EXECUTIVE INFORMATIONAL OVERVIEW

Æterna Zentaris

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Late-Stage Biopharmaceutical Opportunity

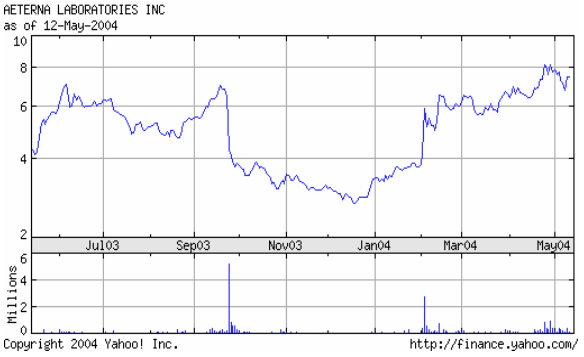
Snapshot

May 14, 2004

Æterna Laboratories Inc., along with its wholly owned subsidiary Zentaris GmbH (hereafter called Æterna Zentaris), is a biopharmaceutical company with an extensive product portfolio that includes two marketed products and a host of product candidates at the clinical and preclinical levels of development in oncology, endocrinology, and infectious diseases. Cetrotide® (cetrorelix) is sold in the U.S., Europe, and several additional countries for ***in vitro*** fertilization and has successfully completed Phase II **clinical trials** for **endometriosis**, **uterus myoma**, and **benign prostatic hyperplasia (BPH)**. Impavido® (miltefosine) is sold in India for **visceral leishmaniasis** (black fever) and has successfully completed a Phase III trial for **cutaneous leishmaniasis** (parasitic skin disease). In development, perifosine is the first orally active AKT inhibitor that is in Phase II trials for multiple **cancers**. Neovastat® is in a Phase III trial for **non-small cell lung cancer (NSCLC)**. Æterna Zentaris benefits from a discovery platform of 100,000 molecules, which is generating promising new compounds. Æterna Zentaris also maintains a 62% ownership of Atrium Biotechnologies Inc., a growing subsidiary that develops, distributes, and markets active ingredients, fine chemicals, cosmetic products, and nutritional products through an established multinational network.

Recent Financial Data

Ticker (Exchange)[1]	AELA (NASDAQ)
Recent Price (05/14/04)	$7.14
52-Week Range	$8.42-2.69
Shares Outstanding (mm)	45.4
Market Cap. (mm)	$324.2
Average 12-month vol.	209,727
Insider +5% Owners	34%
Institutional Owners	42%
EPS (as of 12/31/03)	($0.21)
Employees	220



[1] *All amounts are in Canadian dollars, except pricing data, which is in U.S. dollars.*

Key Points

- Æterna Zentaris benefits from two marketed pharmaceutical products, Cetrotide® and Impavido®, as well as an extensive pipeline of more than 15 compounds at different development stages in oncology, endocrinology, and infectious diseases.
- Among the more advanced stage candidates in the pipeline, perifosine is a novel AKT inhibitor in development for multiple types of cancers that target cell-cycle progression and **apoptosis**. Additionally, cetrorelix could also become a treatment for endometriosis, uterus myoma, and BPH.
- To facilitate development and/or commercialization of its pipeline, Æterna Zentaris has formed several partnerships, including a North American partnership with Keryx Biopharmaceuticals (KERX-NASDAQ) for perifosine and worldwide (except Japan) partnership with Solvay Pharmaceuticals for cetrorelix. These partners fund a significant portion of certain development projects underway.
- Atrium provides Æterna Zentaris with a revenue-generating subsidiary. In 2003, sales were $120.3 million, operating income was nearly $14 million, and net earnings were $7.1 million. Atrium's recent acquisition of Pure Encapsulations, a private U.S. company, affords the opportunity for U.S. expansion.
- Æterna Zentaris is a global biopharmaceutical company—from drug discovery through marketed products. It has managed its business plan to diversify financial and scientific risks and is now on the verge of becoming a major player in the oncology and endocrinology fields.
- The Company carries cash and short-term investments of nearly $52 million as of March 31, 2004. This position gives Æterna Zentaris the necessary capital to pursue its strategic objectives.

†**BOLD** WORDS ARE REFERENCED IN GLOSSARY ON PAGES 40-42.

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Executive Overview

Æterna Laboratories Inc., along with its wholly owned subsidiary Zentaris GmbH (hereafter called Æterna Zentaris), is a biopharmaceutical company with a product portfolio that includes two marketed products and a host of product candidates under development in oncology, endocrinology, and infectious diseases. On the market is Cetrotide® (cetrorelix), which is sold in the U.S., Europe, and several additional countries for *in vitro* fertilization and has successfully completed Phase II clinical trials for endometriosis, uterus myoma, and BPH. Additionally, Æterna Zentaris has an anti-infective product, Impavido® (miltefosine), which has been marketed in India since mid-June 2003 for visceral leishmaniasis (black fever) and has successfully completed a Phase III trial for cutaneous leishmaniasis (a parasitic skin disease). Furthermore, Æterna Zentaris benefits from a discovery platform of 100,000 molecules, which is generating promising new compounds.

Pipeline

Æterna Zentaris' product pipeline includes candidates under development within the areas of oncology, endocrinology, and infectious diseases. Its oncology pipeline features approximately a half-dozen clinical stage products, including perifosine for multiple cancers, Neovastat® (AE-941) for NSCLC, teverelix and D-63153 for prostate cancer, RC-3095 in small cell lung cancer (SCLC), and other candidates at the preclinical level. In endocrinology, the Company is developing in advanced stage cetrorelix for three additional indications—endometriosis, uterus myoma, and BPH—as well as several other preclinical products. In the infectious diseases category, Impavido® (miltefosine) has successfully completed a Phase III clinical trial for cutaneous leishmaniasis.

The majority of Æterna Zenteris' pipeline is being developed along with several strategic partners, which provide the bulk of the funding while leaving Æterna Zentaris' burn rate at a low level. Partners include Ardana Bioscience, Baxter Oncology, German Remedies Ltd., Hainan Chang An, Keryx Biopharmaceuticals, Nippon Kayaku, Produtos Roche QFSA, Serono International S.A., Shionogi & Co., Ltd. (SGIOF.PK), and Solvay Pharmaceuticals B.V. (SVYSY.PK).

Figure 1 (page 4) provides a snapshot of Æterna Zentaris' marketed products as well as its development efforts, including its respective partners—divided by oncology, endocrinology, and anti-infectives—accompanied by brief descriptions of key candidates. Extensive details on each candidate are provided throughout this Executive Informational Overview (EIO).

Oncology

- Perifosine, a phospholipid-like active substance possessing antitumoral activity, was developed as an oral AKT inhibitor. Based on therapeutic responses observed in Phase I clinical trials as well as in preclinical studies, a total of six tumor types have been identified as being of interest for evaluation in Phase II—cancers of the prostate, breast, pancreas, and head and neck, as well as soft tissue **sarcoma** and **melanoma**. In addition, a Phase I study to test perifosine in combination with radiotherapy has recently been completed and results will be presented at the American Society of Clinical Oncology (ASCO) in June of this year. Pending the results from these first trials in monotherapy and in combination with radiotherapy, the Company plans to elect the two most promising indications for priority development up to market authorization. In comparison to competitors' products, perifosine has shown no **hematotoxicity** or **neurotoxicity** thus far. Perifosine is partnered with Keryx Biopharmaceuticals in North America (Canada, U.S., and Mexico) and developed with the contribution of the U.S. National Cancer Institute (NCI) and the Netherland National Cancer Institute. Æterna Zentaris owns the ex-North American rights on perifosine and intends to continue to develop this product up to commercialization. Under the licensing agreement with Keryx, Æterna Zentaris has access (free of charge) to all data generated from the clinical program assumed by Keryx Biopharmaceuticals and is expected to benefit from milestone payments as well as scale-up royalties on future North American sales by Keryx.

Figure 1
Æterna Zentaris
PRODUCT AND PIPELINE SUMMARY

ONCOLOGY							
Products	Indications	Preclinical	Phase I	Phase II	Phase III	Marketed	Partner
Perifosine	Multiple cancers						Keryx (North America), US and Netherland NCI
D-63153	Prostate						Baxter (world)
Teverelix	Prostate						Ardana BioScience (world)
RC-3095	Multiple cancers						
Neovastat	NSC Lung						US NCI
Lobaplatin	Multiple cancers					Approved in China	Hainan Chang An (China)
AN-152 Cytotoxic Conjugate							
AN-215 Cytotoxic Conjugate							
AN-238 Cytotoxic Conjugate							
ZEN-012							
ZEN-014							
Disorazol E1							
LHRH peptidomimetics							

ENDOCRINOLOGY							
Products	Indications	Preclinical	Phase I	Phase II	Phase III	Marketed	Partner
Cetrotide	*In Vitro* Fertilization						Serono (world, except Japan), Shionogi/Nippon Kayaku (Japan)
	In Vitro Fertilization						
Cetrorelix	Uterus Myoma						Solvay (world, except Japan), Shionogi/Nippon Kayaku (Japan)
	BPH						
	Endometriosis						
EP-1572 GHS							Ardana Bioscience
LHRH peptidomimetics							Solvay
Ghrelin antagonist	obesity						

ANTI-INFECTIVE							
Products	Indications	Preclinical	Phase I	Phase II	Phase III	Marketed	Partner
Impavido® (Miltefosine)	Visceral Leishmaniasis (Black Fever)						WHO, Nimrall, German Remedies & action medeor, Roche
Impavido® (Miltefosine)	Cutaneous Leishmaniasis (Parasitic Skin Disease)						Roche

Source: Æterna Zentaris.

- D-63153, an **Luteinizing Hormone-Releasing Hormone (LHRH)** antagonist in development for prostate cancer, is the result of research activities for the identification and characterization of backup candidates for cetrorelix. The aim of development was an active substance, which has special physical-chemical properties and is better suited for long-term depot formulations required for therapy of tumors. D-63153 has completed a Phase Ib-study and has entered Phase II. The Company has a worldwide license agreement in place with Baxter Oncology for this compound. Baxter Oncology will undertake the full development of D-63153 until marketing and Æterna Zentaris is expected to benefit from milestones and royalties on future sales of D-63153.

- Teverelix, a LHRH antagonist, is undergoing a Phase I dose-ranging clinical trial for the treatment of prostate cancer, where administration of a LHRH antagonist has several advantages over the use of LHRH agonists. These advantages include immediate hormone withdrawal without a flare-up effect; avoidance of symptoms related to the flare-up effect; immediate reduction of **prostate specific antigen (PSA)**; immediate reduction in the size of the prostate; and continuous reduction of the **follicle stimulating hormone (FSH)** level. Ardana acquired full global rights and is assigned the intellectual property relating to teverelix and the underlying microcrystalline suspension technology. In return, Zentaris received a substantial payment at signature, and is expected to receive fixed annual guaranteed payments until 2006, as well as potential future royalties on sales of teverelix.

- RC-3095, a bombesin/gastrin-releasing peptide antagonist, is being developed for multiple types of cancers. Monotherapy Phase II has been initiated for prostate and SCLC.

- Neovastat® (AE-941) is an antiangiogenic drug designed to choke off new blood vessel development and halt the growth and proliferation of disease. Æterna Zentaris is pursuing a Phase III study sponsored by the U.S. NCI in NSCLC.

- Lobaplatin, which has already received marketing authorization in China, belongs to the therapeutic group of platinum-based drugs that have proven highly effective in treating many cancer indications. Lobaplatin is partnered with Hainan Chang An of China, where Hainan will manufacture and market Lobaplatin in China. Æterna Zentaris remains owners of rights to market Lobaplatin (ex China).

