAQ). Our share price may be affected by developments directly affecting our business and by developments out of our control or unrelated to us. The biopharmaceutical sector in particular, and the stock market generally, 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;
- other announcements by us regarding technological, product development or other matters;
- arrivals or departures of key personnel;
- government regulatory action affecting our product candidates and our competitors products in the U.S.A., 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.A., Canada or abroad.

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

In the past, following periods of large price declines in the public market price of a company s securities, securities class action litigation has often been initiated against that company. Litigation of this type could result in substantial costs and diversion of management s attention and resources, which would adversely affect our business. Any adverse determination in litigation could also subject us to significant liabilities.

We must meet continuing listing requirements to maintain the listing of our shares on the TSX and NASDAQ. 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. Our shares have recently closed below the $1.00 per share minimum for several consecutive days on the NASDAQ. If the closing bid price falls below the $1.00 minimum for more than 30 consecutive trading days, we will have 180 days to satisfy the $1.00 minimum bid price, which must be maintained for a period of at least ten trading days in order to regain compliance. If our shares continue to close below $1.00 per share during the initial 180 day period following a notice of noncompliance from NASDAQ, we could transfer from the NASDAQ Global Market to the NASDAQ Capital Market. Transferring from the NASDAQ Global Market to the NASDAQ Capital Market would provide us with an additional 180-day calendar day compliance period to regain compliance with the NASDAQ minimum bid price rule. If our shares were delisted from TSX or NASDAQ, you may have difficulty in disposing of your shares.

Our largest shareholders have influence over our business and corporate matters, including those requiring shareholder approval. This could delay or prevent a change in control. Sales of common shares by such shareholders could have an impact on our share price.

Our two largest shareholders, which held 18.65% and 16.57% of our outstanding shares as of December 31, 2007, have influence over our business and corporate matters, including those requiring shareholder approval. This could delay or prevent a change in control. Sales of common shares by such shareholders could have an impact on our share price.

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 expansion of our business. As a result, the return on an investment in our shares will, for the foreseeable future, depend upon any future appreciation in value. There is no guarantee that our shares will appreciate in value or even maintain the price at which shareholders have purchased their shares.

Item 4. Information on the Company

A. History and development of the Company.

Æterna Zentaris Inc. is a global biopharmaceutical company focused on endocrine therapy and oncology with expertise in drug discovery, development and commercialization, primarily targeting the North American and European markets.

We were incorporated on September 12, 1990 under the laws of Canada. Our registered office is located at 1405

du Parc-Technologique Blvd., Quebec City, Quebec, Canada G1P 4P5, our telephone number is (418) 652-8525 and our website is www.aezsinc.com. None of the documents or information found on our website shall be deemed to be included in or incorporated into this annual report.

On December 30, 2002, we acquired Zentaris AG, a biopharmaceutical company based in Frankfurt, Germany. Zentaris was a spin-off of Degussa AG and Asta Medica GmbH, a former pharmaceutical company. With this acquisition, the Company changed its risk profile and inherited an extensive and robust product pipeline with capabilities from drug discovery to commercialization with a particular focus on endocrine therapy and oncology. As part of the acquisition, we also inherited a very experienced pharmaceutical team along with a network of strategic pharmaceutical partners. The total consideration paid for the acquisition of Zentaris was U.S.$51.9 million, net of cash and cash equivalents acquired of U.S.$2.3 million, of which an amount of U.S.$26.7 million was paid cash and the remaining amount of U.S.$25.2 million as balance of purchase price.

In May 2004, we changed our name to Æterna Zentaris Inc.

In early January 2005, we acquired Echelon Biosciences, Inc. inclusive of a product pipeline focused on the emerging field of transduction signalling technology. We completed the acquisition of 100% of the issued and outstanding common shares of Echelon for a total consideration of U.S.$2.9 million, of which an amount of U.S.$36,000 was paid cash, net of cash and cash equivalents acquired of U.S.$162,000, and the balance was paid through the issuance of 443,905 common shares of the Company.

On April 6, 2005, our former subsidiary Atrium Biotechnologies Inc. (now Atrium Innovations Inc.) (Atrium), completed its initial public offering in Canada and began trading on the Toronto Stock Exchange (the TSX) under the ticker symbol ATB .

Throughout 2006, as part of a thorough, strategic planning process, our management and board of directors made the decision to spin-off Atrium in two phases. On September 19, 2006, we initiated the first phase, a secondary offering to sell 3,485,000 Subordinate Voting Shares of Atrium at a price of C$15.80 per share. This secondary offering closed on October 18, 2006, generating net proceeds of nearly $45 million to Æterna Zentaris. With this transaction closed, our remaining interest in Atrium was 11,052,996 Subordinate Voting Shares representing 36.1% of its issued and outstanding shares. Therefore, we no longer had a controlling interest in Atrium as of October 18, 2006.

The second phase was to distribute our remaining interest in Atrium to our Shareholders concurrently with a reduction of the stated capital of our common shares.

On December 15, 2006, our shareholders approved a reduction of the stated capital of our common shares in an amount equal to the fair market value of our remaining interest in Atrium by way of a special distribution in kind to all our shareholders. This special distribution was completed on January 2, 2007. For each common share held as of the record date of December 29, 2006, our shareholders received 0.2078824 Subordinate Voting Shares of Atrium. In May 2007, we opened an office in the U.S.A., located at 20 Independence Boulevard, Warren, New Jersey 07059-2731. We have two wholly-owned subsidiaries, Æterna Zentaris GmbH (AEZS Germany), based in Frankfurt, Germany and Æterna Zentaris, Inc., based in Warren, New Jersey in the U.S.A.

From the formation of Atrium as our subsidiary in 1999 until the distribution of our remaining interest in Atrium on January 2, 2007, Atrium did not declare or pay any dividends to its shareholders. As a result of the disposition of our entire interest in Atrium, we did not have access to liquidity or cash flows generated by Atrium in 2007 nor will we in ensuing years. In addition, our results in 2007 are impacted by the disposition since Atrium s net earnings are no longer included in our consolidated statement of operations. The net earnings previously generated by Atrium are presented as Net earnings from discontinued operations for the comparative years 2006 and 2005 in our consolidated financial statements.

During the last three years, we have advanced our product development pipeline with a specific focus on our lead product candidate cetrorelix along with our partnered late-stage programs, ozarelix and perifosine, as well as our targeted earlier-stage programs, as depicted in the chart reproduced under the heading, Our Product Pipeline

on page 20.

Our common shares are listed for trading on the TSX under the trading symbol AEZ and on the NASDAQ under the trading symbol AEZS .

B. Business overview.

Recent Developments

Our Strategic Plan

On October 2, 2007, we presented a live webcast and conference call hosted by our President and Chief Executive Officer, David J. Mazzo, Ph.D., which highlighted the outcome of management s review of our pipeline and business operations along with key elements of our new strategic plan to achieve our short-term and long-term objectives. Dr. Mazzo discussed in detail the fundamentals of our strategic plan, most notably that: (1) Æterna Zentaris long-term vision is to become a fully integrated biopharmaceutical company; and (2) The management team prioritized its pipeline, developed a strategic partnering strategy and ascribed a value to its most immediate asset, cetrorelix. Key highlights of management s review include the following:

- Cetrorelix, currently in a Phase 3 program for benign prostatic hyperplasia (BPH), is our highest priority, being the product candidate with the largest combination of probability of success, proximity to launch and potential medical and commercial value. We are seeking a commercialization partner for cetrorelix, with the expectation of doing so within 12- 18 months prior to the anticipated launch. After defining the critical path to registration, we expect to launch cetrorelix in the BPH indication in the second half of 2011.

- We will prioritize the advancement of preclinical and very early-stage development programs based on risk-adjusted maximum market potential.

- We have established a clear global partnering strategy moving forward. All commercially viable projects will be developed internally through proof-of-concept in humans. We consider Asia (especially Japan) as a market of interest for us.

- We will divest non-core assets in an effort to ensure focus on our lead value drivers as well as provide an opportunity to infuse non-dilutive sources of funds in to the Company. We identified at that time our former subsidiary, Echelon Biosciences, our marketed product, Impavido® and the building in Quebec City as non-core assets.

Corporate Transactions

Sale of Miltefosine

On March 3, 2008, we announced that we had entered into a definitive purchase agreement with Paladin Labs Inc., whereby we agreed to sell to Paladin Labs Inc. all of the rights related to the manufacture, production, distribution, marketing, sale and/or use of our miltefosine product for an aggregate purchase price of C$9.125 million, subject to certain post-closing purchase price adjustments.

Sale of Echelon Biosciences

On December 3, 2007, we announced we had completed the sale of our Salt Lake City, Utah-based subsidiary, Echelon Biosciences Inc., to Frontier Scientific Inc. for a purchase price of U.S.$3.2 million including U.S.$0.6 million as contingent consideration.

Appointment of Key Executives and Changes to our Board of Directors

On March 27, 2007, we announced the appointment of David J. Mazzo, Ph.D. as our new President and Chief Executive Officer. Prior to joining us, Dr. Mazzo spent more than 20 years in the pharmaceutical industry, and he previously served as President and Chief Executive Officer of Chugai Pharma U.S.A. from April 2003 until March 2007. He also held positions of increasing responsibility with Merck, Baxter, Rhône-Poulenc Rorer, Hoechst Marion Roussel and Schering-Plough. Dr. Mazzo holds a B.A. with Honors (Interdisciplinary Humanities) and a B.S. in Chemistry from Villanova University, as well as an M.S. in Chemistry and a Ph.D. in Analytical Chemistry from the University of Massachusetts (Amherst). He further complemented his education as a research fellow at the Ecole Polytechnique Fédérale de Lausanne, Switzerland.

Shortly after the appointment of Dr. Mazzo, we established an office in Warren, New Jersey in the U.S.A.

On May 7, 2007, we announced the filling of two key management positions with the appointment of Ellen McDonald, M.B.A., as Senior Vice President, Business Operations and Chief Business Officer, and Nicholas J. Pelliccione, Ph.D., as Senior Vice President, Regulatory Affairs and Quality Assurance.

On August 14, 2007, we announced the appointments of Juergen Ernst as Chairman of our Board of Directors and David J. Mazzo, Ph.D., our President and Chief Executive Officer, to our Board of Directors. Mr. Ernst had served as our Vice Chairman since November 2005 and has 35 years of pharmaceutical industry experience, specifically corporate development and pharmaceutical product marketing expertise. He succeeds our founder, Eric Dupont, Ph.D., who served as our Executive Chairman since January 2003 and who stepped down from the Board of Directors on the same day.

On August 16, 2007, we completed the formation of our new management team with the announcement of Paul Blake, M.D. as Senior Vice President and Chief Medical Officer.

Our executive management team is now comprised of the following members:

- David J. Mazzo, Ph.D., President and Chief Executive Officer;
- Paul Blake, M.D., Senior Vice President and Chief Medical Officer;
- Jürgen Engel, Ph.D., Executive Vice President and Chief Scientific Officer;

- Ellen McDonald, M.B.A., Senior Vice President, Business Operations and Chief Business Officer;

- Mario Paradis, C.A., Senior Vice President, Administrative and Legal Affairs, and Corporate Secretary;

- Nicholas J. Pelliccione, Ph.D., Senior Vice President, Regulatory Affairs and Quality Assurance; and

- Dennis Turpin, C.A., Senior Vice President and Chief Financial Officer.

On February 29, 2008, we announced that Mr. Paradis was resigning as Senior Vice President, Administrative and Legal Affairs, and Corporate Secretary effective April 4, 2008.

Pipeline Developments

Cetrorelix: In the first half of 2007, patient dosing commenced for our flagship product candidate, cetrorelix, a luteinizing hormone-releasing hormone (LHRH) antagonist, in the first of three clinical trials of an extensive Phase 3 program in BPH. The program will enroll a total of approximately 1,500 patients. This first trial will enroll approximately 600 patients and will primarily be conducted in the U.S.A. and Canada with the expectation to complete recruitment in the second quarter of 2008. Our partner Shionogi & Co (Shionogi) is currently conducting a 300-patient Phase 2b trial with cetrorelix for the treatment of BPH in Japan and plans to announce results of the trial in the third quarter of 2008.

Additionally, we announced the termination of the license and cooperation agreement for cetrorelix for all remaining indications, including endometriosis, with Solvay. We regained exclusive worldwide ex-Japan rights for cetrorelix in all indications, without any financial compensation payable to Solvay. Cetrorelix was not a priority for Solvay as it shifted its focus to newly defined therapeutic areas as a result of the acquisition of Fournier Pharma, which was announced in March 2005. We now have full rights ex-Japan to cetrorelix and are in the process of conducting an updated, comprehensive strategic analysis to determine how best to proceed with the development for

the endometriosis indication.

Ozarelix: Our partner, Spectrum Pharmaceuticals (Spectrum), presented an abstract outlining detailed Phase 2 BPH results for ozarelix, our fourth-generation LHRH/GnRH antagonist. Results indicated that ozarelix was well tolerated and demonstrated statistically significant as well as clinically meaningful efficacy in the treatment of lower urinary tract symptoms (LUTS) secondary to BPH. The abstract was presented at the American Urological Association (AUA) Annual Meeting in May 2007. In January 2007, a Phase 2b study in the BPH indication was initiated in the U.S.A. and Canada by our partner, Spectrum and results are expected to be announced in the second quarter of 2008.