Endocrinology

- Cetrorelix, a LHRH antagonist that has shown to suppress the formation of certain hormones in the pituitary gland by blocking specific receptors, is a key component of Æterna Zentaris' endocrinology pipeline. Æterna Zentaris benefits from a long term agreement signed with Serono S.A., which triggers significant annual lump sum payments (greater than US$10 million) in addition to manufacturing income and royalties on sales of cetrotide. We note that cetrotide is already on the market for *in vitro* fertilization and is marketed under the name Cetrotide®. Due to its unique mode of action, some of the common side effects that are typically associated with the administration of LHRH agonists can be avoided. Cetrotide® is partnered with Serono S.A. on a worldwide basis for *in vitro* fertilization, except for Japan, where it is partnered with Shionogi & Co. and Nippon Kayaku.

  On April 29, 2004, the Company announced statistically significant positive results from a recently completed Phase II clinical program designed to evaluate cetrorelix in three different indications: endometriosis, pre-surgical treatment of uterine myoma, and BPH, which can benefit from a targeted and controlled decrease in sex hormones, including estrogen and testosterone. Æterna Zentaris' partner for development within this area is Solvay Pharmaceuticals B.V., which has the worldwide rights (except in Japan) for endometriosis, uterus myoma, and BPH. Solvay will undertake the full development of cetrorelix up through marketing. Æterna Zentaris is expected to benefit from potential milestones and royalties on worldwide future cetrorelix sales, except Japan. In addition, Shionogi & Co., Ltd. and Nippon Kayaku are the owners of the Japanese rights.

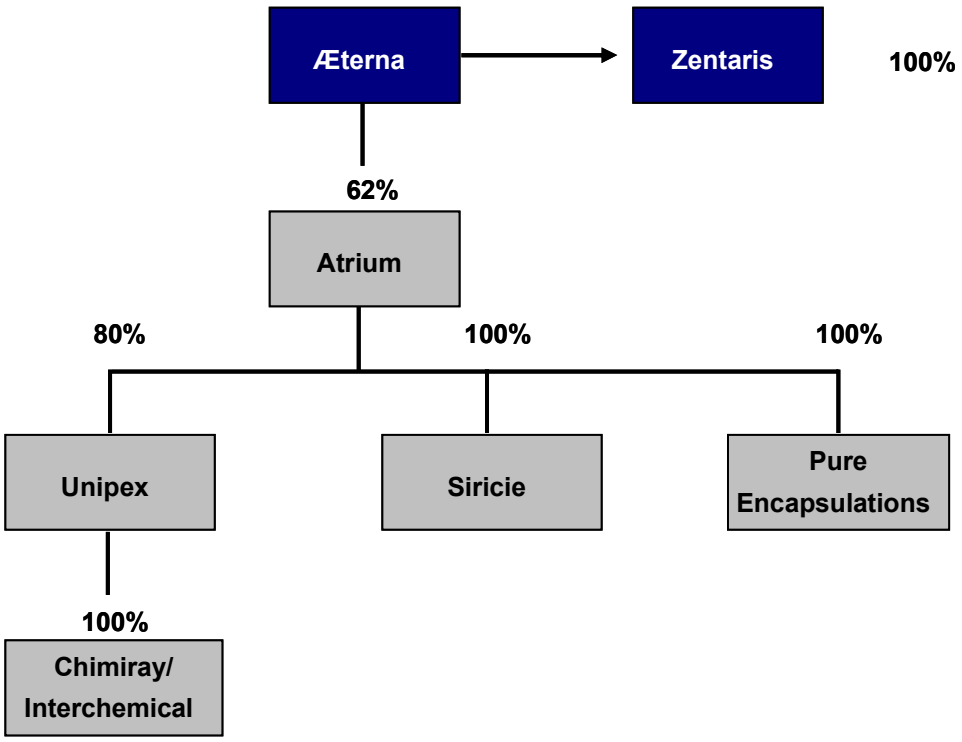
Anti-Infective

- Impavido® (miltefosine) has recently received approval in India for visceral leishmaniasis and Phase III trials in cutaneous leishmaniasis in South America have been completed. Miltefosine is partnered with German Remedies Ltd. for the private sector in India and Bangladesh. For non-governmental organizations, the drug is made available via action medeor, a German medical aid organization.

Atrium Biotechnologies

Æterna Zentaris holds a 62% ownership in Atrium Biotechnologies Inc., a growing subsidiary that develops, distributes, and markets active ingredients, fine chemicals, cosmetic products, and nutritional products through an established multinational network throughout 20 countries to industry leaders such as Estée Lauder, L'Oréal, Clarins, Chanel, Aventis S.A. (AVE-NYSE), Sanofi Synthelabo, and Nestlé. Æterna Zentaris also benefits from its other recently acquired divisions, which include Unipex, ADF Chimie, Chimiray/Interchemical, Sircie, and Pure Encapsulations. A snapshot of Æterna Zentaris' subsidiaries, including Atrium, and its respective ownership in each is provided in Figure 2.

Figure 2
Æterna Zentaris
OWNERSHIP OF SUBSIDIARIES



NOTE: Subsidiaries shaded in grey are not fully owned by Æterna Zentaris.

Source: Æterna Zentaris.

Headquarters, Manufacturing, and Employees

Æterna Zentaris is headquartered in Quebec City, Canada, and employs approximately 280 people throughout its facilities in Canada, the United States, Germany, and France. In the Quebec City region, Æterna Zentaris has a 75,000-square-foot facility that houses its corporate headquarters, its Atrium Biotechnologies subsidiary, a research laboratory, and a production center that meets Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP) standards. Zentaris' facility is located in Frankfurt, Germany in the pharmaceutical infrastructure of its former owner, Degussa AG. Atrium and its affiliates are based in Paris, France, the Boston area (Massachusetts), and Fairfield, New Jersey.

Growth Strategy

Following the acquisition of Zentaris at the end of 2002, Æterna Zentaris is a global biopharmaceutical company with marketed products from its initial oncology, endocrine therapy, and drug discovery units. The Company is focused on developing and bringing to market compounds that address diseases with poor survival rates and limited treatment alternatives. The Company is uniquely positioned since it has a profitable subsidiary in Atrium, in addition to is biopharmaceutical activities, which is focused on the sales and distribution of active ingredients, fine chemicals, cosmetic products, and nutritional products. Additionally, the Company has a number of large and significant partnerships with companies in the biopharmaceutical sector, which assist in funding the research activities and which hold the potential to generate revenues from a variety of areas. Details on these partnerships are provided on pages 26-27.

Intellectual Property

Æterna Zentaris believes that its patent portfolio significantly contributes to the value and the success of its business. Its strategic approach is to build a portfolio that provides broad protection of technology as well as a tiered patent claim structure to provide specific composition of matter, disease indication, and manufacturing process claims.

The Company's policy is to file patent applications in all major markets in the world. The patent portfolio of the Company and its subsidiaries comprises approximately 70 patent families. In addition, roughly 20 patent families are the result of co-operations with external researchers, including the Institute for Biophysical Chemistry of the Max Planck Institute for biophysical Chemistry in Göttingen, Germany for the product candidate Miltefosine, and the Tulane University in New Orleans, Louisiana, for cetrorelix, as well as for the product candidates in the area of bombesin antagonists, LHRH antagonists, and peptide conjugates with **cytotoxic** active groups.

Management, Board Members, and Scientific Advisory Board

Management

Table 1 provides a snapshot of Æterna Zentaris' key management, followed by detailed biographies.

Table 1
Æterna Zentaris
KEY MANAGEMENT

Name	Title	Officer Since
Éric Dupont, PhD	Chairman of the Board	1991
Gilles Gagnon	President, Chief Executive Officer, and Director	2000
Professor Jürgen Engel, PhD	Chief Operating Officer, Executive Vice President, Global Research and Development, Director	2003
Dennis Turpin, CA	Vice President and Chief Financial Officer	1996
Eckhard Gunther, PhD	Vice President, Drug Discovery	2003
Matthias Rischer, PhD	Vice President, Pharmaceutical Development	2003
Goswin Reuschenbach, PhD	Senior Director, Regulatory Affairs	

Source: Æterna Zentaris.

Éric Dupont, PhD, Chairman of the Board

Dr. Dupont founded the Company in 1991 while completing his PhD in physiology-endocrinology and a certificate in business administration at Laval University. Dr. Dupont also completed post-doctoral studies in neuroendocrinology at the Research Centre of the Notre Dame Hospital in Montreal, which is affiliated with the University of Montreal. From 1990 to 1993, he was the recipient of a fellowship from the Medical Research Council of Canada. He has also received numerous awards of excellence for his work.

Gilles Gagnon, President, Chief Executive Officer, and Director

Mr. Gagnon joined the Company in September 2000 as Vice President, Business Development, and became President and Chief Executive Officer (CEO) in January 2003. He spent more than 20 years in the pharmaceutical industry and held senior management positions at Sandoz and Novartis (NVS-NYSE). Mr. Gagnon holds graduate degrees in Pharmacology (M.Sc.) and administration (MBA) from Université de Sherbrooke and a certificate in General Management from the London Business School, U.K.

Jürgen Engel, PhD, Executive Vice President, Global Research and Development and Chief Operating Officer

Dr. Jürgen Engel has been CEO of Zentaris since the beginning of 2001. Before that, he was in charge of all research activities of ASTA Medica AG, after having held several executive positions within that company, including Director of Research Coordination and Director of the Medical Chemical Department. Over a period of 25 years, he has supervised more than 700 scientists and clinical professionals. Dr. Engel holds a doctorate in organic chemistry and was a professor at Regensburg University, where, during the past years, he has been a speaker and honorary professor. He is also honorary professor at the Dresden Technical University. In 1995, he received the Galenus-von-Pergamon prize for having developed alkylphospholipides as a new class of anti-tumor agents. Dr. Engel is the author of more than 200 scientific articles.

Dennis Turpin, CA, Vice President and Chief Financial Officer

Mr. Turpin joined the Company in August 1996 as Finance Director before being appointed Vice President and Chief Financial Officer (CFO) in June 1999. Prior to joining Æterna Zentaris, he spent ten years with Coopers & Lybrand (now PricewaterhouseCoopers) as a Principal for its Tax Department. Chartered Accountant since 1987, Mr. Turpin graduated from Laval University in 1985.

Eckhard G. Günther, PhD, Vice President, Drug Discovery

Dr. Günther joined the Company in December 2002 when Æterna acquired Zentaris. He was Head of Drug Discovery at Zentaris since January 2001. Prior to that, he assumed management positions at ASTA Medica AG. Dr. Günther has more than 15 years of experience in the biotechnology and biopharmaceutical industries. A few years ago, he was instrumental in the discovery of a new class of substances offering a new approach to the inhibition of tubulin in oncology. He is also at the root of a number of patent applications and publications. Dr. Günther earned a Doctorate in Synthetic Organic Chemistry at the University of Halle-Wittenberg in Germany.

Matthias Rischer, PhD, Vice President, Pharmaceutical Development

Dr. Rischer joined the Company in December 2002 when Æterna acquired Zentaris. He was Head of Pharmaceutical Development at Zentaris since January 2001. Prior to that, Dr. Rischer was a top executive at ASTA Medica AG. He has more than ten years of experience in the biotechnology and biopharmaceutical industries, and holds a Doctorate degree in Chemistry from George-August-University in Göttingen, Germany. He is also the author of several publications in the field of chemistry.

Goswin Reuschenbach, PhD, Senior Director, Regulatory Affairs

Head of Drug Regulatory Affairs at Zentaris GmbH since January 2001, Dr. Reuschenbach has developed an expertise in worldwide registration of new drugs with international regulatory agencies and in launching new products through licensing agreements with pharmaceutical companies. Dr. Reuschenbach holds a Doctorate degree in Synthetic Inorganic Chemistry from the University of Cologne and had supervised numerous clinical studies before specializing in regulatory affairs for the past ten years. At Fisons Arzneimittel GmbH in Germany, he held the position of Scientific Manager of their medical department and then became the company's Head of Regulatory Affairs, Drug Safety and Documentation before being appointed Group Head oncological and endocrinological products in the Department of Regulatory Affairs at ASTA Medica, in Frankfurt.