Perifosine: At the American Society of Clinical Oncology s (ASCO) Annual Meeting, our partner, Keryx Biopharmaceuticals (Keryx), presented a poster outlining Phase 1 and Phase 2 results for perifosine, our oral anti-cancer signal transduction inhibitor compound, for the treatment of patients with advanced sarcoma. Results of the Phase 1 and Phase 2 studies of perifosine showed an overall clinical benefit rate (CBR) of 52%, which compares favorably with the activity of mTOR inhibitors. Our partner Keryx is conducting multiple Phase 1 and 2 clinical trials in monotherapy as well as in combination with chemotherapy and biologics for multiple cancers.

On November 14, 2007, we announced the completion of patient recruitment for our European multi-center Phase 2 trial in non-small cell lung cancer (NSCLC) with perifosine. This randomized, double-blind, placebo-controlled trial will assess the efficacy and safety of a 150 mg daily dose of perifosine when combined with radiotherapy in 160 patients with inoperable Stage III NSCLC. The trial is being conducted in collaboration with the Netherlands Cancer Institute and we expect to announce top-line results at the end of 2008.

AEZS-108: Detailed, Phase 1 results for our targeted cytotoxic-LHRH analog conjugate, AEZS-108, were reported in female patients with cancers expressing LHRH at the ASCO Annual Meeting. Evidence of anti-tumor activity was found at 160 mg/m2 or 267 mg/m2 doses of AEZS-108, where 7 of 13 patients showed signs of tumor response, including three patients with complete or partial responses. On February 12, 2008, we reported that dosing of AEZS-108 commenced in a Phase 2 trial in endometrial and ovarian cancers. This open-label, non-comparative multicenter Phase 2 trial will treat up to 82 women with LHRH-receptor positive ovarian and endometrial cancerous tumors. The trial is being conducted in 15 centers in Europe.

AEZS-112: This is a novel small molecule, anti-cancer drug in development involving two mechanisms of action: tubulin and topoisomerase II inhibition. On January 8, 2007, we announced the initiation of a Phase 1 trial for AEZS-112 in patients with solid tumors and lymphoma and expect to announce top-line results at the end of 2008.

On October 25, 2007, we presented an abstract outlining novel data generated from three follow-up candidates of AEZS-112 at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics. Following encouraging results, we will pursue further research aimed at selecting an AEZS-112 follow-up candidate for preclinical development in cancer.

Our Business Strategy

Our strategy is to advance our product development pipeline with a clear focus on our flagship product candidate, cetrorelix for the BPH indication as well as AEZS-108, our lead program in oncology for the treatment of endometrial and ovarian cancer. With the collective experience of our new management team in place and our expertise in drug discovery, pharmaceutical development and commercialization, we

believe we are well positioned to execute our strategy.

Our foremost priority is cetrorelix for the BPH indication. Based on various third-party sources, such as BPH, Urologic Diseases in America 2004; NIH Publication 04-5512:43-67; The American Journal of Managed Care, the prevalence of BPH in 2007 in the U.S.A. is estimated to be 20 million individuals as defined by International Prostate Symptom Score (IPSS) >7. Additionally, it is estimated that approximately 5.6 million men will be treated in the U.S.A. for LUTS associated with BPH. The prevalence of BPH in the U.S.A. is expected to increase to 26.8 million in 2020, and the LUTS treated population to approximately 8 million men in 2020. The potential for base case peak annual sales of cetrorelix is over $500 million in the United States market alone. We intend to

continue to diligently advance the cetrorelix Phase 3 program with the objective of filing a New Drug Application (NDA). We also have the intent to file in Europe a Marketing Authorization Application (MAA).

Our lead oncology product candidate, AEZS-108, currently in Phase 2 clinical trials, is our second priority. AEZS-108 is currently dosing patients with endometrial and ovarian cancer in a multi-center trial in Europe with the expectation of reporting top-line results from this trial in early 2009.

We intend to further advance our earlier-stage product candidate with what we believe to be high potential, namely, AEZS-112.

Additionally, we have a drug discovery unit which includes high throughput screening systems and a library of nearly 120,000 compounds. We also have several preclinical programs underway with targeted potential development candidates. Among the targets for which we expect to propose clinical development candidates in the coming years are: ghrelin receptor ligands, PI3K/Erk inhibitors, LHRH peptidomimetics and erucylphosphocholine derivatives.

Furthermore, we intend to continue marketing Cetrotide® (cetrorelix) in more than 80 countries, in collaboration with our partner, Merck Serono, on a world-wide ex-Japan basis, and with Shionogi in Japan.

We are currently in a phase in which our products and product candidates are being further developed or marketed jointly with strategic partners. We expect we will continue to engage strategic partnerships in the future as we move to realize our vision of becoming a fully integrated specialty biopharmaceutical company.

Our Product Pipeline

Pipeline Table

Discovery	**Preclinical**	**Phase 1**	**Phase 2**	**Phase 3**	**Commercial**
120,000 compound library	AEZS-115 (endometriosis & urology) AEZS-120 (oncology vaccine) Erk & PI3K inhibitors (oncology) Ghrelin receptor	AEZS-112 (oncology) AEZS-130 (endocrinology)	AEZS-108 (endometrial and ovarian cancers) Cetrorelix (endometriosis) (BPH in Japan) Ozarelix (BPH, prostate cancer)	Cetrorelix (BPH)	Cetrotide® (*in vitro* fertilization)

	ligands (endocrinology) AEZS-127 (oncology)		Perifosine (multiple cancers)	
Partners	AEZS-127: Keryx	AEZS-130: Ardana	Cetrorelix: Shionogi in Japan Ozarelix: Spectrum in North America and India, Nippon Kayaku in Japan Perifosine: Keryx in North America	Cetrotide®: Merck Serono (World ex- Japan) Shionogi (Japan)

LHRH Antagonists

Cetrorelix

Cetrorelix is a peptide-based active substance which was developed in cooperation with Nobel Laureate Professor Andrew Schally presently of the U.S.A. Veterans Administration-Miami, University of Miami, and formerly of Tulane University in New Orleans. This compound is a luteinising hormone releasing hormone (LHRH, also known as GnRH) antagonist that blocks the pituitary LHRH receptors resulting in a rapid decrease of sexual hormone levels. Moreover, cetrorelix allows the LHRH receptors on the pituitary gland to be blocked gradually. Conversely, the side effects usually associated with the use of agonists and resulting from total hormone withdrawal can be avoided in conditions that do not require a castrating degree of hormone withdrawal. Therefore, in contrast to treatment with agonists, LHRH antagonists permit dose-dependent hormone suppression which is of critical importance for the tolerability of hormonal therapy.

The mode of action of cetrorelix and the distinction between LHRH antagonists and LHRH agonists

LHRH is released by the hypothalamus in the brain and controls the production of sex hormones (i.e. testosterone in the testes and estrogen and progesterone in ovaries) via the activation of LHRH receptors located on the pituitary gland (hypophysis).

When using LHRH agonists, the LHRH receptors on the pituitary gland are stimulated leading to an initial increased secretion of the hormones luteinizing hormone (LH) and follicle stimulating hormone (FSH), which in turn regulate the formation of testosterone and estrogen. The increase or surge of hormonal levels induces a flare-up effect that can last up to three weeks until the pituitary markedly decreases the release of LH and FSH by desensitization and depletion of LHRH receptors (i.e. down-regulation) resulting in a considerable drop in testosterone and estrogen levels. Though the initial flare-up effect is limited in time, it can sometimes cause, depending on the nature and stage of the particular disorder, considerable additional symptoms or even life-threatening complications, which in turn require additional therapeutic intervention. By simultaneous administration of anti-androgens, the flare-up effect can be attenuated. However, this additional treatment also bears the risk of certain side effects, e.g. disturbances of the function of the stomach, intestines and liver.

During full hormone suppression, LHRH agonists reduce the male sex hormones to ranges below castration level. In women, the hormone levels are far below the ranges observed after the end of the climacteric. Treatment with an LHRH agonist, therefore, is regularly associated with side effects such as hot flashes, depression, muscle weakness, loss of libido and, particularly in women, osteoporosis and ovarian cysts. At the end of treatment, it takes several weeks for the hormone function to return to normal ranges. At the same time, an excessive rebound effect can lead to renewed deterioration of the symptoms.

We believe that cetrorelix, an LHRH antagonist, because of its different mode of action, can avoid the side effects associated with the administration of LHRH agonists. Since LHRH antagonists have a rapid onset of action, the treatment time to response with cetrorelix can be much shorter than with agonists. Moreover, in various clinical studies, the effect of cetrorelix therapy lasted much longer than that of hormone suppression, which consequently confirms the new therapeutic principle of intermittent treatment. Periods with moderate and well-tolerated hormonal suppression can be followed by intervals without treatment during which side effects are avoided and quality of life is restored. Since there is no necessity for long-term therapy and the overall treatment time is much shorter, the risks of side effects are also reduced. In particular, we also believe that the risk of developing osteoporosis in patients taking the cetrorelix therapy regimen is diminished.

Cetrorelix might therefore be useful in a variety of malignant and non-malignant indications in which a suppression of the pituitary-gonadal axis is desired. The degree of suppression of gonadotrophins and sex steroids required is dependent on the clinical circumstances and disease treated. For example, in patients undergoing controlled ovarian stimulation for assisted reproductive techniques, endogenous gonadotrophin secretion has to be controlled, whereas development of the follicle must not be adversely affected.

Cetrorelix in *in vitro* fertilization (COS/ART)

Cetrorelix is the first LHRH antagonist which was approved for therapeutic use as part of fertilization programs in Europe and was launched on the market under the trade name Cetrotide® (cetrorelix acetate) in 1999. In women who undergo controlled ovarian stimulation for recovery of ovocytes for subsequent fertilization, Cetrotide® helps prevent premature ovulation. LHRH is a naturally occurring hormone produced by the brain to control the secretion of LH and, therefore, final egg maturation and ovulation. Cetrotide® is designed to prevent LH production by the pituitary gland and to delay the hormonal event, known as the LH surge which could cause eggs to be released too early in the cycle, reducing the opportunity to retrieve the eggs for the assisted reproductive techniques procedure.

In comparison with LHRH agonists that require a much longer pre-treatment, the use of our LHRH antagonist, Cetrotide®, permits the physician to interfere in the hormone regulation of the women undergoing treatment much more selectively and within a shorter time.

The effectiveness of Cetrotide® has been examined in five clinical trials (two Phase 2 and three Phase 3 trials). Two dose regimens were investigated in these trials: either a single dose per treatment cycle or multiple dosing. In the Phase 2 studies, a single dose of 3 mg was established as the minimal effective dose for the inhibition of premature LH surges with a protection period of at least four days. When Cetrotide® is administered in a multi-dose regimen, 0.25 mg was established as the minimal effective dose. The extent and duration of LH suppression was found to be dose dependent. In the Phase 3 program, efficacy of the single 3 mg dose regimen and the multiple 0.25 mg dose regimen was established separately in two controlled studies utilizing active comparators. A third non-comparative study evaluated only the multiple 0.25 mg dose regimen of Cetrotide®. In the five Phase 2 and Phase 3 trials, 184 pregnancies were reported out of a total of 732 patients (including 21 pregnancies following the replacement of frozen-thawed embryos). In these studies, drug-related side effects were limited to a low incidence of injected site reactions; however, none of them was serious such as an allergic type of reaction - or required withdrawal from treatment. No drug-related allergic reactions were reported from these clinical studies.

Cetrotide® is the only LHRH antagonist that is available in two dosing regimens. With an immediate onset of action, Cetrotide® permits precise control a single dose (3 mg), which controls the LH surge for up to four days, or a daily dose (0.25 mg) given over a short period of time (usually five to seven days). The treatment with Cetrotide® can be accomplished during a one-month cycle with a simplified, more convenient and shorter treatment requiring fewer injections than LHRH agonists.

Cetrotide® is marketed in a 3 mg and a 0.25 mg subcutaneous injection as cetrorelix acetate by Merck Serono in the US and Europe. Approval for Cetrotide® in Japan was gained in April 2006. In September 2006, we announced the launch of Cetrotide® in Japan for *in vitro* fertilization. Cetrotide® is marketed in Japan by our partner Shionogi. We will receive revenue from the supply of Cetrotide® to our Japanese partners. The market competitor is ganirelix (Antagon /Orgalutran®) from Akzo (Organon) indicated for the inhibition of premature LH surges in women undergoing controlled ovarian hyperstimulation, which, however, is not yet approved in Japan.

Partners for Cetrotide®

On August 2000, we entered into a commercialization agreement with Merck Serono for Cetrotide®. Under the terms of this agreement, we granted an exclusive license to Merck Serono to commercialize Cetrotide® for IVF/COS/ART worldwide ex-Japan and we are entitled to receive fixed and sales royalties from Merck Serono. The Japanese rights for this indication are held by Shionogi whereby, according to a commercialization agreement, we received transfer pricing from Shionogi.