Board of Directors

Æterna Zentaris' Board of Directors consists of nine directors, six of whom are independent of management. The Board oversees the conduct and supervises the management and affairs. The Board meets regularly to consider particular issues or conduct specific reviews whenever deemed appropriate. Before the start of each financial year, the Board approves Æterna Zentaris' annual budget and strategic objectives. Table 2 provides a snapshot of key Board members, followed by detailed biographies.

Table 2
Æterna Zentaris
BOARD OF DIRECTORS

Name	Title	Director Since
Éric Dupont, PhD	Chairman of the Board	1991
Gilles Gagnon	President, Chief Executive Officer, and Director	2002
Professor Jürgen Engel, PhD	Chief Operating Officer, Executive Vice President, Global Research and Development, Director	2003
Marcel Aubut, Esq	Director	1996
Francis Bellido, PhD	Director	2002
Stormy Byorum	Director	2001
Henri A. Roy	Director	2003
Pierre Laurin, PhD	Director	1998
Pierre MacDonald	Director	2000

Source: Æterna Zentaris.

Éric Dupont, PhD, Chairman of the Board

(Detailed biography on page 8)

Gilles Gagnon, President, Chief Executive Officer, and Director

(Detailed biography on page 8)

Professor Jürgen Engel, PhD, Director

(Detailed biography on page 8)

Marcel Aubut, Esq., Director

Mr. Aubut is Managing Partner of the law firm, Heenan Blaikie Aubut. He obtained both his law degree (LL.B., 1970) and his Master of Law degree from Université Laval.

Francis Bellido, PhD, Director

Dr. Bellido is President and Chief Executive Officer of Biomundis Biotechnology Investment Fund. Prior to that, he was President and Chief Operating Officer of SGF Santé Inc., an industrial and financial holding company. He obtained his PhD in Medical Microbiology from the University of Geneva in 1988 and his Federal Masters degree in Pharmaceutical Sciences, also from the University of Geneva in 1984.

Stormy Byorum, Director

Ms. Byorum co-founded in 1996 and is a Managing Partner of Violy, Byorum & Partners, a strategic advisory and investment banking firm focused on Latin America. She received her BBA from Southern Methodist University and her MBA from the Wharton School at the University of Pennsylvania.

Henri A. Roy, Director

Mr. Roy is Chairman and President and General Manager of SGF Quebec. He has held executive positions in many key industrial sectors such as telecommunications, food, natural resources (mines, metals, energy and forest products), as well as in the pharmaceutical and venture capital industries, both in North America and overseas. He obtain his MBA from Harvard Business School, 1976, and a Bachelor of Mechanical Engineering, from McGill University, 1970

Pierre Laurin, PhD, Director

Dr. Laurin is Executive in Residence at HEC Montréal (Business School University of Montreal) since January 1999. He holds a Doctorate in Business Administration (DBA) from Harvard University, a "Licence ès Sciences Commerciales" from HEC Montréal and a "Baccalauréat ès Arts" from the Séminaire de Philosophie of Montreal.

Pierre MacDonald, Director

Mr. MacDonald is President and Chief Executive Officer of MacD Consult Inc., a consulting firm in finance and international marketing.

Scientific Advisory Board

Æterna Zentaris' Scientific Advisory Board is listed in Table 3.

Table 3
Æterna Zentaris
SCIENTIFIC ADVISORY BOARD

Name	Title
Gerald Batist, MD, CM, FACP	Director of the McGill Center for Translational Research in Cancer and Professor, Department of Oncology and Medicine, McGill University Jewish General Hospital, Montreal, Canada
Richard Beliveau, PhD	Director of the Molecular Oncology Laboratory of the Cancer Research Centre, Sainte-Justine, Montreal, Canada
W.K. (Bill) Evans, MD, FRCPC	Executive Vice President, Clinical Programs, Cancer Care, Ontario, Toronto, Canada
Fernand Labrie, OC, OQ, MD, PhD	Head, Centre hospitalier de l'Universite Laval, (CHUL) Research Center, Quebec Canada
Hartmut Michel, MD	Director of Max-Planck Institute for Biophysics in Frankfurt, Germany and 1988 Nobel Prize laureate in chemistry
Professor Klaus H.R. Diedrich	Director of the Department of Gynecology and Obstetrics and the University Clinic in Luebeck, Germany
Professor René Frydman	Head, Department of Gynecology and Obstetrics, Hospital Antoine Berciere, Clamart (Paris), France

Source: Æterna Zentaris.

Core Story

Æterna Zentaris is focused on developing and bringing to market products within three therapeutic areas:

- oncology;
- endocrinology; and
- anti-infective.

This Executive Informational Overview (EIO) is designed to provide more details on each of these areas and explain how they relate to Æterna Zentaris' research efforts. Pages 12-18 detail the Company's oncology efforts; pages 19-23 detail the Company's endocrinology efforts; and pages 24-25 detail the Company's anti-infective efforts.

Oncology

Æterna Zentaris has a significant presence in oncology. Figure 3 provides a snapshot of the current oncology pipeline. More details are found in subsequent sections.

Figure 3
Æterna Zentaris
PRODUCT AND PIPELINE SUMMARY

ONCOLOGY							
Products	Indications	Preclinical	Phase I	Phase II	Phase III	Marketed	Partner
Perifosine	Multiple cancers						Keryx (North America), US and Netherland NCI
D-63153	Prostate						Baxter (world)
Teverelix	Prostate						Ardana BioScience (world)
RC-3095	Multiple cancers						
Neovastat	NSC Lung						US NCI
Lobaplatin	Multiple cancers					Approved in China	Hainan Chang An (China)
AN-152 Cytotoxic Conjugate							
AN-215 Cytotoxic Conjugate							
AN-238 Cytotoxic Conjugate							
ZEN-012							
ZEN-014							
Disorazol E1							
LHRH peptidomimetics							

Source: Æterna Zentaris.

Perifosine

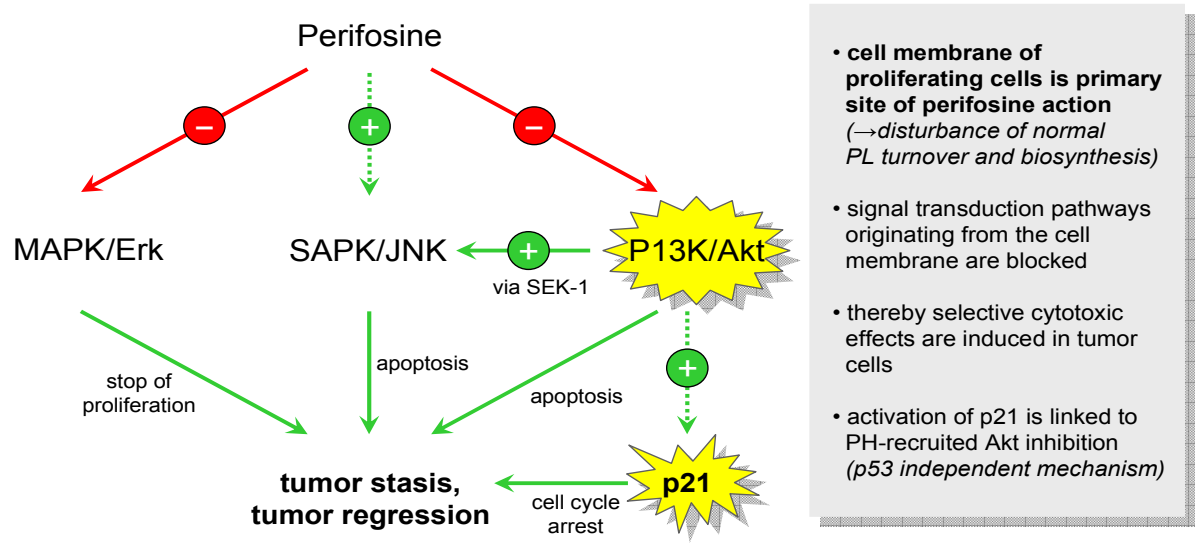
Perifosine (an analogue of Miltefosine, page 24) belongs to the class of anti-tumor agents called alkylphosphocholines (ALKs). This oral AKT inhibitor is being developed to treat multiple cancers. Perifosine has a molecular structure similar to phospholipids, which play a crucial role in the structure and function of cell membranes. Additionally, the compound has been shown to inhibit crucial membrane processes, such as the transmission of growth signals. Æterna Zentaris believes that this approach could enable the division of cancer cells to be stopped. Unlike comparable preparations, perifosine is taken orally, is well tolerated, and has shown fewer side effects, particularly in the gastrointestinal tract.

Following its recent acquisition of Access Oncology, Keryx Biopharmaceuticals obtained North American rights for perifosine and intends to sponsor additional single-agent and combination studies with the drug candidate. However, Æterna Zentaris retains rights for the rest of the world. Zentaris' research and development team had synthesized perifosine in 1997 and licensed North American development and commercialization rights to Access Oncology in September 2002 for US$18 million in upfront and milestone payments, plus a scale up royalty on North American sales.

Mechanism of Action

Perifosine is an alkyl-lysophospholipid (ALP) compound similar in structure to the phospholipids of biological membranes. The drug targets AKT/Protein Kinase B (PKB) serine/threonine protein kinase activity by localizing to the inner plasma membrane of cells where it blocks AKT/PKB activation by phosphatidylinositol 3-kinase (PI3K). Activation of PI3K by growth factors and cytokines normally leads to a cascade of pro-cancer events medicated throughout AKT/PKB. This includes inhibition of apoptosis through the phosphorylation of Bad and members of the caspase family, and promotion of cell growth through phosphorylation of tumor suppressor protein p21, and activation of Raf. As a targeted inhibitor of AKT/PKB, perifosine has shown potent anti-tumor activity in preclinical cancer cell line and animal tumor models. Figure 4 provides a snapshot of the proposed model of anti-tumor response activity of perifosine.

Figure 4
Æterna Zentaris
PROPOSED MODEL OF ANTI-TUMOR ACTIVITY OF PERIFOSINE



Source: Æterna Zentaris.

Development Program

Perifosine's development program is focused on nine NCI sponsored Phase II trials examining the drug as a single agent across six cancer types—prostate (2 trials), sarcomas (2 trials), breast, pancreatic (2 trials), melanoma, and head and neck. Each of these ongoing trials and are expected to be completed later this year and released in early to mid 2005. Eight of the nine studies are multi-centered, all are open label, and all are non-controlled. Eight of nine involve a loading plus maintenance schedule, however exact dosing is not available at this time. Æterna Zentaris expects to enroll up to 412 patients in all trials and efficacy is expected to be measured as a primary endpoint in seven of the trials (2 survival, 4 response, and 1 progression). A snapshot of the Phase II clinical program for perifosine is provided in Table 4, page 14.

Additionally, a European Phase I trial of perifosine as a combination therapy with **radiation therapy** has recently been completed and results will be presented at ASCO in June of this year. The results of this Phase I trial evaluating perifosine in combination with radiotherapy in patients with unresectable locally advanced tumors will be presented at the upcoming American Society of Clinical Oncology (ASCO) Annual Meeting, June 5 through 8, 2004. The Phase I results to be presented at ASCO will form the basis for a Phase II trial evaluating perifosine in combination with radiotherapy in patients selected for specific tumor types. Æterna Zentaris plans to evaluate perifosine in combination with radiotherapy as a treatment for multiple types of cancer through the ongoing collaboration with the Netherlands Cancer Institute of Amsterdam.

Table 4
Ætena Zentaris
PERIFOSINE PHASE II CLINICAL PROGRAM

	NCI Clinical Trials Groups	NCI Princess Margaret (Toronto)	NCI Princess Margaret (Toronto)	NCI California Cancer Consortium	NCI Eastern Cooperative Oncology Group	NCI Center for Cancer Research	NCI University of Chicago	NCI Mayo Clinical Cancer Center	NCI Center for Cancer Research
Clinical Stage	**Phase II**	**Phase II**	**Phase II**	**Phase II**	**Phase II**	**Phase II**	**Phase II**	**Phase II**	**Phase II**
Centers	5 in Canada	3 in Canada	4 in Canada	4 in U.S.	3 in U.S.	1 in U.S.	12 in U.S.	7 in U.S.	2 in U.S.
Patients									
Number	15-30	17-37	18-35	21-41	35-84	22-46	22-48	17-46	<45
Cancer Type	Metastatic or locally advanced soft tissue sarcoma	Advanced adenocarcinoma of the pancreas	Recurrent or refractory, locally advanced or metastatic breast cancer	Biochemically recurrent, hormone-sensitive prostate cancer	Locally advanced, unresectable or mestatic pancreatic cancer	Metastatic androgen-independent prostate cancer	Recurrent or metastatic squamous cell head and neck cancer	Advanced soft tissue sarcoma	Refractory solid tumors, HL and NHL, CLL and myelodysplastic syndromes
Performance Status	ECOG 0-2	ECOG 0-2 or Karnofsky 60-100%	ECOG 0-2 or Karnofsky 60-100%	Karnofsky 60-100%	ECOG 0-1	ECOG 0-2 or Karnofsky 60-100%	ECOG 0-2 or Karnofsky 60-100%	ECOG 0-1	ECOG 0-2
Prior Therapy	Radiation and adjuvant chemotherapy allowed; no prior systemic chemotherapy	Radiation allowed previously; no more than one prior chemotherapy regimen	Surgery, radiation, hormone and 2 lines of prior chemotherpay regimens allowed	Prior hormone, vaccine, brachytherapy, radiotherapy and surgery allowed; no prior chemotherapy	Radiation and surgery allowed; no prior chemotherapy directed at pancreatic cancer	Continuing LHRH agonist therapy; surgery radiation and one prior chemotherapy regimen allowed	Prior radiation allowed; no more than one biological therapy; no more than one adjuvant or other chemotherapy	Prior biologic; chemotherapy and radiotherapy allowed; no more than two chemotherapy regiments	Radiotherapy and chemotherapy allowed
	At least one measurable site of disease; exclusind bone and some other sarcomas	Not amenable to curative local therapy	At least one measurable lesion; no brain metastates	Rising PSA following a nadir after local curative therapy; no evidence of metastases		Metastatic, androgen-independent; no brain metastases	Metastatic or recurrent disease, unsuitable for radiotherapy or surgery, no brain metastases	Progression since prior radiation; no uncontrooled brain metastases	No standard therapeutic options; requires systemic therapy
Tumor Description									
Administration									
Route	Oral	Oral	Oral	Oral	Oral	Oral	Oral	Oral	Oral
Schedule	Intermittent; loading on D1 plus daily maintenance D2-21, then 7D break; 28D cycle	Daily for three weeks, one week rest; monthly cycle	Intermittent; loading on D1-2 plus maintenance D3-21, then 7D break; 28D cycle	Loading on D1 plus maintenance D2-28; 28D cycle	Loading on D1 plus continuous dialy maintenance dose	Intermittent; for cycle 1, loading on D1, maintenance, D3-21, 7D break; no loading for subsequent cycles	Loading on D1-2 plus maintenance D3-28; 28D cycle	Loading on D1 plus continuous daily maintenance dose	Intermittent; loading on D1 followed by maintenance BID or TID on D2-21, 7D break; dose escalate to MTD

Source: Ætena Zentaris and National Cancer Institutes PDQ Clinical Trials Database.

D-63153

D-63153, a microcrystalline suspension formulation with sustained release properties, is being developed for prostate cancer and is the result of research activities for identification and characterization of backup candidates for currently marketed cetrorelix (pages 20-22). With D-63153, an active substance possessing special physico-chemical properties—better suited for long-term depot formulations—was targeted. In August 2002, a license agreement for D-63153 was signed with Baxter Oncology. Based on the Phase I dose-ranging clinical trial results, the dosing schedule for Phase II is expected to be determined using Æterna Zentaris' proprietary technology. D-63153 has successfully completed a Phase Ib study proving long-lasting suppression of testosterone to levels after castration. The compound has entered Phase II for prostate cancer. The current U.S. market for prostate cancer treatments is approximately $1.5 billion.

Teverelix

Teverelix, a LHRH antagonist with favorable physico-chemical characteristics, is undergoing a Phase I dose-ranging clinical trial for the treatment of prostate cancer. Æterna Zentaris recently announced that it's wholly owned subsidiary Zentaris and Ardana Bioscience had signed a new agreement for the compound. Ardana acquired full global rights and is assigned the intellectual property relating to teverelix and the underlying microcrystalline suspension technology. In return, Zentaris receives a substantial payment at signature, fixed annual guaranteed payments until 2006, as well as potential future income on sales of teverelix. As part of the agreement, Æterna Zentaris is to provide certain development services and supply clinical samples to Ardana Bioscience.

Teverelix works by suppressing the formation of the male sex hormone, testosterone, by blocking the receptors of the pituitary gland. Specifically, the drug docks on LHRH receptors and eventually blocks the release of testosterone. Sufficiently high doses of Teverelix cause the testosterone level to drop post-castration levels. The response of prostate **carcinoma** to a hormone reduction of this kind is to stop growing or recede.

In prostate cancer, administration of a LHRH antagonist has several advantages over the use of LHRH agonists:

- immediate hormone withdrawal without a flare-up effect;
- avoidance of symptoms related to the flare-up effect;
- immediate reduction of PSA;
- immediate reduction of the size of the prostate; and
- continuous reduction of the FSH level.

Teverelix was co-developed by Æterna Zentaris and its former subsidiary, Europeptides. The compound has shown low histamine release but similar potency compared to second-generation LHRH antagonsists. Ardana Bioscience is developing a sustained release formulation for prostate cancer, which is currently in a Phase I program in healthy male volunteers and is nearing conclusion. Additionally, formulations for BPH, endometriosis, and infertility are being developed.

RC-3095

RC-3095 is a hormone-like peptide that is being developed for multiple types of cancers. As a gastrin-releasing peptide inhibitor, the compound has proven **angiogenesis** inhibition ***in vivo*** and down regulation of HER-2 receptor. Phase I has been completed, though this compound is not yet partnered. The Phase I trial tested the subcutaneous injection of dosages ranging from 8 μg/kg daily to 96 μg/kg twice daily in patients with various solid tumors. Up to the highest dose level tested, RC-3095 was tolerated without clinically relevant side effects aside from a slight reaction at the injection site. Additionally, systemic tolerability of RC-3095 was shown to be very good.

Although tumor response was not a primary endpoint in Phase I, patients with different tumor types showed clinical response to treatment at dosages ranging between 32 μg/kg once daily and 96 μg/kg twice daily. At the highest dosage, a patient with **Zollinger-Ellison Syndrome** demonstrated a 50% drop in his pathologic gastrin levels within six hours after dosing. In addition, a patient with hormone-refractory prostate cancer with rapidly rising PSA showed a drop in serum PSA as a biochemical indicator of tumor response. Finally, a patient with a thyroid cancer who was treated at the low dosage of 32 μg/kg once daily showed a transient decrease in the size of a cervical lymph node and qualified for a minor remission. Based on these Phase I data, Phase II studies are currently exploring the activity of RC-3095 in prostate cancer and SCLC.

Neovastat® (AE-941)

Neovastat® is an **angiogenesis inhibitor** that is unique from other antiangiogenesis therapies since it possesses multiple mechanisms of action on antiangiogenic activity. Æterna Zentaris reports that Neovastat® (1) inhibits MMPs (enzymes that breakdown surrounding tissue); (2) blocks receptor sites for the angiogenic molecule **vascular endothelial growth factor (VEGF)**, thus preventing **endothelial cells** from responding to the angiogenic activator; (3) induces apoptosis in endothelial cells; (4) stimulates tissue-type plasminogen activator (tPA) enzymatic activity; and (5) prevents endothelial cells from proliferating and forming new blood vessels**—**called **tubulogenesis**.

The multiple biological activities of Neovastat® distinguish it from other angiogenesis inhibitors due to its potential to interfere with different stages of the angiogenic process, such as selectively inhibiting MMPs 2, 9, and 12, and blocking the action of VEGF to its receptor. In numerous preclinical and clinical studies, Neovastat® has shown an excellent safety profile with few side effects among more than 800 patients with various diseases over four years.

Æterna Zentaris is collaborating with the NCI to develop Neovastat® for NSCLC, which is currently in Phase III with results expected in 2007.

The American Cancer Society estimates that lung cancer is responsible for 28% of all U.S. cancer deaths—an estimated 157,200 deaths per year. In Canada, 12,000 new cases are expected to be diagnosed this year, accounting for 17% of all new cancer cases and responsible for 10,700 deaths.

Lobaplatin

Lobaplatin has demonstrated activity in a wide range of preclinical tumor models, appearing to overcome tumor resistance to **cisplatin** and **carboplatin** in some models. The compound remains largely intact until removed by glomerular filtration. Exposure of the body to lobaplatin correlates with dose, creatinine clearance, and the degree of **thrombocytopoenia**. An impaired renal function results in an increase of the plasma half-life time and results in a higher exposure of the body to the drug. As a result, a formula was developed that allows a doctor to calculate the dose that is expected to lead to an acceptable extent of thrombocytopenia in a patient with a given renal function. Depending on the variable excretory function of the kidney, the dosage would be adjusted to ensure the target level of drug exposure, which could lead to a more predictable reduction of thrombocyte count. Phase I clinical trials of different administration schedules found the same dose-limiting toxicity (thrombocytopoenia) and similar maximum tolerated doses (60 mg/m^2 per three-four weeks).

In Phase I studies, lobaplatin demonstrated activity in ovarian cancer patients pretreated with platinum. A Phase II trial with lobaplatin was performed in patients with refractory or relapsed ovarian cancer to define activity and pharmacokinetics. Twenty-two patients were treated with lobaplatin administered as an intravenous bolus every four weeks, with dosage of Lobaplatin being adapted according to pre-existing impairment of renal function. Toxicity was confined to mild nausea and vomiting, and mild leucocytopenia (WHO grade 3 in 18% of the courses).

While lobaplatin induced no renal toxicity, thrombocytopenia (WHO grade 3/4 in 53% of the courses) varied with severity of pre-existing renal impairment. Five of 21 evaluable patients (24%) achieved a response (four complete remissions and one partial remission). Remissions occurred mainly in patients who relapsed more than six months after primary treatment. The median survival from start of lobaplatin

treatment was eight months. Broad Phase II evaluation in Chinese clinical trials showed safety and efficacy of lobaplatin in different indications, leading to marketing authorization for the treatment of breast cancer, lung cancer, and chronic myelogenous leukemia.

PRECLINICAL EFFORTS

Peptide Drug Conjugates: AN Series

Æterna Zentaris is investigating several hormonal receptor-binding peptide conjugates for the treatment of a variety of malignant indications. Preclinical data have yielded favorable results, with the conjugates demonstrating significant *in vivo* reduction of tumor volumes following a single injection and reduced toxicity. The following candidates are currently under investigation with potential to move at least one candidate into clinical testing this year while continuing clinical investigation of the remaining conjugates.

AN-152. LHRH-doxorubicin conjugate for prostate, breast, endometrial, and ovarian cancers.