Clinical Development Overview of Cetrorelix in BPH, Endometriosis and Uterine Myoma

In October 2004, cetrorelix completed an extensive program of seven Phase 2 trials in urology and gynaecology, a significant part of which was sponsored by our partner, at the time, Solvay.

Cetrorelix in BPH

BPH is a hormone-driven enlargement of the male prostate gland. The prostate is located directly at the vesicle outlet in the male surrounding the first part of the urethra. The enlargement puts pressure on the urethra, causing difficulty in urinating. BPH is classified into three stages according to symptoms: 1) the irritant phase, where the patient suffers dysuria (pain when urinating) and nocturia (the urge to urinate during the night); 2) residual urine occurring in the bladder thus increasing problems during urinating; and 3) overflow of the bladder. These can result in formation of bladder stones, congestion of urine and engorged kidneys which can in turn lead to life-threatening kidney damage.

Because LHRH agonists decrease testosterone to castration levels, treatment of BPH with LHRH agonists is not convenient and therefore not the best approach. Drug therapy with plant-based drugs, alpha-blockers or alpha-reductase inhibitors (5-ARIs) is possible but the plant-based drugs and alpha-blockers cannot delay further prostate growth, they merely improve the symptoms in 50% of patients. Treatment with alpha-reductase inhibitors decreases the size of the prostate; however, this form of therapy is successful only in patients with a greatly increased prostate volume and only after a treatment period of at least six months. In contrast, clinical studies suggest that cetrorelix improves the symptoms of BPH and reduces the size of the prostate after a short treatment period without chemical castration. The effects are independent of the prostate volume and are maintained for a long period following treatment withdrawal.

BPH Clinical Trials

All Phase 2 studies performed so far in patients with symptomatic BPH revealed that cetrorelix is therapeutically active in this indication as demonstrated by an improvement in symptoms as assessed primarily by the International Prostate Symptom Score (IPSS) as well as an increase in urinary peak flow rate and a reduction in prostate volume.

On April 29, 2004, we announced the results of two placebo-controlled Phase 2 trials that were conducted in BPH. As early as one month following initiation of therapy, both trials demonstrated improvement of clinical symptoms, classified and graded according to the IPSS which

was paralleled by an increase in maximum uroflow in patients receiving cetrorelix treatment group, compared with patients on the placebo group. The positive effect lasted three months without additional administration of cetrorelix. Furthermore, the use of cetrorelix was associated with a slight reduction of prostate size and moreover did not have an adverse influence on sexual activity or libido.

On October 7, 2004, we announced additional results for cetrorelix in BPH, which was a randomized, double-blind, placebo-controlled Phase 2 trial that enrolled patients with symptomatic and objectively defined BPH (decreased urine flow). This trial was conducted in Europe under the coordination of Professor Frans MJ Debruyne from the Department of Urology, University Medical Center in Nijmegen, the Netherlands. During a run-in period, all patients received two intramuscular injections of placebo, two weeks apart. Thereafter, 250 patients with persisting symptomatic BPH were randomized into five equal groups receiving either placebo injections or four different dosage regimens from 60 to 120 mg in two or three injections of a depot formulation of cetrorelix over the course of four weeks.

Patients were followed up for about six months after the last injection for efficacy and safety assessments, as well as for levels of testosterone and quality of life and sexual function. As early as one month following the initiation of therapy, the use of cetrorelix was associated with a dose-dependent, statistically significant improvement of clinical signs and symptoms, including IPSS and maximum uroflow, compared to placebo. Importantly, for all dosage regimens the therapeutic response lasted until the last observation point, i.e. 24 to 26 weeks following cessation of cetrorelix administration.

On March 16, 2005, we announced that our partner Shionogi was pursuing the development of cetrorelix by initiating the first Phase 2a trial in the Japanese market with cetrorelix in BPH. This trial will evaluate the safety (systemic and local tolerability) and explore efficacy (effects on BPH-related parameters such as the IPSS) of cetrorelix.

On January 30, 2006, we announced that we regained our worldwide rights (ex-Japan) from our partner Solvay to develop and potentially market Cetrorelix in BPH, and the ongoing development of cetrorelix in endometriosis was pursued by Solvay until we regained the rights in May 2007 in endometriosis as described in further detail on page 25 of this annual report.

Our Phase 3 program began in January 2007. The Phase 3 program consists of two placebo controlled efficacy studies, an open label safety study and a Thorough QT/QTc Study consistent with the ICH E14 Guideline.

The two placebo controlled studies each compare two intermittently administered dose regimes with placebo in patients with BPH who are then assessed one year after beginning therapy. The primary end-point in each trial is the change in IPSS between the beginning of treatment to the end of follow-up after 52 weeks. The IPSS has been used successfully as the primary endpoint in a number of other drug development programs for BPH. Other measures that are evaluated in these studies are urine flow, general aspects of safety, quality of life issues and some that are particularly relevant to males aged 50 and over who are suffering from BPH. One of our trials, the one being conducted principally in North America, is approaching full recruitment of the planned approximately 600 patients. The other study is being conducted in Europe, has been opened to recruitment in the first quarter of 2008 and will include approximately 400 patients.

The third study in the Phase 3 program is an open label study of the dose regime we are planning to market. It is more focused on aspects of general safety, quality of life and tolerability of cetrorelix, although the effects of cetrorelix on the patients symptoms are also being evaluated. It is also opening to patient recruitment in the first quarter of 2008 and will include approximately 500 patients. The final component of the Phase 3 program, the Thorough QT/QTc Study, is being designed with input from the FDA in order to ensure that we meet the regulatory guidance on this topic for novel drugs under development.

On March 22, 2007, our partner Shionogi announced positive results for a Phase 2a Japanese trial with cetrorelix in BPH that was initiated in 2005. This trial was designed to evaluate primarily pharmacokinetics and safety (systemic and local tolerability) in Japanese subjects, whereas evaluation of efficacy was only exploratory. A total of 50 patients were included in five dosing groups corresponding to single administration of 30 mg, 60 mg or 90 mg cetrorelix and multiple administration of 60mg and 90 mg, three times eight weeks apart. The observation period was up to 32 weeks in the multiple administration dosing groups. The Japanese patients responded to cetrorelix with a transient reduction of testosterone concentration in blood, which did not reach or remain at the castration level. IM injection of cetrorelix pamoate was safe and well tolerated at all dosages tested. None of the dosage regimens tested caused a suppression of prostate specific antigen (PSA) levels. Results also showed that the bioavailability of cetrorelix in Japanese patients is similar to what is observed in non-Japanese patients. The sizes per dosage group were too small to evaluate efficacy trends for statistical significance. On the basis of this study, Shionogi initiated a 300-patient Phase 2b study to assess primarily the efficacy of cetrorelix in BPH in Japanese patients.

In connection with our strategic review, we announced on October 2, 2007 that we had decided to seek a commercialization partner for cetrorelix in the BPH indication and, subject to favorable Phase 3 clinical results and regulatory approval, we expect to launch cetrorelix in this indication in the second half of 2011.

Regarding the potential market of cetrorelix in BPH, based on various third-party sources, such as BPH, Urologic Diseases in America 2004; NIH Publication 04-5512:43-67; The American Journal of Managed Care, the prevalence of BPH in 2007 in the U.S.A. is estimated to be 20 million individuals as defined by International Prostate Symptom Score (IPSS) >7. Additionally, it is estimated that approximately 12.2 million men have been diagnosed and 5.6 million men treated for BPH. As population demographics shift toward an elderly population, BPH treated population in the U.S.A. is expected to grow by 41% between 2007 and 2025, exceeding 8 million. The potential for base case peak annual sales of cetrorelix is over $500 million in the United States market alone.

Cetrorelix in Endometriosis

Endometriosis is the estrogen-driven displacement of endometrium-like tissue (tissue from the mucous membranes of the uterus) to other organs outside the womb. In the abdomen, the tissue can spread to the fallopian tubes, the ovaries, the bladder, the small and large intestines, the stomach, the lungs or the legs. Estrogen-dependent diseases often regress when estrogen production is reduced (endometriosis, and the pelvic pain associated with it, improves when estrogen production is reduced). Excessive and prolonged reduction of estrogen production, however, is typically associated with adverse side effects, such as vasomotor symptoms and bone loss.

A similar, very low estrogen level can be induced by oophorectomy (surgical removal of the ovaries) and by chronic LHRH agonist treatment. In both cases, estrogen replacement treatment is necessary to reduce the hypo-estrogenic effects (e.g. bone loss, climacteric symptoms) associated with these therapeutic approaches. Administration of LHRH agonists can initially lead to a deterioration of symptoms due to the flare-up effect, then, due to the complete suppression of estrogen to below castration levels values for many months. These symptoms can further deteriorate upon withdrawal of hormonal replacement. The longer the treatment period with traditional LHRH agonists is, the higher the risk of developing osteoporosis. Its use is therefore restricted to six months and can be extended only if estrogens and progesterones are administered concomitantly.

We believe that the side effects could be avoided with our LHRH antagonist cetrorelix due to the absence of flare-up effects and to the possibility of controlling estrogen levels at values comparable to the ones observed at the beginning of the regular monthly cycle. Since the controlled hormone withdrawal is achieved in a very short period of time, complaints from monthly bleeding are reduced while inflammatory *foci* of endometriosis are depleted of their basis. Therefore, we believe that treatment time can be reduced. Initial experiences show that the effect of therapy persists for many months. Since the effect of cetrorelix starts within a short period of time and the risk of developing osteoporosis is low, we believe that cetrorelix therapy can be repeated in several cycles.

Endometriosis Clinical Trials

In earlier Phase 2 clinical trials, cetrorelix was given at a rate of 3 mg per week over a period of eight weeks. All patients were free of pain during the course of treatment. A second laparoscopy (direct visualization of the peritoneal cavity, ovaries, outside of the tubes and uterus,) was performed after eight weeks and an improvement of the disease was shown in 60% of the cases. The efficacy was comparable to agonists but with the benefit of an almost complete absence of side effects. Cetrorelix allowed targeted control of the hormone level to show rapid effects, while avoiding the problems of menopause and risks (e.g. osteoporosis) associated with an otherwise complete and long-term withdrawal of hormones. We believe that the rapid onset of action would be ideal for intermittent therapies, allowing for treatment-free intervals with re-dosing at the time when the therapeutic effect starts to fade.

On April 29, 2004, we announced the results of Phase 2 placebo-controlled studies demonstrating that cetrorelix use was associated with a rapid and durable therapeutic response, namely improvement of endometriosis-related symptoms, such as pelvic pain, extending up to several months following only two intramuscular injections of cetrorelix with a one month interval.

On March 16, 2005, we announced that our worldwide (ex-Japan) exclusive development and marketing partner, Solvay, initiated a full development program for the potential treatment of endometriosis with cetrorelix. On May 8, 2007, we and Solvay announced the termination of the license and cooperation agreement for cetrorelix for all remaining indications, including endometriosis, effective on that date. We have regained exclusive worldwide (ex-Japan) rights for cetrorelix in all indications without any financial compensation payable to Solvay. The move

by Solvay out of the women s health care field resulted from a change in their strategic focus to newly defined therapeutic areas following the acquisition of the Fournier group in France.

In connection with our strategic review, we announced on October 2, 2007 that, after optimization of formulation and trial design, we plan to move into Phase 2b with cetrorelix in the endometriosis indication. The decision to proceed with development was made based on the proven safety and efficacy of Cetrotide®, the overall database from preclinical and clinical studies in endometriosis and the large unmet medical needs and commercial opportunity in the area of endometriosis. We will announce timelines relative to the further development of this program in the near future.

Cetrorelix in Uterine Myoma

As part of the seven Phase 2 programs, cetrorelix was also evaluated for the indication of uterine myoma. A uterus myoma is a benign tumor of the uterine muscles. If the entire uterine wall is penetrated by myoma, one refers to uterus myomatosus. Depending upon the length and the direction, it is either referred to as a subserous myoma, which is located below the peritoneal covering of the uterus and grows towards the intestinal cavity, or a submucous myoma, which is located below the mucous membrane and grows into the uterine cavity. The most frequent form however, is the intramural myoma bound in the muscular layer of the uterus. Intramural myoma leads to pain in the lower abdomen and in some cases to prolonged or severe monthly bleeding outside the normal cycle. This can cause severe blood loss leading to anemia. Infertility and pregnancy problems such as miscarriage or premature delivery are also frequent consequences. When the myoma puts pressure on the intestine or the bladder, the result can be constipation, bladder pain or a desire to urinate. If the myoma exerts pressure on nerves leaving the spinal cord, the result can be back and neuralgic pain in the legs.

Uterine Myoma Clinical Trials

On April 29, 2004, we disclosed positive Phase 2 results from a double-blind, placebo-controlled, multi-center trial evaluating the subcutaneous formulation of cetrorelix, administered weekly for four weeks, as a pre-surgical treatment to 109 women with uterine myomas. In addition to evaluating the safety and tolerability of different doses of the new formulation, the trial also evaluated whether cetrorelix use could lead to the reduction of myoma and uterine volumes within a shorter treatment period than that normally required for LHRH agonists. Data from this trial demonstrated that cetrorelix use led to a reduction of myoma and uterine volumes after a one-month treatment period, which is significantly shorter than the two- to six-month treatment period typically required for LHRH agonists. The best response rate was obtained at a dose of 10 mg of cetrorelix per week. Cetrorelix use did not lead to castration-like symptoms.

Partners for Cetrorelix

We previously licensed cetrorelix to Solvay worldwide (ex-Japan) for all indications with the exception of IVF/COS/ART, which rights belong to Merck Serono and Japanese rights are held by Shionogi. In the BPH indication, for which we regained exclusive worldwide (ex-Japan) rights, Japanese rights are held by Shionogi.

On March 22, 2007, we announced that Nippon Kayaku had terminated its development agreement pertaining to cetrorelix pamoate to focus solely in oncology.

On May 8, 2007, we and Solvay announced the termination of the license and cooperation agreement for cetrorelix for all remaining indications, including endometriosis, effective on that date. We have regained exclusive worldwide (ex-Japan) rights for cetrorelix in all indications without any financial compensation payable to Solvay.

Competition for Cetrorelix

The market leaders in the indication of BPH are Pfizer, Astellas/Boehringer Ingelheim, Sanofi-Aventis and Abbott with alpha-blockers and Merck and GlaxoSmithKline with alpha-reductase inhibitors. Worldwide, there are four LHRH agonists for the treatment of endometriosis, including those of TAP Pharmaceutical Products (Abbott and Takeda), Astra Zeneca, Pfizer and Sanofi-Aventis.

Ozarelix

Ozarelix is a modified LHRH antagonist which is a linear decapeptide sequence. Ozarelix is a fourth generation LHRH antagonist aiming at extended suppression of testosterone levels that does not require a sophisticated depot formulation for long-lasting activity. The aim of this project is to identify an active substance with superior properties for the development of longer-acting formulations that we believe are particularly suitable for tumor therapy.

Single doses of ozarelix depot were tested in healthy male volunteers. Ozarelix was well tolerated and produced a dose-dependent suppression of testosterone. An immediate decrease in testosterone plasma levels was observed in all dose groups reaching levels below 1 ng/ml within the first 12 hours after application. Duration of suppression was dose-dependent and at the highest dose of 60 mg caused testosterone suppression for one month.

On August 12, 2004, we entered into a licensing and collaboration agreement with Spectrum for ozarelix and its potential to treat hormone-dependent cancers as well as benign proliferative disorders, like BPH and endometriosis. Under the terms of the agreement, we granted an exclusive license to Spectrum to develop and commercialize ozarelix for all potential indications in North America (including Canada and Mexico) and India while keeping the rights for the rest of the world. In addition, Spectrum is entitled to receive 50% of upfront, milestone payments and royalties received from our Japanese partner, Nippon Kayaku, that are generated in the Japanese market for oncological indications.

BPH clinical trials

In October 2006, we announced positive and highly statistically significant Phase 2 results for ozarelix in BPH. The multi-center double-blind, randomized, placebo-controlled dose-ranging Phase 2 trial included 144 patients who received different intramuscular dosage regimens of ozarelix, or a placebo, to assess its safety and efficacy. Ozarelix was administered on day 1 or day 1 and 15. The primary efficacy endpoint of improving clinical symptoms of BPH at week 12, as measured by significant changes in IPSS, was achieved at all dosage regimens. However, the best results in terms of the most important decrease of the IPSS score were obtained with a dose of 15 mg administered on day 1 and 15. The observed mean decrease of the IPSS score at week 12 was minus 8.6, it peaked at minus 9.4 at week 20 and was still at minus 8.7 as of week 28. Testosterone suppression levels were maintained above castration levels at all times. Secondary efficacy parameters such as uroflow, residual urinary volume, quality of life and circulating testosterone levels were also measured and showed good results. The outcome of the trial demonstrated an excellent safety profile with ozarelix as patients had no serious side effects. The erectile function was also not affected at any dose regimens.

On January 3, 2007, Spectrum announced the FDA s acceptance of an IND for ozarelix in BPH. Spectrum initiated a Phase 2b study in January 2007 which will involve approximately 70 patients. Dr. Claus Roehrborn from the UT Southwestern Medical Center at Dallas, Department of Urology, serves as the lead investigator. The Phase 2b study is a randomized placebo-controlled trial of ozarelix. Patients are dosed with 15 mg of ozarelix (administered intramuscularly) or placebo on day 1 and 15 and are followed for six months. The primary endpoint of the study is the improvement of BPH symptoms as measured by IPSS. The study will also measure urine flow, residual urine volume and quality of life. On January 25, 2007, Spectrum announced the dosing of the first patient of this Phase 2b study. Spectrum also announced that it had reached its enrolment target for this study on May 1, 2007. Data from this Phase 2b trial are expected to be available during the second quarter of 2008. Spectrum has announced plans to utilize the results of the Phase 2b trial to design and execute a Phase 3 clinical program for ozarelix.

On May 23, 2007 and September 5, 2007, Spectrum disclosed detailed Phase 2 results for ozarelix in BPH at two medical conferences. Results indicate that ozarelix was well tolerated and demonstrated statistically significant as well as clinically meaningful efficacy in the treatment of LUTS secondary to BPH. The effect developed rapidly, with noticeable activity at four weeks from starting treatment, were maximal at 12-16 weeks, and persisted for the six month observation period. At week 12, all ozarelix-treated groups showed improvement with the greatest improvement in the 15mg + 15mg group. Change from baseline in IPSS was 8.6 ($p<0.001$); change from baseline in urine flow was 4.7 ($p=0.002$); testosterone levels declined transiently and returned to baseline in most patients by four weeks and all patients by six weeks following dosing. Results also showed no statistically significant impact on

quality of life or erectile function. Serious adverse events were reported in four patients on ozarelix (myocardial infarction, pneumonitis, hypotension, renal colic) but were not considered treatment-related. No systemic allergic reactions were seen and the injections were well tolerated.

Prostate cancer clinical trials

In August 2006, we announced positive Phase 2 result for ozarelix in hormone-dependent inoperable prostate cancer. This open-label, randomized-controlled dose-finding trial enrolled 64 patients receiving different intramuscular dosage regimens of ozarelix to assess its safety and efficacy. The study achieved its primary endpoint of defining a tolerable dosage regimen of ozarelix that would ensure continuous suppression of testosterone at castration level for a three-month test period. A secondary efficacy endpoint aimed at assessing tumor response as determined by a 50% or greater reduction of serum PSA level, compared to baseline, was also achieved. The best results regarding the primary endpoint of continuous suppression were obtained with a dose of 130 mg per cycle where all patients remained suppressed to castration until at least day 85. In patients with continuous testosterone suppression below castration level, tumor response as measured by PSA levels was 97%. Following these results, we, in collaboration with Spectrum, initiated an additional Phase 2 study in European centers to verify and optimize the findings derived from the cohort of patients having received 130 mg of ozarelix per cycle.

On August 3, 2006, we announced a licensing and collaboration agreement with Nippon Kayaku for ozarelix. Under the terms of the agreement, we granted Nippon Kayaku an exclusive license to develop and market ozarelix for all potential oncological indications in Japan. In return, we received an upfront payment upon signature and are eligible to receive payments upon achievement of certain development and regulatory milestones, in addition to low double-digit royalties on potential net sales. Spectrum is entitled to receive 50% of the upfront, milestone payments and royalties received from Nippon Kayaku.

AEZS-115 Non-Peptide LHRH Antagonist

As outlined above, the LHRH receptor plays an important role in a number of benign and malignant tumors. Our drug discovery unit searches for small, non-peptide molecules which have the same effect on the receptor. Their advantage lies in the potential for oral administration.

AEZS-115 is a new orally bioavailable LHRH antagonist with LHRH-receptor binding affinity in the nanomolar range which is developed for hormone therapy of endocrinological disorder and of benign and malignant tumors. The compound demonstrates excellent selectivity to LHRH-receptor and has advanced to a preclinical stage where the *in vivo* activity has been confirmed. Major advantages are the dose-dependent reduction of sexual hormones without flare-up effect whereas no decrease down to castration level is necessary and therefore side effects are reduced.

In January 2006, we regained the exclusive worldwide rights to develop and commercialize AEZS-115 from Solvay. Attractive *in vivo* activity of this orally available peptidomimetic LHRH-antagonist was demonstrated with a single, oral administration (20mg/kg) in rats which led to efficient and revocable suppression of plasma testosterone levels for up to 12 hours. Furthermore, a repeat of the dosing of AEZS-115 increased the suppression time without accumulation in the plasma.

In 2007, an oral formulation was selected and pharmacokinetic data were obtained.

Signal Transduction Inhibitors

Perifosine

Perifosine is an alkylphosphocholine compound with structural similarity to phospholipids, which are the main constituents of cellular membranes and it is an active ingredient with anti-tumor capacities. In tumor cells, perifosine has demonstrated interactions with vital signal transduction mechanisms and induction of programmed cell death (apoptosis).

Perifosine exerts a marked cytotoxic effect in animal and human tumor cell lines. The most sensitive cancer cell lines were larynx carcinoma, breast, small cell lung, prostate and colon. Based on the *in vitro* trials, the mode of action of perifosine appears to be fundamentally different from that of currently available cytotoxics. Pharmacodynamic data have demonstrated that perifosine possesses anti-tumor activity, including tumor models that are resistant to currently available agents for cancer therapy. This activity is based on a direct and relatively specific action on tumors. A dose relationship was also shown.

In preclinical and clinical Phase 1 trials (solid tumors), this orally administered agent has been found to have good tolerability. Five Phase 1 trials have been conducted on perifosine, including the trial presented at the June 2004 ASCO meeting in combination with radiotherapy.

In four trials, the use of perifosine as a single agent in a total of 94 patients provided initial encouraging evidence of anti-tumor activity. In particular, investigators observed two partial responses (>50% reduction) in patients with sarcoma and 16 stable diseases in patients with breast, prostate, pancreatic and other forms of cancer.

Based on findings in various tumor models, the U.S. National Cancer Institute, along with our North American partner, Keryx, investigated additional dosage regimens of perifosine in oncology patients. A number of screening Phase 2 studies examine perifosine as a single agent in

several tumor types, including prostate, breast, pancreatic, head and neck, sarcoma and melanoma. Encouraging results showing anti-tumor activity were obtained in soft tissue sarcoma, breast and prostate cancers and lead to further development in these indications.

A proof-of-concept Phase 1 study of perifosine in combination with radiotherapy conducted by the National Cancer Institute of the Netherlands was completed in 2004. Results from this trial were presented at ASCO 2004. A total of 21 radiotherapy-naïve patients, 17 of whom had advanced non-small cell lung cancer (NSCLC) and 14 had become refractory to prior chemotherapy, received oral perifosine doses ranging from 50 mg to 200 mg/day concurrently with standard doses of radiotherapy. The trial data demonstrated an acceptable safety and tolerability profile, with 150 mg/day established as the dose recommended for use in subsequent clinical trials. Also demonstrated was preliminary evidence of anti-tumor activity at all dosage levels, including complete or partial responses (complete disappearance and decreased tumor size, respectively), or stable disease, with a median follow-

up for responders of eight months. Importantly, in the cohort of 10 patients who were treated with 150 mg/day, the established dose recommended for use in subsequent clinical trials, there were three complete responses, three partial responses, and four patients with stable disease.

On September 22, 2005, we announced the commencement of a Phase 2 clinical study of perifosine in combination with radiotherapy in patients suffering from NSCLC. This is a randomized, double-blind, placebo-controlled trial to assess the efficacy and safety of a 150 mg daily dose of perifosine when combined with radiotherapy in 160 patients with inoperable Stage III NSCLC. The trial is being conducted in collaboration with the Netherlands Cancer Institute. The lead investigator is Marcel Verheij, MD PhD, of the Department of Radiation Oncology / Division of Cellular Biochemistry, at The Netherlands Cancer Institute in Amsterdam.

On March 2, 2006, our North American partner, Keryx, announced the initiation of a corporate-sponsored Phase 2 trial, multi-cancer, clinical program to evaluate perifosine as a treatment for leukemia. Dr. Frank Giles, Professor, Department of Leukemia, at the MD Anderson Cancer Center in Houston, TX, is the principal investigator. This Phase 2 trial will assess the objective response rate and evaluate the pharmacokinetics and safety and tolerability of perifosine as a single agent in relapsed or refractory acute myeloid leukemia, acute lymphocytic leukemia,, chronic lymphocytic leukemia, high-risk myelodysplastic syndrome and chronic myeloid leukemia in the blastic phase.

In June 2006, we announced positive data of perifosine in patients with advanced renal cell carcinoma (RCC). Keryx disclosed results from an interim analysis performed at the end of the first year of accrual, and the results of the RCC group met protocol requirements for expansion of this cohort of a Phase 2, multi-center trial of perifosine that included multiple types of tumor. Of the 13 patients with RCC, seven were evaluable for response. Three of them (43%) had a partial response and an additional two patients (29%) achieved long-term stable disease. Two patients (29%) had progressive disease. Additional patients will be enrolled in this study.