AN-215. Bombesin-2-pyrrolino-DOX conjugate for brain, gastric, prostate, and SC lung cancers.

AN-238. Somatostatin-2-pyrrolino-DOX conjugate for prostate, NSCLC, ovarian, pancreatic, and other cancers.

Tubulin Inhibitors: ZEN-012 and ZEN-014

Tubulin is a protein found in all cells, which 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 death of the affected cell. The anti-tumor agents Taxol and Vincristine, which are widely and successfully used in therapy, are based on this principle. Both compounds are expensive natural substances that cause severe side effects when used in humans. A tubulin inhibiting drug can be used, for example, for the treatment of breast cancer and ovarian carcinomas. The Company is developing two product candidates in preclinical trials which we describe below.

ZEN-012. ZEN-012 has shown potent *in vitro* antiproliferative activity against a panel of more than 35 established human tumor cell lines including multidrug resistant phenotypes. Additionally, it has shown a markedly differential sensitivity profile in a panel of 14 human tumor xenografts in this clonogenic assay. The compound is not cross-resistant to cisplatin, vincristine, and doxorubicine resistant cell lines. With these values of activity, ZEN-012 is comparable to vindesine and could be significantly superior to paclitaxel. ZEN-012 inhibits the polymerization of map rich bb-tubulin. The cancer cells subsequently undergo apoptosis after treatment with low concentrations of ZEN-012. During *in vivo* activity, ZEN-012 proved to be a potent inhibitor of *in vivo* tumor growth in different xenograft models including mammary and renal cancers after i.p. and p.o. treatment. Based on the determination of cytotoxic activity, Æterna Zentaris has also identified ZEN-012 as a highly cytotoxic compound with cell cycle specific mode of action.

ZEN-014. ZEN-014 is a novel pyrazole derivative that was discovered by Zentaris. It represents a new class of small molecule tubulin binders with antiangiogenic properties, which are assumed to be novel highly potent anticancer drugs. ZEN-014 exhibits promising *in vivo* activity in a **renal cell carcinoma (RCC)** model at a dose of 50 mg/kg after oral application. Based on these *in vitro* and *in vivo* activities, ZEN-014 is a promising new candidate for further preclinical development. ZEN-014 combines antiproliferative activity at nanomolar concentrations with strong inhibition of angiogenesis. These preclinical results were recently presented at the American Association for Cancer Research (AACR) meeting in Orlando, Florida.

Disorazol E1

Disorazoles are aromatic polyketides first isolated in 1994 from the bacterium, Sorangium cellulosum. Although the mechanism of action is still being elucidated, it remains one of the most cytotoxic compounds with activity at picomolar concentrations. Zentaris is expected to evaluate the use of Disorazol E1 as a single agent, however, due to its potency, it may be better utilized in the context of a peptide or antibody conjugate.

Endocrinology

LHRH antagonists act by blocking the release of LHRH, a pituitary hormone that triggers the production of estrogen in women and testosterone in men. These hormones, which have been connected to the spread of prostate, breast, ovarian, and endometrial malignancies, have surfaced as an immediate target for several therapeutic drugs. Initially, LHRH antagonists lacked the needed potency to represent a viable therapeutic. However, as newer generations of LHRH antagonists have been developed, they have begun to overcome these obstacles, achieving stronger efficacy and gaining broader application.

The current generation of LHRH antagonists has demonstrated a faster mode of action and broader safety profile than several of its counterparts. Additionally, the LHRH antagonists have demonstrated the ability to reach beyond the treatment of malignant disorders and address a variety of benign disorders, such as endometriosis and uterine myoma.

While LHRH antagonists continue to gain acceptance, they are only approved for infertility and as an injectable treatment for prostate cancer. However, scientists are exploring additional ways to deploy LHRH antagonists for further indications and investigating methods to boost their bioavailability and ease of administration. A significant portion of Æterna Zentaris' product portfolio is dedicated to the discovery and application of LHRH antagonists for the treatment of a variety of diseases. A snapshot of the Company's endocrinology pipeline is provided in Figure 5, followed by descriptions of each compound.

Figure 5
Æterna Zentaris
PRODUCT AND PIPELINE SUMMARY

ENDOCRINOLOGY							
Products	Indications	Preclinical	Phase I	Phase II	Phase III	Marketed	Partner
Cetrotide	*In Vitro* Fertilization						Serono (world, except Japan), Shionogi/Nippon Kayaku (Japan)
	In Vitro Fertilization						
Cetrorelix	Uterus Myoma						Solvay (world, except Japan), Shionogi/Nippon Kayaku (Japan)
	BPH						
	Endometriosis						
EP-1572 GHS							Ardana Bioscience
LHRH peptidomimetics							Solvay
Ghrelin antagonist	obesity						

Source: Æterna Zentaris.

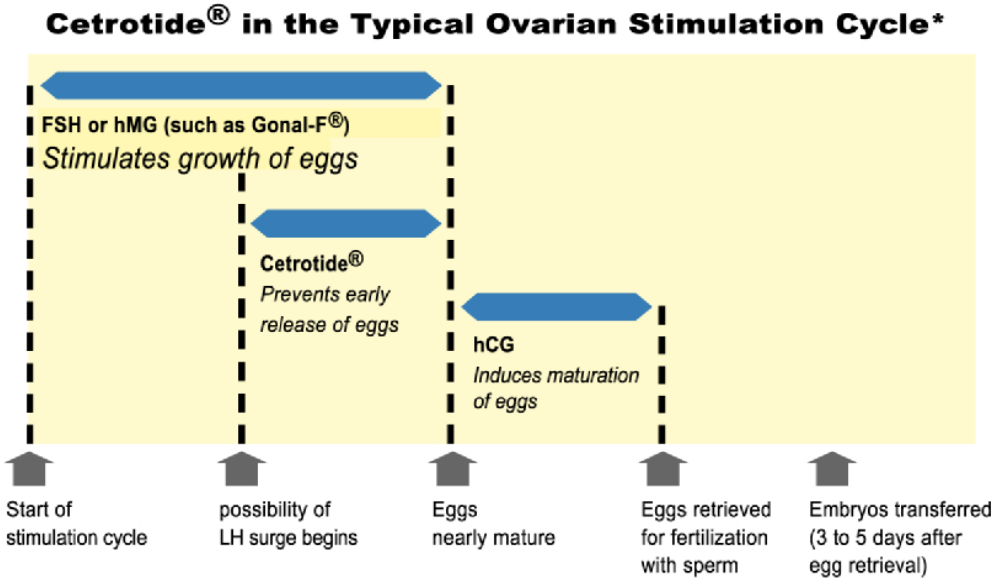
Cetrotide® (cetrorelix)

Serono S.A. of Switzerland, markets Cetrotide® in the U.S. and Europe and other countries (except Japan) to prevent premature ovulation in controlled ovarian stimulation prior to **assisted reproductive technologies (ARTs)**. Marketing rights for Japan are held by Shionogi & Co. and Nippon Kayaku. Cetrotide®, a new LHRH antagonist, is the only LHRH antagonist offering a choice of two highly effective dosage strengths that enable precise control. Thus, treatment with Cetrotide® can be accomplished during one monthly cycle. Additionally, due to its immediate onset of action, Cetrotide® permits a simplified, more convenient, and shorter treatment regiment involving fewer injections than with competitive LHRH antagonists.

As an injectable LHRH antagonist that controls hormonal responses in the body that impact the development of eggs in the ovaries, the drug works by delaying a hormonal event, known as the "LH Surge," which can result in premature ovulation. The LH Surge is a natural hormonal response that signals the release of mature eggs from the ovaries. If an LH Surge occurs too early in a cycle, eggs are released before expected. This greatly reduces the opportunity to retrieve the eggs for later use in ART procedures. The LH Surge is caused by a series of changes involving two hormones—gonadotropin-releasing hormone (GnRH) and **luteinizing hormone (LH)**. Figure 6 (page 20) illustrates how Cetrotide® fits into the typical ovarian stimulation cycle. Cetrotide® is available in two dosing regimens—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).

Figure 6

CETROTIDE® IN THE TYPICAL OVARIAN STIMULATION CYCLE



Source: Æterna Zentaris.

Clinical Trial Results

The effectiveness of Cetrotide® has been examined in five clinical trials (two Phase II and three Phase III trials). Two dose regimens were investigated in these trials, either a single dose per treatment cycle or multiple dosing. In the Phase II studies, a single dose of 3 mg was established as an 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 has been established as the minimal effective dose. The extent and duration of LH suppression was found to be dose dependent. In the Phase III 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 II and Phase III trials, 184 pregnancies were reported out of a total of 732 patients (including 21 pregnancies following the replacement of frozen-thawed embryos). No drug related allergic reactions were reported from these clinical studies.

Cetrorelix

Cetrorelix, a LHRH antagonist that has shown to suppress the formation of certain hormones in the pituitary gland by blocking specific receptors, is a key component of Æterna Zentaris' endocrinology pipeline. The drug also has proven effective in treating a number of diseases in which reducing the production of sex hormones is expected to create improvements.

On April 29, 2004, the Company announced statistically significant positive results from a recently completed Phase II clinical program designed to evaluate cetrorelix in three different indications: endometriosis, pre-surgical treatment of uterine myoma, and BPH, which can benefit from a targeted and controlled decrease in sex hormones, including estrogen and testosterone. The positive results of six Phase II trials, which also demonstrated good tolerability in all indications, will form the basis for further development of cetrorelix in different indications through collaboration with Solvay Pharmaceuticals, the Company's worldwide (except Japan) exclusive development and marketing partner for cetrorelix for the above indications. Each of these indications is described below.

Uterus Myoma

A uterus myoma, or a fibroid, is a benign tumor of the uterine muscles that penetrates the uterine wall. Depending upon the length and the direction, the condition is either referred to as a **subserious 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.

Patients with uterus myoma suffer from menstrual pain along with increased and often extended menstrual bleeding, which in certain cases can cause **anemia**. As soon as 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 neuralogic pain in the legs. During pregnancy, myoma can cause abnormal positions of the embryo, premature labor and pain, or possibly miscarriage. Additionally, in approximately a half of one percent of cases, the myoma can develop into a malignant tumor (sarcoma).

While the causes of uterus myoma are unknown, estrogen does have a very strong stimulating influence on the growth of the tumors in spite of the fact that a quarter of all women affected have no complaints. Post menopause, the myoma typically recedes on its own. An estimated 15% of all women between 14 and 45 will suffer a uterus myoma. Exact details concerning spending for this indication are difficult since drugs used to treat uterus myoma are also used for other indications. The Company estimates that the total market size in both the U.S. and Europe is approximately $290 million.

Cetrorelix in Treating Uterus Myoma

While invasive curative measures, such asmyomectomy, endometrial resection, myolysis, or hysterectomy currently exist, LHRH agonists have demonstrated the ability to reduce fibroid volume and vaginal bleeding. As the first LHRH antagonist in advanced clinical development, cetrorelix allows the hormone level to be specifically controlled such that the effect is rapid, avoiding the menopausal problems associated with an otherwise complete and long-term withdrawal of the hormone seen with LHRH agonists. Fast effectiveness could also be used in intermittent therapy. The growth of uterus myoma depends on the level of estrogen. Reducing the estrogen level using cetrorelix has produced rapid shrinkage of the myoma and fewer complaints.

Benign Prostatic Hyperplasia (BPH)

BPH is a hormonal enlargement of the male prostate gland. The prostate is located directly at the vesical outlet in the male surrounding the first part of the urethra. The enlargement squeezes the urethra, causing problems when urinating. BPH is classified into three stages according to symptoms. The first phase, or the irritant phase, is where the patient suffers **dysuria** (pain when urinating) and **nocturia** (the urge to urinate during the night). The second phase occurs when there is residual urine in the bladder, increasing problems during urination. Overflow of the bladder is typical for the third phase of the illness. This can result in the formation of bladder damage, congestion of urine, engorged kidneys, and life-threatening kidney damage. Enlargement of the male prostate is controlled by testosterone. Normally testosterone is responsible for proper functioning of the prostate. With increasing age, however, testosterone can cause benign cell growth.