In November 2006, Keryx presented intermediary results of the Phase 2 study of imatinib plus perifosine in patients with imatinib-resistant gastrointestinal stromal tumor (GIST). The primary endpoint of this study is to evaluate the efficacy and toxicity of the combination imatinib and perifosine in patients with imatinib-resistant GIST. To date, 16 patients have been enrolled in the current study. Of the 12 patients with evaluable disease, there were two partial responses by Choi criteria (17% objective response rate (ORR)) and one partial response by RECIST criteria (8% objective response rate). Grade 3 and 4 adverse events were rare and included fatigue, myalgias, ocular toxicity and nausea/emesis. The early data from the current study suggest that the addition of perifosine to imatinib is well-tolerated and may have efficacy in the treatment of patients with imatinib-resistant GIST.

In December 2006, we announced positive interim Phase 2 data on perifosine in patients with relapsed and refractory multiple myeloma (MM). Investigators concluded that perifosine alone or in combination with dexamethasone has activity in patients with advanced, relapsed/refractory MM, achieving response and/or stabilization of disease in 69% of evaluable patients to date. In this ongoing Phase 2 study, patients with relapsed/refractory MM are treated with perifosine (150 mg oral daily dose) to assess the single agent activity of perifosine in this patient population. If patients progress on perifosine alone, Dexamethasone (20 mg, twice weekly) is added to their perifosine regimen.

In June 2007, our partner Keryx presented outlined results of Phase 1 and 2 studies for the treatment of patients with advanced sarcoma at the ASCO meeting. The dose schedules in the Phase 1 trials were weekly 100-800mg or loading dose 300-1800mg on Day 1 followed by 50-150mg daily for Days 2-21 every 28 days or loading dose 400-900mg and daily 50-100mg continuously. In the Phase 2 trial, doses were loading dose 900mg on Day 1 and 150mg daily for days 2-21 every 28 days; loading dose 9 mg and 100 mg daily continuously; 50mg daily continuously without a loading dose; and 900-1500mg weekly. 145 patients with sarcoma were entered into studies and were assessed for clinical benefit rate (CBR). Partial responses were seen, in one patient each, with chondrosarcoma, extra-skeletal myxoid chondrosarcoma, leiomyosarcoma and a

desmoid tumor. At lower doses with 52 patients fully evaluable for CBR, the CBR was 52% with four partial responses and 23 stable disease at ≥ 4 months. At higher doses with 30 patients fully evaluable for CBR, CBR was 53% with 16 stable disease at ≥ 4 months. Toxicities were mainly gastrointestinal and/or fatigue. The percentage of patients with grade 0 nausea, vomiting, diarrhea and fatigue for lower dose perifosine (76 patients) was 46%, 49%, 38% and 55% respectively compared to 26%, 32%, 20%, and 58% for higher dose perifosine (69 patients). The proportion of patients with grade 2+ nausea, vomiting,

diarrhea and fatigue was 20%, 13%, 15%, and 21% for lower dose perifosine and 49%, 35%, 42%, and 25% for higher dose perifosine.

Also in June 2007, Keryx announced positive Phase 1 and Phase 2 data on perifosine in patients with relapsed/refractory multiple myeloma and Waldenstrom s Macroglubulinemia. Data demonstrated clinical activity of perifosine in combination with bortezomib (overall response rate (partial response + minimal response) of 31%), dexamethasone (78% of patients treated with perifosine and low dexamethasone had at least stable disease, including 26% that had partial or minimum response), and lenalidomide plus dexamethasone (50% of patients achieving a partial response or better) in patients with relapsed/refractory multiple myeloma. Perifosine also showed clinical activity as a single agent in patients with relapsed/refractory Waldenstrom s Macroglobulinemia, 36% of the patients having a partial or a minimal response.

In November 2007, Keryx announced positive preliminary Phase 2 data of perifosine in patients with chemo-insensitive sarcoma. Data demonstrated the tolerability and clinical activity of perifosine as a single agent with an overall clinical benefit of 40% (stable disease > 3 months) in patients with refractory rare sarcomas. Perifosine was well tolerated with the most common grade 1 & 2 adverse events reported as nausea, vomiting, diarrhea and fatigue. During this month, Keryx also announced Phase 1 and 2 data of perifosine in patients with advanced renal cell carcinoma. The Phase 2 trial included 24 patients with advanced renal cell carcinoma who were randomized to receive either the daily (50mg or 100mg) or the weekly (900mg or 1200mg) dose of perifosine. Thirteen of those patients were evaluable for response. Four (31%) had a partial response and an additional four patients (31%) achieved long-term stable disease for a 62% overall clinical benefit. Five patients progressed. The Phase 1 trial assessed perifosine in combination with sorafenib. Eighteen patients with advanced cancers were enrolled in one of four cohorts. Ten of these patients had advanced renal cell carcinoma with some patients having received a prior treatment. No grade 4 toxicities were reported and one grade 3 hand/foot syndrome has been seen. The combination has been generally well tolerated. The Phase 1 will enroll an additional 20 patients to confirm the selected maximal tolerated dose.

Also in November 2007, Keryx announced early results of a Phase 2 trial of perifosine as a single agent for the treatment of recurrent malignant gliomas (malignant glioblastoma and malignant anaplastic gliomas). Twenty-five patients with advanced malignant gliomas were treated with a loading dose of 600mg (150mg x4) followed by a 100mg daily dose of perifosine. The median progression free survival and overall survival in the anaplastic glioma group was nine weeks (range 2-50 weeks) and 49 weeks respectively. Toxicity was minimal with the following reported events: one grade 1 nausea, one grade 1 diarrhea, one grade 2 pain, and one grade 4 gout exarcebation. The study was designed to enroll at least 12 evaluable malignant glioblastoma patients and at least 10 evaluable malignant anaplastic gliomas patients. If at least one patient achieves six month progression free survival, the study would continue to enrol an additional subset of patients. Therefore, the malignant glioblastoma arm has been halted and the malignant anaplastic gliomas arm will continue to enroll.

On November 14, 2007, we announced completion of patient enrolment for our multi-center Phase 2 trial with perifosine in combination with radiotherapy for NSCLC. Patients receive perifosine daily for five to six weeks and are followed for at least 12 months. The primary endpoint of this trial is the extent and duration of local control, i.e. the absence of tumor recurrence or progression in the area that has been irradiated.

On December 10, 2007, Keryx announced Phase 1 and 2 data on perifosine in patients with relapsed/refractory multiple myeloma. Phase 1 results demonstrated clinical activity of perifosine in combination with bortezomib in patients previously treated with bortezomib. Eighteen patients with advanced multiple myeloma (83% relapsed and refractory) were enrolled in one of four cohorts. Perifosine was escalated from 50 to 100mg daily while bortezomib was escalated from 1.0 to 1.3mg/mm2. No dose-limiting toxicity and no grade 3 peripheral neuropathy were reported. Dexamethasone 20mg (day of and day after each Velcade dose) was added in patients with progressive disease on perifosine plus velcade alone. Sixteen patients on either Velcade plus perifosine alone or with dexamethasone were evaluable for response. An overall response rate of 56% (complete + partial + minimal response) was reported with an additional 31% of patients achieving stable disease. The Phase 2 portion of the study is open with 12 patients enrolled as of December 2007 with perifosine 50mg daily and Velcade 1.3mg/mm2 on Day 1, 4, 8, 11

every 21 days as the selected Phase 2 dose. Phase 2 results demonstrated that perifosine as monotherapy appears to have modest activity with 33 of 50 evaluable patients (66%) achieving stable disease. Sixty-seven highly pre-treated MM patients were treated with perifosine at 150mg daily to assess the single agent activity. If a patient

progressed on perifosine alone, dexamethasone (20mg twice weekly) was added to the perifosine regimen. Toxicity was manageable with no deep vein thrombosis or peripheral neuropathy reported. Twenty-one patients had perifosine reduced from 150 to 100mg daily with no difference in response noted and dexamethasone was added in 39 of 55 patients with progressive disease. Out of 29 patients currently evaluable for response on the combination, an overall response rate (complete + partial + minimal responses) of 35% (10/29) was achieved, with an additional 52% (15/29) of patients achieving stable disease. Six patients remain on treatment with duration of response ranging from 15-70 weeks. Enrollment objectives were met and the study is now closed.

The following are the ongoing trials sponsored by Keryx:

Therapeutic category	**Trial description**
Renal	Phase 1 study of perifosine+ sorafenib for patients with advanced cancers
	Phase 1 study of perifosine+ sunitinib for patients with advanced cancers
	Phase 2 study of perifosine following tyrosine kinase inhibitors (TKI)-failure in patients with renal cancer
	Phase 2 study of perifosine for patients with carcinoma of the kidney
Sarcoma	Phase 2 trial of perifosine in patients with chemo-insensitive sarcomas
	Phase 2 study of imatinib plus perifosine in patients with imanitib-resistant gastrointestinal stromal tumor (GIST)
	Phase 2 study of perifosine in treating patients with advanced soft tissue sarcoma
Blood	Phase 2 study of efficacy of perifosine alone and in combination with dexamethasone for patients with multiple myeloma
	Phase 1/2 study of safety & efficacy of perifosine & bortezomib+/- eexamethasone for myeloma patients
	Phase 2 study of perifosine in patients with refractory and relapsed leukemia
	Phase 1 study of perifosine+ lenalidomide and dexamethasone for patients with multiple myeloma
	Two Phase 2 studies of perifosine in patients with relapsed/refractory waldenström s macroglobulinemia
	Phase 1 study of UCN-01 in combination with perifosine in patients with relapsed and refractory acute leukemias, chronic myelogenous leukemia or high risk myelodysplastic syndromes (trial sponsored by the National Cancer Institute)
Lung	Phase 1/2 trial of perifosine in the treatment of non-small cell lung cancer
Breast	Phase 2 trial of perifosine plus trastuzumab in patients with breast cancer
	Phase 2 trial of perifosine in combination with endocrine therapy for breast cancer
Prostate	Phase 2 trial of perifosine in combination with chemotherapy (trial sponsored by the National Cancer Institute)
Glioma	Phase 2 clinical trial of perifosine for recurrent/progressive malignant gliomas
	Phase 2 clinical and molecular-metabolic trial of perifosine for recurrent/progressive malignant gliomas
Ovarian	Phase 1 perifosine and docetaxel pharmacodynamic study
Head and Neck	Phase 2 study of perifosine in treating patients with Recurrent or metastatic head and neck cvancer (trial sponsored by the National Cancer Institute)

Exploratory trials	Phase 1 trial of docetaxel with perifosine
	Phase 1 trial of paclitaxel with perifosine
	Phase 1 perifosine and gemcitabine study (trial completed)
	Phase 2 trial of perifosine in patients for whom no standard therapy exists
	Phase 2 placebo-controlled study of perifosine in combination with single agent chemotherapy for metastatic cancer patients

Partners for Perifosine

A Cooperative Research and Development Agreement (CRADA) was put in place with the National Institute of Health/the National Cancer Institute in May 2000. A cooperation and license agreement was signed in September 2002 with Access Oncology, Inc. (AOI), for the use of perifosine as an anticancer agent covering the United States, Canada and Mexico. In January 2004, AOI was acquired by Keryx, which is pursuing the clinical development of perifosine under the same conditions as AOI. The agreement, in particular, provides us free access to all data from Keryx and its partner s studies, as well as milestone payments and scale-up royalties to be paid to us on future net sales of perifosine in North America. We own rest of the world rights to perifosine.

AEZS-127 Erucylphosphocholine

On January 6, 2005, we announced the initiation of preclinical development of erucylphosphocholine (AEZS-127), an analog of perifosine which is suitable for intravenous administration. Like perifosine, AEZS-127 belongs to a new class of compounds based on alkylphosphocholines. AEZS-127 possesses distinctive reduced haemolytic activity thus allowing for intravenous injection.

On January 6, 2005, we also licensed to Keryx certain rights to develop and market AEZS-127 in North America, South Africa, Israel, Australia and New Zealand while keeping rights for the rest of the world. According to the agreement with Keryx, the preclinical development costs of AEZS-127 are shared between Keryx (50%) and us (50%).

In 2006, studies for acute toxicity and dose range finding of erucylphosphocholine were actively pursued. The 4-week toxicity studies in rats and dogs as well as the safety pharmacology package was completed in 2007. These preclinical data are a prerequisite for the performance of a Phase 1 clinical study which is planned in 2008. Expenditures for the clinical development of erucylphosphocholine will be covered by Keryx.

Erk/PI3K Inhibitors (dual kinase inhibitors)

In addition to our activities with alkylphosphocholines, we are screening small molecules for activity as agonists and antagonists to lipid-protein signaling interactions, which are seen as new and potentially important therapeutic targets.

We are focusing our efforts on single and dual inhibitors of Ras-Raf-Mek-Erk and PI3K-Akt pathways. The Ras-Raf-Mek-Erk and the PI3K-Akt pathways are constitutively activated in many cancer types, and influence both tumor development and progression.

Both signaling pathways represent promising therapeutic targets for the treatment of tumors. We have now identified a new compound class with inhibitory activity against both the Erk and PI3K kinases. These small molecules inhibit the kinases at nanomolar concentrations in a dose-dependent manner by competing directly at the ATP binding site. In a broad kinase panel, the molecules are very selective against other kinases. In cellular experiments the compounds inhibit the activation of downstream targets Akt and Rsk1, and can stop the proliferation of various human cancer cell lines. Moreover, a new generation of aniline-substituted pyridopyrazine-urea derivative show highly selective PI3K inhibition. We are currently performing first *in vivo* studies with front-

runner compounds in four mouse xenograft models (HCT116, U87, A549 and PC3) as well as pharmacokinetic studies in rodents using an oral pre-formulation In addition, initial Absorption, Distribution, Metabolism, and Excretion (ADME) parameters were collected. Further optimization of the lead class is ongoing with respect to pharmacokinetic parameters, in order to select a development candidate as soon as possible.