Cetrorelix in Treating BPH

Cetrorelix has been shown to suppress the formation of the male sex hormone testosterone, which plays a principal role in cell growth of the prostate. Since cell growth is stopped, surgical removal of the prostate can be avoided. According to Decision Resources (a Massachusetts-based company that provides in-depth research on the trends, emerging developments, and market potential of the drug industry), BPH presently affects approximately 51 million men above the age of 40. In the age group over 60, BPH is found in half of all men.

The first proof of concept trial testing cetrorelix was published in 1994. The uncontrolled trial, which tested 11 patients, yielded a 44% decrease in prostate volume after only four weeks of treatment. Patients also experienced several improved functions, such as urinary frequency. Additionally, Lepor et al (Proscar and Fomax lead investigator) published an abstract describing a randomized, placebo-controlled study, where cetrorelix was shown to improve International Prostate Symptom Score (I-PSS) and urinary incontinence within four weeks. Finally, an uncontrolled study by Comaru-Schally et al further solidified these findings in a 144-patient proof of concept trial confirming cetrorelix's safety and efficacy.

Endometriosis

Endometriosis is a chronic disease in which endometrial tissue is found in locations outside of the endometrial (uterine) cavity, most often in neighboring and/or more distant organs where the tissue is subject to the same hormonal fluctuations as the menstrual cycle. Endometriosis centers form cysts and growths that respond sensitively to the ovarian hormones during menstruation with bleeding and inflammation. Pain of varying intensity occurs and further complications can include irregular and often severe monthly bleeding; bladder, and intestinal cramps; increased susceptibility to infection; allergies and general feelings of malaise and exhaustion.

While the causes of endometriosis are not yet known, if left untreated, possible consequences could include damage to organs and infertility. According to the U.S. Endometriosis Association, between 10-20% of all women of child-bearing age in the U.S. are affected by this disease. Of this population, approximately 30-40% of these patients are no longer or at least only partially fertile. The figures for other Western industrialized countries are similar. The Company estimates that the U.S. market potential for current treatments that target endometriosis is approximately $2.5 billion.

Cetrorelix in Treating Endometriosis

The growth of the endometrium tissue is dependent upon the level of the female sex hormone estrogen. Reducing the estrogen level using cetrorelix produces a rapid regression of endometriosis and associated complaints. Cetrorelix allows targeted control of the hormone level to give fast effects, while avoiding the problems of menopause and potential risks associated with an otherwise complete and long-term withdrawal of hormones. The fast effectiveness can also be used for intermittent therapies.

Results of a 2002 Phase II study investigating cetrorelix for endometriosis concluded that patients experienced a reduction in the Retrospective American Fertility Society Score (rAFS) and remained symptom free throughout the eight-week treatment regimen. The study demonstrated that weekly subcutaneous administration of cetrorelix effectively controls the symptoms endometriosis and yields fewer side effects than LHRH agonists.

EP-1572

Æterna Zentaris is developing EP-1572, a human growth secretagogue, which is responsible for the stimulation of human growth hormone (GH). In preclinical evaluation, this oral hormone therapy has demonstrated significant oral bioavailability and may prove beneficial for treating indications such as GH-deficiency, wasting diseases, **diabetes**, **osteoporosis**, and aging. Ardana Bioscience, which has partnered with Æterna Zentaris for the development of Teverelix (page 15), is planning a Phase I study in healthy volunteers with the eventual goal of targeting the growth hormone deficiency market. EP-1572 has already demonstrated a marked increase of GH production in rats, an observation that was replicated in two human volunteers in a 2001 proof-of-concept study.

PRECLINICAL EFFORTS

LHRH Peptidomimetics

The LHRH receptor plays an important role in the number of benign and malignant tumors. Cetrorelix, which was developed by Æterna Zentaris, is a peptide that blocks the receptor and can therefore be used for cancer therapy. Drug discovery searches for small non-peptide molecules, which cause the same effect on the receptor. Their advantage lies in the potential for oral administration and producing them in a cost-efficient manner. A drug based on these substances would be especially useful for the treatment of BPH, breast cancer, and prostate carcinoma. The development of new orally bioavailable LHRH antagonists for hormonal therapy has yielded several promising compounds. The project has advanced to a stage where the *in vivo* activity has been confirmed for two compounds.

In January 2004, an agreement with Solvay Pharmaceuticals was put in place. Based on the agreement, Solvay and Æterna Zentaris intend to jointly push ahead this research project aimed at developing novel, low molecular weight and orally-bioavailable peptidomimetic LHRH antagonists. Potential indications include endometriosis, uterus myoma, BPH, as well as malignant disorders such as breast and prostate cancer. As part of the agreement, Solvay Pharmaceuticals secures itself exclusive worldwide rights to all gynecological indications as well as to BPH, while Æterna Zentaris retains exclusive rights to all other indications, including oncology.

Ghrelin Receptor Antagonists

In collaboration with university laboratories in France, Germany, and Italy, Æterna Zentaris has recently added to its portfolio a ghrelin receptor antagonist compound that could be a promising agent for the management of obesity. Ghrelin is a natural peptide hormone produced by the stomach that increases appetite and induces accumulation of fat tissue. The recent discovery of ghrelin and its receptors opens up new opportunities for the treatment of obesity and eating disorders through the use of ghrelin receptor antagonists to suppress appetite.

Æterna Zentaris has recently signed two agreements for the development of ghrelin antagonists with the Laboratory of Aminoacids, Peptides, and Proteins of the University of Montpellier, France, directed by Professor Jean Martinez, and with the Department of Experimental and Environmental Medicine of the University of Milan, Italy, directed by Professor Vittorio Locatelli. Research projects are targeting the chemical synthesis and pharmacological investigation of new compounds acting as ghrelin receptor antagonists.

The design, synthesis, and *in vitro* screening of new chemical entities with ghrelin receptor antagonist properties is expected to be undertaken by Professor Martinez's group in Montpellier, building upon the significant experience of this laboratory in the preparation of analogues of peptide molecules. This is expected to be followed by a pharmacological investigation of the most promising compounds by Professor Locatelli's group in Milan, who has developed experimental models for the study of eating behavior.

It is estimated that 34 million to 61 million Americans are obese, with the worldwide incidence increasing by approximately 1% per year. The global market for obesity treatments is expected to reach $1.4 billion by 2008, with annual growth of 12.5%.

Anti-Infective

Miltefosine (Impavido®)

Visceral Leishmaniasis

Miltefosine (Impavido®) has recently received approval for marketing in India and Bangladesh for visceral leishmaniasis (a disease also known as Kalar-Azar or black fever). Visceral leishmaniasis, or internal leishmaniasis (a more hazardous form), is a parasitic infectious disease transmitted by the sandfly. It occurs when a parasite enters a person's immune system via the blood stream, multiplies, and again via the blood stream, attacks primarily the spleen, liver, lymph nodes, and bone marrow. Symptoms of this disease include fevers lasting many weeks, swelling of the spleen and liver, deficiencies of the blood forming system, bleeding of mucous membranes, and severe weight loss. If untreated, this disease can result in death between six months and two years after infection.

The World Health Organization (WHO) estimates that 12 million individuals are currently infected by leishmaniasis in 88 countries, including Africa, Asia, Europe, and North and South Americas. Infection with the parasite is possible any place where sandfly populations are found, particularly in rural areas. In Europe, leishmaniasis is principally found in the Mediterranean zone, including Portugal, Spain, France, Italy, and Greece. Following the massive depletion of sandfly populations in the 1950s due to insecticide use, the leishmaniasis pathogen is now multiplying again.

Impavido® is the first oral drug approved against visceral leishmaniasis and has been proven to be highly effective and less toxic than current therapies (*New England Journal of Medicine*, 2002 Vol.347, No.22, p.1739). Today, antimonial therapies tend to fail increasingly because of resistance. Additionally, since the injectable therapies available require the hospitalization of patients due to severe side effects, an oral drug is able to engender overall cost efficiencies. A Phase IV clinical trial has commenced and is sponsored by the Indian Council of Medical Research (ICMR). Æterna Zentaris expects that the product could soon be widely available in India through the public health system.

The WHO estimates that approximately 315,000 patients develop visceral leishmaniasis in India each year. Compared with resistance of approximately 80% to the standard antimony therapy, the Impavido® rate of cure is approximately 95%. Impavido® has comparatively few side effects (occasional vomiting and diarrhea) and is suitable for children.

Cutaneous Leishmaniasis

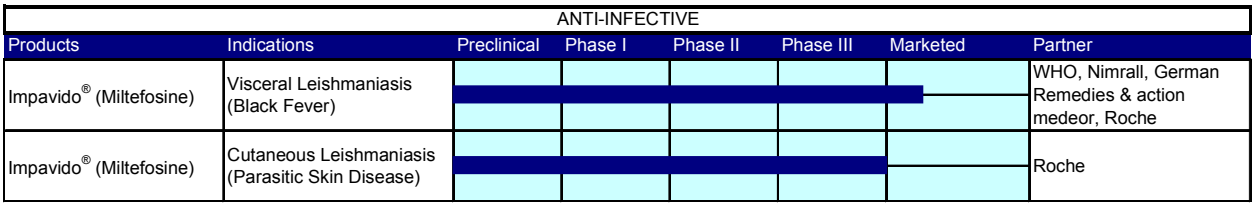
While Impavido® is approved in India for visceral leishmaniasis, it is also in development for cutaneous leishmaniasis, a skin disease mainly found on the head, neck, and arms. Its symptoms are either in the form of dry lumps or seeping cutaneous sores. The initially lumpy skin lesions open by themselves after weeks or months. After the lesions appear, spontaneous, if somewhat delayed healing can occur, leaving scars.

Phase III Clinical Results

In July 2003, Æterna Zentaris announced positive Phase III results for Impavido®, demonstrating patients taking the drug had a 220% better cure rate compared with those in the placebo group. The average cure rate after treatment with Impavido® was 70%. The double-blind, placebo-controlled study tested 133 patients in Columbia and Guatemala suffering from cutaneous Leishmaniasis. Of these patients, 89 were treated with Impavido® at a dosage of 150 mg/day for four weeks, while 44 received placebo. Cure from the disease was assessed six months after the end of treatment. All skin lesions had to be healed at that time and no new skin lesions were allowed to appear. Importantly, patients with newly diagnosed cutaneous leishmaniasis responded to treatment equally well as patients who were not cured by prior therapy. The new treatment was well tolerated. Side effects of Impavido® were limited to short episodes of vomiting or diarrhea, similar to earlier findings in patients with visceral Leishmaniasis.

These favorable results enable Æterna Zentaris to immediately apply for a marketing authorization in South American countries where the cutaneous form of the disease is predominant. We provide a snapshot of Æterna Zentaris' anti-infective timeline for Impavido® in Figure 7.

Figure 7
Æterna Zentaris
PRODUCT AND PIPELINE SUMMARY



Source: Æterna Zentaris.

Distribution and Marketing Agreements

At the end of February 2003, Æterna Zentaris announced that it had signed an exclusive distribution and marketing agreement with German Remedies Limited for the marketing of Impavido® in India and Bangladesh. German Remedies Limited, a member of the Zydus Cadila Group, is a public company since 1973 and is one of the leading Indian pharmaceutical companies with 1,700 employees. It manufactures pharmaceutical specialties in various therapeutic groups with major emphasis in the fields of female healthcare, gastroenterology, respiratory care, oncology, and diagnostics.