Competitor for Erk/PI3K Inhibitor

Novartis PI3K inhibitor NVP-BEZ 235, which is currently being investigated in a clinical Phase 1, was used as a reference compound for the evaluation of our candidate compounds.

Tumor Targeting Cytotoxic Conjugates and Cytotoxics

Cytotoxic Conjugates

In view of the non-specific toxicity of most chemotherapeutic agents against normal cells, targeting such drugs to cancerous tissue offers a potential benefit for patients with advanced or metastatic tumors. Targeted cytotoxic peptide conjugates are hybrid molecules composed of a cytotoxic moiety linked to a peptide carrier which binds to receptors on tumors. Cytotoxic conjugates are designed to achieve differential delivery, or targeting, of the cytotoxic agent to cancer vs. normal cells.

Our cytotoxic conjugates represent a novel oncological strategy to control and reduce toxicity and improve the effectiveness of cytotoxic drugs. The development strategy was to create targeted conjugates with high cytotoxic activity based on doxorubicin, an approved and commercialized product or 2-pyrrolino-doxorubicin which is 500 to 1,000 times more active than the parent compound. We are exploring several candidates in which doxorubicin or 2-pyrrolino-doxorubicin are coupled to the peptide carriers targeting LHRH (AEZS-108 & AN-207), somatostatin (AN-238 & AN-162) or bombesin (AN-215) receptors. These conjugates are less toxic and more effective *in vivo* than the respective radicals in inhibiting tumor growth in LHRH receptor-positive models of human ovarian, mammary or prostatic cancer.

In AEZS-108, the most advanced of the cytotoxic conjugates, doxorubicin is chemically linked to an LHRH agonist, a modified natural hormone with affinity for the LHRH receptor. This design 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 more favorable safety profile with lower incidence and severity of side effects, as normal tissues are spared from toxic effects of doxorubicin. In addition, the targeted approach may enable treatment of LHRH receptor positive cancers that have become refractory to doxorubicin which has been administered in its non-targeted form.

In preclinical studies conducted to date in several animal models of LHRH receptor positive human cancer cell lines, AEZS-108 anti-tumor activity and tolerability were shown to be superior to that of doxorubicin. As would be expected, AEZS-108 was not active or was significantly less active than doxorubicin in LHRH receptor negative cancer cell lines. On January 18, 2005, we announced the initiation of a company-sponsored Phase 1 dose-ranging study with this targeted anti-cancer agent AEZS-108.

In June 2006, we announced positive Phase 1 results for AEZS-108 in patients with gynaecological and breast cancers which showed that the compound has a good safety profile and no dose-limiting toxicities. Eight patients received AEZS-108 by intravenous infusion. Infusion was well tolerated at all dosages, without supportive treatment. Pharmacokinetic analyses showed dose-dependent plasma levels of AEZS-108 and only minor (10-20%) release of doxorubicin. Stabilization of disease was observed in one of eight patients in the ongoing Phase 1 study.

On November 27, 2006, we disclosed additional positive Phase 1 results regarding AEZS-108 in patients with gynaecological and breast cancers. Further data showed the compound s good safety profile and established the maximum tolerated dose at 267 mg/m2, which is equimolar to a doxorubicin dose of 77 mg/m2. This dose will be the recommended dose for a Phase 2 trial. The Phase 1 open-label, multi-center, dose-escalation, safety and pharmacokinetic study conducted in Europe include 17 patients suffering from breast, endometrial and ovarian cancers with proven LHRH receptor status. Evidence of anti-tumor activity was found at 160mg/m2 and 267 mg/m2 doses of AEZS-108 where seven of 13 patients showed signs of tumor response, including 3 patients with complete or partial responses. The Phase 2 trials will focus on advanced or recurrent ovarian and endometrial cancers, two forms of cancer where LHRH receptors are highly expressed. Recommended dose will be 267 mg/m2 given once every three weeks.

In 2007, a Phase 2 open label, non-comparative, multicenter two indication trial stratified with two stage Simon Design was prepared, where 82 patients are planned for this trial and up to 41 patients each with diagnosis of platinum-resistant ovarian cancer (stratum A) and disseminated endometrial cancer (stratum B). On February 12, 2008, we reported that the treatment of first patients had commenced in this Phase 2 trial. Results of this trial are expected in the first half of 2009.

AEZS-105 - Lobaplatin

Lobaplatin is a platinum derivative that has demonstrated lower toxicity in preclinical studies compared with cisplatinum, specifically renal toxicity, and incomplete cross-resistance with other platinum derivatives suggesting potential therapeutic use even in tumor indications not routinely treated with platinum derivatives.

Clinically, lobaplatin was well tolerated at recommended dosages. Treatment was not associated with typical side effects often seen with cisplatinum, such as nephrotoxocity (impairment of kidney function), otoxicity (loss of hearing capacity), neurotoxicity (effects on sensory function). In addition, vomiting was less severe than published data from both cisplatinum and carboplatinum. Characteristic toxicity of

lobaplatin is a short-lasting, spontaneously reversible drop in thrombocyte count (blood platelets).

In a Phase 2 study conducted in China that included 284 patients with a broad range of solid and non-solid tumors, safety and particularly good therapeutic efficacy were demonstrated in patients with breast cancer, small cell lung cancer (SCLC), and chronic myeloid leukemia (CML) (a cancer of the hematopoietic system). The primary endpoint in solid tumor patients was the remission rate according to WHO criteria, while response in CML was assessed according to the disease-specific criteria of Talpaz. The favorable results of this study were the basis for approval of the product in China including all three indications: breast cancer, SCLC and CML.

In China, lobaplatin has been approved by the Chinese health authorities for the treatment of inoperable, advanced breast cancer, SCLC and CML. In December 2002, we signed a contract with Hainan Chang An Pharmaceuticals Ltd. for the marketing in China of lobaplatin. The contract includes the worldwide manufacturing rights of lobaplatin by Hainan Chang An Pharmaceuticals. The technology transfer agreement provided for a first payment to us upon signature and a later manufacturing-related payment.

In 2007, lobaplatin was licensed to Atani for the territory of Japan. Atani is planning to perform preclinical studies and will conduct a Phase I clinical trial at the end of 2008/beginning of 2009.

Tubulin Inhibitors / Vascular Targeting Agents

AEZS-112 - Development of a Low Molecular Weight Tubulin Inhibitor with anti-angiogenic properties

Tubulin is a protein found in all cells that plays an important role during cell division, in that it helps to transmit genetic information to the daughter cells. Inhibition of this process leads to the death of the affected cell. The anti-tumor agents taxol and vincristine, which are widely used in cancer therapy, are based on this principle. Both compounds are expensive natural substances and cause severe side effects when used in humans.

We are currently identifying and developing novel tubulin inhibitors which, compared with currently used products, exhibit in animal models improved efficacy, have a more acceptable side effect profile, an incomplete or no cross-resistance and are administered orally.

AEZS-112 is a drug development candidate with an excellent tolerability profile showing excellent *in vivo* activity in various tumor models including mammary, colon, melanoma and leukemia cancers after *per os* administration. This compound expresses different modes of action. Strong anticancer activity is combined with pro-apoptotic and anti-angiogenic properties. AEZS-112 inhibits the polymerization of cancer tubulin rather than bovine brain tubulin, it destroys the mitotic spindel of the cancer cells and it inhibits topoisomerase II activity. AEZS-112 arrests the cancer cells in the G_2M phase at a nanomolar concentration and induced apoptosis. AEZS-112 is not cross-resistant to cisplatin, vincristine and doxorubicine in cell lines resistant to these drugs. Given orally once weekly, AEZS-112 proved to be a potent inhibitor of *in vivo* tumor growth in melanoma, mammary, colon, lung, renal as well as in leukemia cancers at acceptable and very well tolerated doses. Furthermore AEZS-112 showed favorable safety and toxicity profiles. No findings with respect to cardiotoxicity and neurotoxicology parameters could be observed during the toxicological evaluation in mice, rats and dogs. With this profile of activity, AEZS-112 is a promising candidate for further clinical development.

On January 8, 2007, we announced the initiation of a Phase 1 trial for AEZS-112 in patients with solid tumors and lymphoma. This open-label, dose-escalation, multi-center, intermittent treatment Phase 1 trial is being conducted in the United States with Daniel D. Von Hoff, MD, Senior Investigator at the Translational Genomics Research Institute in Phoenix, AZ, as the lead investigator. The trial includes up to 50 patients who have either failed standard therapy or for whom no standard therapy exists. Primary endpoint of the Phase 1 trial focuses on determining the safety and tolerability of AEZS-112 as well as establishing the recommended Phase 2 dose and regimen. Secondary endpoints are aimed at establishing the pharmacokinetics and determining the efficacy based on standard response criteria.

As of December 11, 2007, 22 patients have entered this Phase 1 dose escalating clinical trial. To date no Maximum Tolerated Dose (MTD) has been achieved and no clinical relevant drug-related adverse events have been encountered.

GH-RH Modulators

Development of a Growth Hormone Secretagogue

Growth hormone secretagogues (GHS) represent a new class of pharmacological agents that directly stimulate growth hormone (GH) secretion from the pituitary gland without the involvement of growth hormone-releasing hormone GH-RH or somatostatin. We believe that there is currently no GHS on the pharmaceutical market. Since GH is a potent regulator of lipid, sugar and protein metabolism, the potential clinical uses of GHS are

numerous. They include growth retardation in children and treatment of cachexia in AIDS patients, which are currently the only approved uses of therapy of GH. The administration of GH, which has to be injected every day, is cumbersome. Therefore, we believe that there would be a demand for new orally active drugs like GHS.

As part of our university collaboration, we accessed new peptidomimetic compounds with GH secretagogue properties. The lead development candidate, AEZS-130 (EP-1572), is a novel peptidomimetic GHS with potent and selective GH-releasing activity in humans. AEZS-130 underwent limited clinical pharmacology tests that demonstrated a potent stimulation of the GH secretion after oral administration in human volunteers. This product has been licensed to Ardana Bioscience Ltd. (Ardana) (ARD-07), which initiated an open, randomized, placebo-controlled Phase 1 dose-ranging study in April 2004. Thirty-six healthy subjects were included in this study to receive either the reference hormone GH-RH by intravenous route or one of the following dose levels of AEZS-130: 0.005, 0.05 or 0.5 mg/kg by oral route. AEZS-130 at the dose of 0.5 mg/kg orally caused an increase in growth hormone release equivalent to that induced by GH-RH intravenously. The compound was well tolerated and no other hormones showed a significant modification after any dose of AEZS-130.

In June 2006, Ardana presented results regarding AEZS-130 at the 2006 Endo Convention. These results referred to the Phase 1 trial regarding the stimulating effects of AEZS-130 on growth hormone following both oral and intra-duodenal administration in healthy males. This study showed that AEZS-130 was well tolerated by the 36 volunteers enrolled and no adverse events were reported. Administration of AEZS-130 either orally or via intra-duodenal infusion results in increased levels of growth hormone in the blood. This stimulation of growth hormone appears to be selective as no other hormones/analytes that were measured (cortisol, ghrelin, prolactin, insulin, glucose and ACTH (adrenocorticotropic hormone)) were affected in a dose-dependent or statistically significant way by administration of AEZS-130 either orally or via intra-duodenal infusion.

In May 2007, Ardana gained orphan drug status for AEZS-130, which it is developing as a diagnostic for growth hormone deficiency in adults. The clinical development and toxicology programs are ongoing and, subject to clinical outcome, Ardana announced the commencement in the U.S.A. of the planned pivotal registration study and the enrolment of the first patient in August 2007. This Phase 3 study is a multi-center, randomized, cross-over study investigating the safety and effectiveness of oral GHS as a growth hormone sitmulation test compared to intravenous L-Arginine plus growth hormone releasing hormone. The study will be conducted in 10 centers in the U.S.A. with 80 subjects. Half of the subjects will be patients with proven deficiency and the other half will be matched controls (healthy subjects).

Ghrelin Receptor Ligands

Ghrelin is a peptide predominantly produced by the stomach. Apart from a potent GH-releasing action, ghrelin has other activities including stimulation of lactotroph and corticotroph function, influence on the pituitary gonadal axis, stimulation of appetite, control of energy balance, influence on sleep and behavior, control of gastric motility and acid secretion, and influence on pancreatic exocrine and endocrine function as well as on glucose metabolism. The recent discovery of ghrelin and its receptors opens up new opportunities for the development of drugs that will treat metabolic disorders. There is indeed a possibility that ghrelin analogs, acting as either agonists or antagonists, might have clinical impact without affecting GH level. The use of ghrelin antagonists as appetite suppressants or inhibitors of lipogenesis could open up new opportunities for the treatment of obesity and associated diseases (e.g. diabetes, cardiovascular diseases). The use of ghrelin agonists could have therapeutic benefits which are expected to offer hope for cachexic or anorexic patients.

In 2004, we established a research and license collaboration agreement with Le Centre National de la Recherche Scientifique and University Montpellier I and II, France, acting in their own names, as well as in the name and on behalf of the Laboratoire des Aminoacides, Peptides et Protéines (LAPP) (UMR 5810), directed by Dr. Jean Martinez, for the synthesis and characterization of new chemical entities acting as ghrelin receptor ligands. According to the agreement, we have the worldwide rights to develop and exploit the new compounds for any indication. Compounds with the most potent affinity for the ghrelin receptors will be investigated further through an international network of academic

investigators with expertise in the field of endocrinology in order to identify clinical development candidates.

Additionally, we also established a research contract with the Department of Experimental and Environmental Medicine of the University of Milan, Italy, under the direction of Prof. Vittorio Locatelli, for the pharmacological characterization of potentially ghrelin receptor ligands.

In August 2005, we filed a first patent application to protect a series of new chemical entities characterized as ghrelin receptor ligands.

In May 2006, we established a research project agreement with the University of Montreal. This research project will focus on the characterization of ghrelin receptor ligands on fat tissue. This project is led by Huy Ong, Professor at the Faculty of Pharmacy, at the University of Montreal.

In August 2006, we also initiated a research collaboration with the Hôpital Laval (Quebec City) under the direction of Dr. Denis Richard. This research collaboration will focus on the pharmacological characterization of ghrelin receptor ligands *in vivo* (e.g. the effects in diet-induced obesity models).

In October 2006, we presented for the first time our *in vivo* data on the capacity of ghrelin antagonists of selectively inhibiting food intake. This study, using a rat model, outlined the capacity of ghrelin antagonists ability to inhibit appetite without affecting growth hormone secretion and represents evidence that ghrelin antagonist compounds can selectively inhibit food intake. It further supports the hope that ghrelin antagonist compounds have the potential to be useful for the treatment of obesity.

During 2007, several preclinical candidates have been investigated which demonstrated an interesting decrease in body weight gain and fat accumulation in a diet induced obesity mouse model. The ongoing work will focus on the improvement of oral bioavailability.

GH-RH Antagonists

Growth hormone-releasing hormone (GH-RH) is a hormone secreted in the brain by the hypothalamus that acts on the pituitary gland to stimulate the synthesis and the release of GH. Many tumor types are potentially dependent on levels of GH and insulin-like growth factors, IGF-I and IGF-II, which stimulate cell proliferation while inhibiting programmed cell death (apoptosis).

GH-RH antagonists represent a potential novel class of promising anti-cancer agents that may offer distinct advantages compared to other classes of anti-tumor agents, with utility in a variety of tumor types. GH-RH antagonists possess the ability to exert both direct (by blocking GH-RH receptors on tumor cells) and indirect (by blocking the secretion of GH from the pituitary and thereby suppressing the production of IGF-I in the liver) anti-proliferative effect. Early evidence for the anti-tumor activity of GH-RH antagonists was provided by research conducted at Tulane University, which demonstrated that GH-RH antagonists inhibit the growth of a broad range of cancer cell lines, including pancreatic, colorectal, prostate, breast, renal, small-cell/non small-cell lung cancer, osteosarcoma and glioblastoma. Importantly, GH-RH antagonists were shown to have a direct anti-proliferative effect *in vitro* on certain cancer cell types, an action that is thought to be mediated by the presence of locally-produced GH-RH, which may act as an autocrine growth factor, and its receptors in the respective cancer cell lines. GH-RH antagonists also inhibit indirectly the production of IGF-I and IGF-II in tumors.

In 2006, selected GH-RH antagonists have been provided to several of our academic partners for further preclinical evaluation.

In 2007, we disclosed *in vivo* data on GH-RH antagonist JMR-132 demonstrating anti-tumor activity of JMR-132 in MX-1 human experimental doxorubicin-resistant breast cancers, as well as on the anti-proliferative effect in combination with docetaxel chemotherapy, which is frequently used for the treatment of early and metastatic breast cancer.

Immunotherapy / Vaccines

Cellular proteins expressed by oncogenes have been recognized as a major cause of tumor development. One of the central oncoproteins involved in cancer formation are the Raf proteins. Based on these proteins, new unique

therapeutic strategies, new predictive animal models and new development products have been generated to efficiently combat cancer. These consist of virulence attenuated, genetically modified bacteria expressing tumor antigens, including oncoproteins or enzymes. Such bacteria are used for vaccination as well as tumor targeting and delivery of antitumoral compounds towards the tumor tissues. This new vaccine approach, therefore, exploits the ability of bacteria to induce potent immune responses as well as direct these responses against malignancies. The immunogenicity of the vaccine will be further enhanced by the capacity of bacteria to colonize tumor tissues. This property will be used to transport substances, e.g. proteins, into the tumor tissue, which are capable of converting non-toxic pro-drugs into active drugs. The use of bacterial carriers for therapeutic vaccination against tumors and the concept of bacterial tumor targeting will be further developed with the Julius-Maximilians-University of Würzburg, including the highly recognized researchers Prof. Dr. Ulf R. Rapp, who is member of our Scientific Advisory Board, and Prof. Dr. Werner Goebel. Prof. Rapp is a known expert in the field of cell and tumor biology and Prof. Goebel is a pioneer in the field of vaccines based on recombinant bacteria.

The preclinical proof of principle has already been shown in a transgenic animal model and is supported by several patent applications that we have filed. The most advanced products are bacterial tumor vaccines which are based on the approved human vaccine strain *Salmonella typhi* Ty21a. The principle of these recombinant vaccine strains is the secretion of the tumor antigen using a so-called Type I secretion machinery derived from *Escherichia coli*. To date, two different vaccine strains have been generated up to GMP scale production a melanoma vaccine encompassing a mutated form of the oncogene B-Raf, which is present in more than 65% of melanomas, and a prostate cancer vaccine strain expressing and secreting PSA. For both vaccines, the preclinical proof of principle has been demonstrated in distinct animal models and the immunogenicity could be further enhanced compared to our already published strains (patent application filed in November 2006).

In 2007, the PSA vaccine (AEZS-120) was selected as the first preclinical development candidate of an anti-tumor vaccine. In September, scientific advice from the Paul Ehrlich Institute, the German health authority for vaccines, was sought and the preclinical development program presented by us was in principle accepted.

A grant application was filed in Germany and was approved in 2008. In accordance with this grant, 50% of our preclinical development costs and 100% of those of our university partner will be reimbursed by the German Ministry of Science and Education. The preclinical development is planned to be initiated in mid-2008.

Drug Discovery

There is an increasing demand on the world market for active substances. Our internal drug discovery unit provides an important prerequisite for the provision of new patented active substances, which can then be developed further or licensed to third parties.

Our drug discovery unit concentrates on the search for active substances for innovative targets which open the door to the introduction of new therapeutic approaches. Further, this unit searches for new active substances having improved properties for clinically validated targets for which drugs are already being used in humans and which produce inadequate effects, cause severe side effects, are not economical or are not available in a patient-friendly form.

To this end, we possess an original substance library for the discovery of active compounds with a comprehensive range of promising natural substances which can serve as models for the construction of synthetic molecules. The initial tests involve 120,000 samples from our internal

substance library in the form of high-throughput screening. The hits, i.e. the first active compounds found in the library, are tested further and built up specifically into potential lead structures. Based on two to three lead structures, they are then optimized in a further step to potential development candidates.

Intellectual Property Patents

We believe that we have a comprehensive intellectual property portfolio that covers compounds, manufacturing processes, compositions and methods of medical use for our lead drugs. Our patent portfolio consists of more than 70 patent families (issued, granted or pending in the U.S.A., Europe and other jurisdictions).

Of the issued or granted patents, the seven described below form the core of our patent portfolio with regard to our lead drugs.

- US patent 5,198,533 provides protection in the U.S.A. for the compound cetrorelix and other (LHRH) antagonists. This U.S. patent will expire in October 2010 pursuant to a granted request for patent term extension.

- US patent 6,828,415 protects a method for preparing sterile lyophilizate formulations of cetrorelix. It specifically protects the lyophilization process used to manufacture cetrorelix. This U.S. patent will expire in December 2021.

- US patent 5,773,032 covers a long-acting formulation of cetrorelix consisting of poorly soluble particles of 5 µm to 200 µm in size. The patent not only protects cetrorelix pamoate as a long-acting formulation but also prevents the development of other LHRH antagonist drugs that are based on this drug-delivery system. This U.S. patent will expire in November 2014. A patent term extension of up to five years may be possible and will be requested upon marketing approval of Cetrorelix pamoate.

- US patent 6,054,432 is a method-of-use patent covering a therapeutic regimen for treating BPH, where Cetrorelix is administered at a dosage of about 0,5 mg per day over time without effecting testosterone castration. The U.S. patent will expire in August 2017.

- US patent 7,005,418 is a method-of-use patent covering the therapeutic management of extrauterine proliferation of endometrial tissue (endometriosis), chronic pelvic pain and/or fallopian tube obstruction by administering an LHRH antagonist in the form of a short-term induction treatment for a period of about 4 to 12 weeks. The U.S. patent will expire in August 2022.

- US patent 6,172,050 provides protection in the U.S.A. for the compound perifosine and other related alkyl phospholipid derivatives, pharmaceutical compositions comprising the compounds as well as their medical use for the treatment of tumors. This U.S. patent expires in July 2013. A patent term extension of up to five years may be possible and will be requested upon receiving marketing approval of perifosine.

- US patent 6,627,609 provides protection in the U.S.A. for the compound ozarelix and related third-generation LHRH antagonists and pharmaceutical compositions comprising them. This U.S. patent will expire in March 2020. A patent term extension of up to five years may be possible and will be requested upon marketing approval of ozarelix.

The table below lists some of our issued or granted patents in the United States and Europe:

Patent No	Title	Country	Expiry Date
Cetrorelix			

EP 0 299 402	LHRH antagonists	Germany, Great Britain, France, Switzerland and others	2013-07-10
US 5,198,533	LHRH antagonists	U.S.A.	2010-10-24
EP 0 611 572	Process to prepare a cetrorelix lyophilised composition	Germany, Great Britain, France, Switzerland and others	2014-02-04
US 6,828,415	Oliogopeptide lyophilisate, their preparation and use	U.S.A.	2017-12-07
US 6,716,817	Method of treatment of female infertility	U.S.A.	2014-02-22
US 6,863,891	Oligopeptide lyophilisate, their preparation and use	U.S.A.	2014-02-22
US 6,867,191	Preparation and use of oligopeptide lyophilisate for gonad protection	U.S.A.	2014-02-22

EP 1 150 717	Sustained release salts of pharmaceutically active peptides and their production	Germany, Great Britain, France, Switzerland and others	2020-01-29
EP 1 309 607	Method for producing LHRH antagonists	Germany, Great Britain, France, Switzerland and others	2021-08-09
US 6,780,972	Method for the synthesis of peptide salts, their use and the pharmaceutical preparations, containing peptide salts	U.S.A.	2021-08-24
US 5,773,032	Long-acting injection suspensions and a process for their preparation	U.S.A.	2014-11-25

C. Organizational structure.

The following chart presents our corporate structure, the jurisdiction of incorporation of our subsidiaries and the percentage of shares that we hold in those subsidiaries as of March 14, 2008.

Æterna Zentaris Inc.
(Canada)

100% 100%

Æterna Zentaris GmbH
(Germany)

Æterna Zentaris, Inc
(U.S.A.)

D. Property, plants and equipment.

Our corporate head office and facilities are located in Quebec City, Province of Quebec, Canada The following table sets forth information with respect to our main facilities as of March 14, 2008.

Location	Use of space	Square Footage	Type of interest
1405 Parc Technologique Blvd Quebec City (Quebec), Canada	Partially occupied for R&D, manufacturing and administration	69,070(1)	Owned
20 Independence Blvd Warren, New Jersey, U.S.A.	Fully occupied for management and administration	10,741	Leased
Weismüllerstr. 50 D-60314 Frankfurt am Main, Germany	Fully occupied for R&D, product management and administration	46,465	Leased

(1) Approximately 60% of this facility is leased to our former subsidiary, Atrium Innovations Inc., and approximately 30% is not occupied.

Item 4A. Unresolved Staff Comments

None.

Item 5. Operating and Financial Review and Prospects

The following analysis provides a review of our results of operations, financial condition and cash flows for the three-month period and full year ended December 31, 2007. In this Management s Discussion and Analysis the Company , we , us , and our mean Æterna Zentaris Inc. and its subsidiaries on a consolidated basis. This discussion should be read in conjunction with the information contained in our annual consolidated financial statements and related notes for the years ended on December 31, 2007, 2006 and 2005. Our consolidated financial statements are reported in United States dollars and have been prepared in accordance with generally accepted accounting principles in Canada, or Canadian Generally Accepted Accounting Principles (Canadian GAAP). All amounts are in US dollars unless otherwise indicated.

Company Overview

Æterna Zentaris Inc. (TSX: AEZ, NASDAQ: AEZS) is a global biopharmaceutical company focused on endocrine therapy and oncology.