Zentaris has state-of-the-art manufacturing plants and adheres to International Standards of Good Manufacturing Practices (GMP) and Quality Management. Zydus Cadila is the fourth largest pharmaceutical group in India. The contract allows for German Remedies to market the product in the private sectors of India. In addition, German Remedies will distribute the product in Bangladesh upon registration.

Additionally, February 2004, Æterna Zentaris entered into a partnership with Produtos Roche QFSA of Sao Paulo for the marketing of Impavido® in Brazil. Under the agreement, Roche will support the registration process and will market the product in Brazil, while Zentaris will supply Impavido® to Roche. This represents the registration of the first oral treatment for leishmaniasis in Brazil, the South American country most afflicted by the disease. Estimates state that every year, up to 50,000 Brazilians are newly infected; 10% of them with the deadly visceral form.

Alliances/Partnerships

In an effort to maximize the development efforts of its therapies, Æterna Zentaris has formed worldwide partnerships to ensure the successful codevelopment and marketing of its products. The Company receives the bulk of the funding for certain development projects underway, while leaving its burn rate to a low level. Partners include Ardana Bioscience, Baxter Oncology, German Remedies Ltd., Hainan Chang An, Keryx Biopharmaceuticals, Nippon Kayaku, Produtos Roche QFSA, Serono International S.A., Shionogi & Co., Ltd., and Solvay Pharmaceuticals B.V. A snapshot of the Company's partners is provided in Figure 8, followed by descriptions of each as it relates to a specific product.

Figure 8
Æterna Zentaris
PARTNERSHIPS

Source: Æterna Zentaris.

Cetrotide® and cetrorelix

Æterna Zentaris and Serono have an agreement in place for worldwide marketing rights, except in Japan, for Cetrotide®. The agreement provides for Æterna Zentaris to receive a signature fee, as well as fixed annual payments until 2010 followed by royalties starting in 2011. In addition, Æterna Zentaris supplies Serono with the finished product at a fixed price. In turn, Serono is granted perpetual fully paid-up license upon expiry of the last relevant patent held by Zentaris.

In Japan, a semi-exclusive license and distribution agreement is in place with Shionogi & Co. Ltd., Japan, granting Shionogi & Co., Ltd. the ability to develop and commercialize Cetrotide® for *in vitro* fertilization/controlled ovarian stimulation/assisted reproductive technology (IVF/COS/ART). Additionally, a joint development agreement with Shionogi & Co., Ltd., Japan is in place, where under the agreement, Shionogi & Co., Ltd. receives a semi-exclusive license in Japan for the development of cetrorelix as an **antineoplastic agent** for human use and, if agreed, for other indications.

EP-1572

Ardana Bioscience is planning a Phase I trial of EP-1572 in healthy volunteers with the eventual goal of targeting the growth hormone deficiency market. EP-1572 has already demonstrated a marked increase of GH production in rats, an observation that was replicated in two human volunteers in a 2001 proof-of-concept study.

LHRH Peptidomimetics

Solvay and Æterna Zentaris have an exclusive collaboration agreement in which the two companies intend to jointly push ahead Æterna Zentaris' research project aimed at developing novel, low molecular weight, and orally-bioavailable peptidomimetic LHRH antagonists for potential indications such as endometriosis, uterus myoma, BPH, as well as malignant disorders, such as breast and prostate cancer.

Perifosine

On February 6, 2004, Keryx Biopharmaceuticals, Inc. announced that it had completed the acquisition of Access Oncology, Inc., a privately held cancer-focused biotechnology company. Perifosine was partnered with Access Oncology in North America and was developed with the contribution of the U.S. NCI.

D-63153

In 2002, Æterna Zentaris granted an exclusive worldwide license to Baxter Healthcare S.A. of Switzerland to develop, manufacture, and commercialize D-63153 for all oncological indications. In addition, Baxter Healthcare S.A. received an exclusive option, until December 31, 2002, to acquire an exclusive unrestricted license from Æterna Zentaris to use D-63153 for all non-oncological indications. The option was exercised by Baxter Healthcare S.A. on December 13, 2002.

Teverelix

On April 2, 2004, Æterna Zentaris announced the signature of a new agreement with Ardana Bioscience for the compound teverelix. Ardana acquired full global rights and is assigned the intellectual property relating to teverelix and the underlying microcrystalline suspension technology. In return, Æterna Zentaris receives a payment at signature, fixed annual guaranteed payments until 2006, as well as potential future income on sales of teverelix. As part of the agreement, Æterna Zentaris is to provide certain development services and supply clinical samples to Ardana Bioscience. Teverelix' Phase I clinical trial evaluating a sustained release formulation for use in prostate cancer is nearing conclusion.

Neovastat®

Æterna Zentaris benefits from strategic alliances in place for the distribution and commercialization of Neovastat® in southern Europe, France, Belgium, and Central and South Americas markets with Grupo Ferrer Internacional, S.A., one of the largest Spanish pharmaceutical companies based in Barcelona. In addition, Mayne Pharma is also having a distribution and marketing agreement covering Australia, New Zealand, Canada, and Mexico. Finally, the company signed an agreement with LG Life Sciences Ltd., an affiliate of the LG Group, to market Neovastat® in South Korea. LG Life Sciences develops, manufactures, and sells proprietary prescription drugs on a global basis in pharmaceuticals, pharmaceutical intermediates, animal health, and agrochemical sectors.

Atrium Biotechnologies Inc.

In addition to Æterna Zentaris' biopharmaceutical business, which is detailed in the preceding sections, the Company holds a 62% ownership in a cosmetics and nutritional business. This division, called Atrium Biotechnologies Inc., was originally a division within Æterna Laboratories, where from 1991 to 1999, Æterna Zentaris developed a limited number of products mainly to generate cash flow to finance its pharmaceutical research. Some of these products were successfully marketed to the cosmetic and nutraceutical industries, leading Æterna to officially establish Atrium as a separate subsidiary in December 1999. Atrium and its subsidiaries currently market more than 500 active products to a network of more than 1,000 industrial clients, including industry leaders such as Estée Lauder, L'Oréal, Clarins, Chanel, Aventis, Sanofi Synthelabo, and Nestlé.

Prior to creating Atrium, Æterna carefully studied the market dynamics in the cosmetic and nutraceutical sectors in order to establish a long-term strategy focused on becoming a world leader in the development and marketing of innovative products and raw materials in the health and personal care industry. Largely inspired by the major pharmaceutical companies' business models, Atrium recognized the need to rapidly and efficiently fill the product pipeline through acquisition and in-licensing of innovative technologies. The Company also believed a critical success factor would be to take control of specialized distribution structures in order to rapidly reach critical mass and secure access to markets for both its in-house products and those that it would in-license from research-based companies.

The need to control distribution led Atrium to purchase Unipex Finance S.A. and ADF Chimie S.A. in July 2001 and April 2002, respectively, as the first steps toward the development of an international network of channel partners. Unipex was acquired because of its credibility and efficiency with operating costs below 10% of sales compared to competitors' performance (up to 30% in some cases). ADF was selected because of its solid product portfolio, innovative products, and strong gross margins. With such a diversified portfolio, combining its proprietary products and those of respected third parties, Atrium has a competitive advantage compared to other raw material suppliers. As such, Atrium is now focused on expanding this network into the U.S. and other strategic European countries.

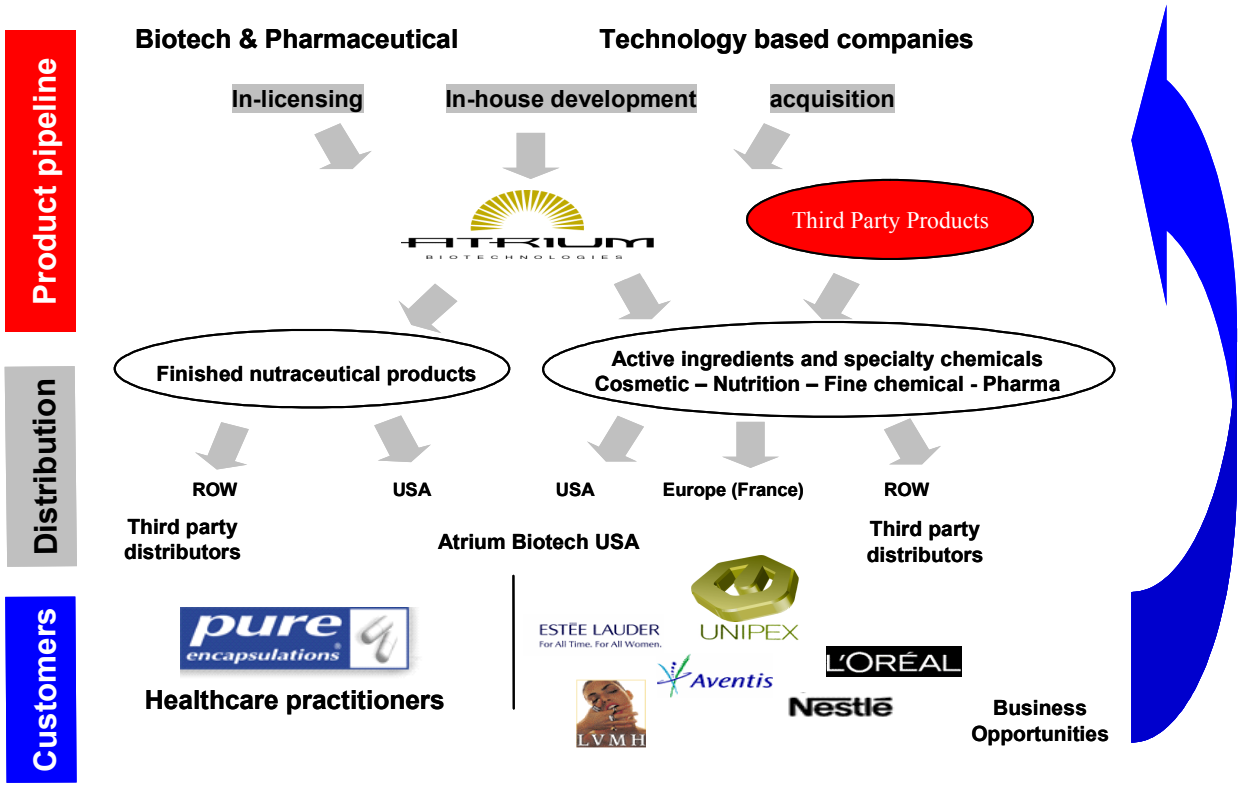
To rapidly expand its proprietary product portfolio, Atrium acquired nutraceutical product lines in September 2000 and April 2002, and hired qualified personnel to form a highly effective in-licensing team in 2002. The Company has stated that its in-licensing team expects to review over 2,000 technologies this year and has already achieved successful in-licensing of two technologies from Fytokem Products Inc. and Eukarion Inc. Eukarion, a U.S.-based biotechnology company, was recognized for the novelty and future of its research on aging by *Science, Nature*, and the British Broadcasting Corporation (BBC). Atrium has exclusive commercial rights for the cosmetic sector.

The proprietary active ingredients marketed worldwide by Atrium are mostly derived from biotechnologies and present exclusive characteristics proven by *in vitro*, or more frequently, in clinical trials, to provide the expected activity and perceived benefit (a visible outcome) for the customer. These active ingredients are mainly sold to the cosmetic industry, but some are sold in the nutraceutical field. Some of these products are the result of Atrium's own internal research. Others have been obtained through in-licensing agreements with emerging and established biotechnology companies that have partnered with Atrium to focus and complete their development, as well as to gain rapid access to a network of major clients, thereby generating short-term benefits. Atrium's cosmetic ingredients and raw materials are sold directly through its subsidiary Unipex in France, or through its network of distributors.