Our pipeline encompasses compounds at all stages of development, from drug discovery through marketed products. The two highest priority clinical programs are our lead value driver, cetrorelix for benign prostatic hyperplasia (BPH) and our lead oncology program, AEZS-108 for endometrial and ovarian cancers.

Key Developments for the Year Ended December 31, 2007

CORPORATE

In January 2007, we completed the spin-off of Atrium Biotechnologies Inc., now known as Atrium Innovations (Atrium) by distributing to our shareholders our remaining interest in Atrium.

In March 2007, the board of directors appointed David J. Mazzo, Ph.D. as new President and CEO of the Company.

Between May and August 2007, the Company appointed three key members to the executive management team:

- Ellen McDonald, M.B.A. SVP and Chief Business Officer
- Nicholas Pelliccione, Ph. D., SVP, Regulatory Affairs and Quality Assurance
- Paul Blake, M.D., SVP and Chief Medical Officer

On August the 14, 2007, the Board of Directors appointed Juergen Ernst as Chairman of the Board, replacing the founder and former Executive Chairman, Éric Dupont, Ph.D.

In the autumn of 2007, the new management team completed a rigorous analysis of the drug development pipeline and business operations and disclosed the key priorities of the corporate drug development and the partnering strategy.

In November 2007, we completed the sale of our Utah-based subsidiary, Echelon Biosciences Inc. (Echelon), to Frontier Scientific Inc. for $3.2 million, including $2.6 million upfront payable upon signing and $0.6 million in contingent consideration based on specific sales levels to be reached in 2008 and 2009.

In December 2007, we opened our operational headquarters in Warren, New Jersey where the majority of the executive management team resides.

Subsequent to year-end, we entered into an agreement, on March 1, 2008, for the sale of our intangible property held for sale Impavido® (miltefosine) for approximately $9.2 million, subject to customary closing conditions.

CETRORELIX

In March 2007, our Japanese partner Shionogi & Co. (Shionogi) presented encouraging Phase 2a trial (performed in Japan) results with cetrorelix in BPH. Results showed that cetrorelix, the Company s lead luteinizing hormone-releasing hormone (LHRH) antagonist, was safe and well tolerated at all dosage regimens. Furthermore, Japanese patients responded to cetrorelix with a transient reduction of testosterone concentration in blood, which did not reach or remain at castration level. Additionally, none of the dosage regimens tested caused a suppression of prostate specific antigen (PSA) levels. Finally, data generated with Japanese patients showed that the bioavailability of cetrorelix was similar

to that observed in non-Japanese patients. Following these results, our partner, Shionogi, initiated a 300-patient Phase 2b study with cetrorelix in BPH in Japanese patients. Shionogi is conducting and sponsoring this study.

In April 2007, we commenced dosing of cetrorelix in the first study of our sponsored Phase 3 program in BPH. This first study, a one-year placebo-controlled efficacy study, is assessing an intermittent dosage regimen of cetrorelix as a potential safe and tolerable treatment providing prolonged improvement in BPH-related signs and symptoms. This 600-patient Phase 3 study is being conducted in North America and Europe.

In May 2007, we regained exclusive worldwide rights (ex-Japan) for cetrorelix from Solvay for the endometriosis indication. The Company now owns worldwide ex-Japan rights for cetrorelix in BPH and endometriosis.

In the first quarter of 2008, we expect to initiate additional trials related to our Phase 3 program in BPH, including a second European efficacy trial as well as a long-term safety trial.

AEZS-108

In June 2007, we presented encouraging detailed Phase 1 results for AEZS-108, our cytotoxic conjugate (LHRH agonist linked to doxorubicin) in female patients with cancers expressing LHRH receptors.

The study conclusion was:

- AEZS-108 was well tolerated by patients with gynecological tumors;

- AEZS-108 is the first drug in a clinical study that targets the cytotoxic activity of doxorubicin specifically to LHRH-receptor expressing tumors;

- Signs of anti-tumor activity were observed in seven out of 13 patients treated with 160 or 267 mg/m(2) of AEZS-108, including three patients with complete or partial response; and

- Recommended dose for further clinical studies will be 267 mg/m(2) given once every three weeks.

At the end of December 2007, we commenced patient enrollment for our European open-label, non-comparative multi-center Phase 2 trial that will treat up to 82 women with LHRH-receptor positive ovarian and endometrial cancerous tumors.

AEZS-112

In January 2007, we announced the initiation of a Phase 1 trial for AEZS-112 in patients with solid tumors and lymphoma. This open-label, dose-escalation, multi-center, intermittent treatment Phase 1 trial is being conducted and sponsored by the Company in the United States. The trial will include up to 50 patients who have either failed standard therapy or for whom no alternative therapy exists. We expect progression of this trial in 2008 to identify maximum tolerated dose of AEZS-112.

OZARELIX

During 2007, our partner Spectrum Pharmaceuticals, Inc. (Spectrum) continued the development of ozarelix, a fourth generation LHRH antagonist, by conducting and sponsoring a North American Phase 2b trial in BPH. Spectrum is also conducting and sponsoring a program with ozarelix in prostate cancer. Additional results are expected in 2008.

PERIFOSINE

In November 2007, we completed patient recruitment for our Company-sponsored European multi-center Phase 2 trial with perifosine, an oral signal transduction inhibitor, combined with radiotherapy, in 160 patients with inoperable Stage III non-small cell lung cancer (NSCLC). We expect to announce results in the first quarter of 2009.

During 2007, our partner Keryx Biopharmaceuticals, Inc. (Keryx) continued the development of perifosine with multiple Phase 1 and Phase 2 studies in North America in multiple cancers. We expect Keryx to move perifosine into Phase 3 in at least one indication in North America in 2008.

Consolidated Results of Operations

On January 2, 2007, we completed the special distribution to all shareholders of our remaining position in Atrium. Since we disposed of our entire position in Atrium in January 2007, we had no access to liquidity or cash flows from Atrium in 2007 and we do not expect to access to cash flows from operations of Atrium in ensuing years. Since Atrium is renting space in our facility in Quebec City, we receive rent from Atrium and share administrative costs, which amount are not significant.

For the years ended December 31, 2006 and 2005, the previously consolidated revenues and expenses of Atrium, representing the former Active Ingredients & Specialty Chemicals Segment as well as the Health & Nutrition Segment, have been reclassified as discontinued operations.

On November 30, 2007, we disposed of our former subsidiary Echelon which was involved in the business of selling reagents. As a consequence, we have no access to liquidity or cash flows from Echelon since the end of November 2007 and we do not expect to access to cash flows from operations of Echelon in ensuing years, beyond possible contigent considerations payments based on Echelon s performance in 2008 and 2009.

For the years ended December 31, 2007, 2006 and 2005, the previously consolidated revenues and expenses of Echelon have been reclassified as discontinued operations.

The following table sets forth Canadian GAAP consolidated financial data in thousands of US dollars, except per share data.

	Years ended December 31,		
	2007	**2006**	**2005**
	$	**$**	**$**
Consolidated revenues			
Sales and royalties	**28,825**	25,123	21,252
License fees	**12,843**	13,652	23,530
Other	**400**	24	31
	42,068	38,799	44,813
Operating expenses			
Cost of sales, excluding depreciation and amortization	**12,930**	11,270	8,250
Selling, general and administrative (SG&A)	**20,403**	16,478	14,403
Research and development (R&D) costs	**39,248**	27,422	25,544
R&D tax credits and grants	**(2,060)**	(1,564)	(317)
Depreciation and amortization (D&A)	**5,566**	8,964	5,944
Impairment of long-lived asset held for sale	**735**		
	76,822	62,570	53,824
Loss from operations	**(34,754)**	(23,771)	(9,011)
Other revenues (expenses)			
Interest Income	**1,904**	1,441	1,235
Interest expense	**(85)**	(1,433)	(7,010)
Foreign exchange gain (loss)	**(1,035)**	319	(87)
Other	**(28)**	409	
	756	736	(5,862)
Share in the results of an affiliated company		1,575	
Loss before income taxes	**(33,998)**	(21,460)	(14,873)
Income tax recovery (expense)	**1,961**	29,037	(609)
Net earnings (loss) from continuing operations	**(32,037)**	7,577	(15,482)
Net earnings (loss) from discontinued operations	**(259)**	25,813	26,053
Net earnings (loss) for the year	**(32,296)**	33,390	10,571
Net earnings (loss) per share from continuing operations			
Basic	**(0.61)**	0.14	(0.34)
Diluted	**(0.61)**	0.14	(0.34)
Net earnings (loss) per share from discontinued operations			
Basic	**(0.00)**	0.50	0.57
Diluted	**(0.00)**	0.48	0.57
Net earnings (loss) per share			
Basic	**(0.61)**	0.64	0.23
Diluted	**(0.61)**	0.62	0.23

45

Consolidated Revenues

Consolidated revenues are derived from sales and royalties as well as license fees. Sales are derived from Cetrotide® (cetrorelix acetate solution for injection) marketed for reproductive health assistance for *in vitro* fertilization, Impavido® (miltefosine) marketed for the treatment of leishmaniasis and active pharmaceutical ingredients. Royalties are derived from Cetrotide® and paid by our partner Merck-Serono. Furthermore, license fees are derived from non-periodic milestone payments, R&D contract fees and amortization of upfront payments received from our different licensing partners.

Sales and royalties increased to $28.8 million for the year ended December 31, 2007 compared to $25.1 million and $21.3 million for the same periods in 2006 and 2005, respectively. The year-over-year increase in sales and royalties is related to new sales of Cetrotide®, following the September 2006 launch in Japan and year-over-year increased sales of Impavido®.

Subsequent to year-end, the Company entered into an agreement, on March 1, 2008, with respect to the sale of its intangible property held for sale Impavido® (miltefosine), for approximately $9.2 million. This transaction is subject to customary closing conditions, including the parties receiving certain third-party consents and approvals. In 2007, sales of Impavido® represented $3.3 million. As a result of the sale of the product, we expect a corresponding decrease in sales and royalties for 2008.

License fees revenues decreased to $12.8 million for the year ended December 31, 2007, compared to $13.7 million and $23.5 million for the same periods in 2006 and 2005, respectively. The year-over-year decrease is mainly attributable to a reduction in license fees revenues related to services rendered through our collaboration with Solvay Pharmaceuticals (Solvay). We regained from Solvay the worldwide ex-Japan rights for cetrorelix in BPH during 2006 and for endometriosis in 2007. License fees revenues are expected to slightly decrease in 2008.

Consolidated Operating Expenses

Consolidated cost of sales, excluding depreciation and amortization, increased to $12.9 million for the year ended December 31, 2007 compared to $11.3 million and $8.2 million for the same periods in 2006 and 2005, respectively. The year-over-year increase in the cost of sales is directly related to additional generated sales and royalties. The cost of sales as a percentage of sales and royalties was 44.86% in 2007 compared to 44.86% in 2006 and 38.82% in 2005. The lower percentage of cost of sales in 2005 compared to 2006 and 2007 is due to favorable product mix sold in 2005 since we sold more active ingredients with higher margins to our partners. The cost of sales as a percentage of sales and royalties is expected to increase to nearly 50% in 2008, assuming the sale of the Impavido® intangible assets and corresponding inventory during the first part of the year 2008.

Consolidated selling, general and administrative (SG&A) expenses increased to $20.4 million for the year ended December 31, 2007 compared to $16.5 million and $14.4 million for the same periods in 2006 and 2005 respectively. The increase in SG&A expenses for the year 2007 compared to 2006 is primarily due to non-recurring corporate expenses of nearly $2.7 million related to the appointment of David J. Mazzo, Ph.D., as the President and CEO of the Company, as well as Juergen Ernst as Chairman of the Board, the departure of the former CEO, Gilles Gagnon, as well as the departure of the founder and former Executive Chairman, Éric Dupont, Ph.D. The increase in SG&A is also related to the appointment of new key executive management, combined with the opening of operational headquarters in New Jersey and increased royalties and commissions expenses directly related to sales and royalties of Cetrotide®.

The increase in SG&A of 2006 compared to 2005 is in part related to $0.6 million of non-recurrent SG&A expenses with regard to a thorough review of the Company s strategic plan combined with nearly $0.3 million of increased royalties and commission expenses directly related to sales and royalties of Cetrotide® as well as increased support of our R&D efforts.

We expect that SG&A expenses for 2008 will remain consistent with 2007.

Consolidated R&D costs were $39.2 million for the year ended December 31, 2007 compared to $27.4 million and $25.5 million for the same periods in 2006 and 2005 respectively. Additional R&D expenses of $11.8 million spent in 2007 compared to 2006 are mainly related to the advancement of our lead product cetrorelix, our LHRH

antagonist in Phase 3 for BPH; as well as to further advancement of targeted, earlier-stage development programs including AEZS-108, our cytotoxic conjugate and AEZS-112, our tubulin inhibitor, both of which are in oncology.

The following table summarizes the 2007 R&D external costs supported by the Company.

(in thousands of US dollars)

			Year ended December 31, 2007	
Products	**Status**	**Indication**	**Net R&D costs (*)**	
			$	**%**
	Phase 3			
Cetrorelix	Phase 2	BPH and endometriosis	11,589	54.47
AEZS-108				