Atrium also has a core competency in the nutraceuticals sector with its own line of finished proprietary products and commenced building a dedicated sales force in Canada and the U.S. at the end of 2002. Currently, the Company's sales force is focused on the smaller, yet more profitable, professional market (i.e. healthcare professionals and practitioners), rather than the retail market as they believe that the retail market is in the midst of change with low growth rates and intense competition resulting in low profit margins.

Over time, Atrium has gained credibility and size, which it believes are necessary to penetrate the retail market in a meaningful way. With its proven development record and its direct sales force (coupled with more than 20 distributors globally), Atrium can control product introduction timelines. This allows the Company the opportunity to benefit when a newly developed or in-licensed product finds applications outside of its sector—most notably in the cosmetic industry. We provide a snapshot of Atrium's business model in Figure 9.

Figure 9
Atrium Biotechnologies Inc.
BUSINESS MODEL



Source: Atrium Biotechnologies Inc.

Atrium has 74 full-time salaried employees: 26 employees located at the head office in Quebec City, Canada, 6 in the U.S., and 42 in Paris, France. Atrium received several awards in 2002, including being recognized as one of the 50 best-managed companies in Canada by the Financial Post.

Products

As a group, Atrium (including Unipex and other subsidiaries) currently markets over 1,000 active ingredients, specialty chemicals, and proprietary products to a network of 2,000 industrial clients in 20 countries. The active ingredients and specialty chemicals from third parties are covered under commercial agreements and represent 90% of Atrium's products. The remaining 10% are comprised of Atrium's proprietary products, which are primarily geared toward the cosmetic and nutraceutical industries.

Third-Party Products

The majority of Atrium's third-party products are offered through Unipex. Unipex offers a broad line of specialty and active ingredients to the cosmetic, nutrition, pharmaceutical, and fine chemical sectors, including Atrium's proprietary products, as well as those of other industry leaders selected for the quality of their products. This enables its customers to call upon the Company as a single source of specialty

chemicals and innovative active ingredients. Unipex represents more than 80 companies in Europe and sells more than 500 products in various categories, including amino acids, additives, excipients, surfactants, specialty lipids, active ingredients, and Active Pharmaceutical Ingredients (API) for the generic market. Unipex's approach is well perceived by customers as they have a guaranteed access to a wide range of products without developing a strategic dependency with one single manufacturer.

Sales and Marketing

Atrium has a broad distribution network and is continuing to develop its sales organization to distribute its products throughout the world. As an innovation-driven company, Atrium has deemed it important to develop solid relationships with industry leaders through strategic collaborations, such as the one established with Estée Lauder. In addition to its long-lasting collaboration with Estée Lauder, Atrium now has privileged relationships with decision makers of various corporations such as Chanel, Dior, L'Oréal, and Kanebo, to name a few. A snapshot of Atrium's marketing network is provided in Figure 10.

Figure 10
Atrium Biotechnologies Inc.
MARKETING NETWORK

Source: Atrium Biotechnologies Inc.

Recent Developments

Atrium is developing a direct sales force within the U.S. and Canada to better understand and manage its market. This enhances its existing international distribution network of approximately 30 distributors. In addition, the division is focused on in-licensing innovative products or technologies. In particular, Atrium has created and participates in OcéaNova, a marine biomass research initiative in which Atrium has a first right of refusal on all technologies. Also, Atrium has potential access to 100,000 molecules through Zentaris.

In 2003, the Company acquired the commercial rights to another line of products through a license agreement with Fytokem Inc. These products totaled approximately $700,000 in sales in 2002. Moreover, an exclusive technology was licensed from the Massachusetts-based biotechnology company, Eukarion Inc. The Company believes that this technology could provide exceptional products for the anti-aging and sun care market segments.

On March 3, 2004, Atrium completed the acquisition of Pure Encapsulations Inc. for approximately $50 million in cash. Based in the Boston area, Pure Encapsulations is a privately-held company focused mainly on the development, manufacturing, and marketing of nutritional supplements for physicians and other healthcare professionals. With sales exceeding $25 million in 2003, Pure Encapsulations is among the leaders in this growing specialized sector, which generates annual sales of over $1 billion in the United States. This acquisition is intended to support Atrium Biotechnologies in establishing a critical mass and in substantially increasing its sales in the United States. Furthermore, it is intended to greatly contribute in attaining Æterna Zentaris' global growth objectives and support its goal to be cash flow positive in 2004 while working toward profitability.

Key Points to Consider

- *Æterna Zentaris' value continues to be driven by its extensive pipeline with two already marketed products*—Cetrotide®, which is marketed in the U.S. and Europe and other countries (except Japan) for *in vitro* fertilization, and Impavido® for visceral leishmaniasis, which is marketed in India for black fever.

- *Partnered with Keryx Biopharmaceuticals in North America, Æterna Zentaris is developing perifosine, a phospholipid-type active ingredient with anti-tumor capacities.* This oral AKT inhibitor is being developed for the treatment multiple cancers. In preclinical trials and in clinical Phase I tests, this preparation has been found to have good tolerance.

- *Other worldwide drug development partners include* Ardana Bioscience, Baxter Oncology, German Remedies Ltd., Hainan Chang An, Serono International S.A., Shionogi & Co., Ltd., and Solvay Pharmaceuticals B.V. These partners provide the bulk of the funding for certain development projects underway, while leaving Æterna Zentaris' burn rate under control.

- *Æterna Zentaris has a strong and diversified intellectual property position, with 70 patent families.* In addition, roughly 20 patent families are the result of co-operations with external researchers, including the Institute for Biophysical Chemistry of the Max Planck Institute for biophysical Chemistry in Göttingen, Germany for the product candidate miltefosine, and the Tulane University in New Orleans, Louisiana, for cetrorelix, as well as for the product candidates in the area of bombesin antagonists, LHRH antagonists, and peptide conjugates with cytotoxic active groups.

- *Æterna Zentaris owns 62% of Atrium, a cash-generating subsidiary.* Atrium develops and markets nutritional supplements and active ingredients and fine chemicals intended for cosmetics, nutritionals, fine chemicals, and pharmaceuticals used in over 1,000 products throughout 20 countries to leaders such as Estée Lauder, L'Oréal, Clarins, Chanel, Aventis S.A., Sanofi Synthelabo, and Nestlé.

- *Atrium acquired 100% of all issued and outstanding shares of Chimiray/Interchemical for approximately €11.5 million ($18.4 million), payable by the issuance of a long-term debt of €5 million ($8 million) and the residual of €6.5 million ($10.4 million) in cash.* Paris-based Chimiray/Interchemical is focused mainly in the distribution of fine chemicals and active ingredients. Net sales for the last 12-month period were approximately €35 million ($52 million) and the Company generated net earnings.

- *Æterna Zentaris benefits from an experienced management and pharmaceutical development team.*

- *Æterna Zentaris and Atrium carries cash and short-term investments of $52 million as of March 31, 2004*. This position places the Company with the necessary capital to pursue its strategic objectives.

Historical Financial Results

Tables 5, 6, and 7 provide a snapshot of Æterna Zentaris' key historical financial statements, including its Statement of Operations, Balance Sheet, and Cash Flow Statement.

Table 5
Æterna Zentaris
CONSOLIDATED STATEMENT OF OPERATIONS
(Expressed in thousands of Canadian Dollars)

	December 31,		
	2001	2002	2003
	$	$	$
REVENUES	43,777	101,204	166,413
Operating Expenses			
Cost of sales	29,950	77,443	98,048
Selling, general and administrative	13,039	17,777	29,103
Research and development costs	22,681	26,062	45,347
Research and development tax credits and grants	(5,989)	(1,933)	(1,223)
Depreciation and amortization			
Property, plant and equipment	1,353	1,992	3,745
Intangible assets	330	429	5,676
Goodwill	167	—	—
	61,531	121,770	180,696
OPERATING LOSS	(17,754)	(20,566)	(14,283)
Operating revenues (expenses)			
Interest income	3,569	3,079	2,146
Interest expense			
On redeemable common shares of the subsidiary	(437)	—	—
On long-term debt and convertible term loans	(274)	(485)	(4,113)
Other	(75)	(23)	(722)
Foreign exchange gain (loss)	127	(195)	(1,574)
	2,910	2,376	(4,263)
Loss before income taxes	(14,844)	(18,190)	(18,546)
Income tax recovery (expense)	4,752	(4,425)	(5,932)
Loss before the following items	(10,092)	(22,615)	(22,478)
Gain (loss) on dilution	10,223	424	(64)
Non-controlling interest	(3,600)	(3,591)	(3,605)
Net loss for the year	(3,469)	(25,782)	(28,147)
Basic and diluted net loss per share	($0.11)	($0.67)	($0.65)
Weighted average number of shares outstanding	30,968,710	38,584,537	42,993,432

Source: Æterna Zentaris.

Table 6
Æterna Zentaris
CONSOLIDATED BALANCE SHEET
(Expressed in thousands of Canadian Dollars)

	December 31, 2002	2003
	$	$
ASSETS		
Current assets		
Cash and cash equivalents	12,494	22,414
Short-term investments	69,040	41,953
Accounts receivable	74,840	48,191
Inventory	16,335	16,169
Prepaid expenses and deferred changes	20,141	3,314
Future income tax assets	1,682	2,604
	176,432	134,645
Property, plant and equipment	21,688	19,599
Deferred charges	1,047	1,322
Intangible assets	90,300	65,513
Goodwill	24,252	61,184
Future income tax assets	17,249	13,516
	330,968	295,779
LIABILITIES		
Current liabilities		
Promissory note	43,000	—
Accounts payable andaccrued liabilities	42,557	53,062
Income taxes	3,783	3,490
Balances of purchase price	39,690	1,113
Current portion of long term-debt	3,202	3,777
	132,232	61,442
Deferred revenues	12,438	10,563
Convertible term loans	—	19,920
Long-term debt	9,969	15,132
Employee future benefits	6,042	6,658
Future income tax liabilities	35,275	25,991
Non-controlling interest	24,676	29,952
	220,632	169,658
SHAREHOLDERS' EQUITY		
Share capital	153,578	187,601
Other capital	854	7,486
Deficit	(44,864)	(73,011)
Cumulative transition adjustment	768	4,045
	110,336	126,121
Subsequent event	330,968	295,779

Source: Æterna Zentaris.

Table 7
Æterna Zentaris
CONSOLIDATED STATEMENT OF CASH FLOWS
(Expressed in thousands of Canadian Dollars)

	December 31,		
	2001	2002	2003
	$	$	$
Cash flows from operating activities			
Net loss for the year	3,469	(25,782)	(28,147)
Items not affecting cash and cash equivalents			
Depreciation and amortization	1,850	2,421	9,421
Stock-based compensation costs	—	53	477
Future income taxes	(5,674)	1,860	1,866
Interest expense	437	—	—
Loss (gain) on dilution	(10,223)	(424)	64
Non-controlling interest	3,600	3,591	1,605
Employee future benefits	—	18	528
Deferred charges	—	—	141
Deferred revenues	—	—	(1,177)
Accretion on convertible term loans	—	—	1,245
Change in non-cash operating working capital items	(2,327)	(3,634)	2,516
	(15,806)	(21,897)	14,493
Cash flows from financing activities			
Issuance (repayment) of promissory note	—	43,000	(4,300)
Net proceeds from theissuance of convertible term loans	—	—	24,415
Payments on balance of purchase price	—	—	(2,358)
Increase in long-term debt	—	—	7,904
Repayment of long-term debt	(2,620)	(2,608)	(3,109)
Issuance of warrants	—	747	—
Issuance of shares	19,459	57,442	26,580
Share issue expenses	(1,954)	(1,324)	(2,557)
Issuance of shares by a subsidiary, net of redemption	—	2,000	41
	14,885	99,257	17,916
Cash flows from investing activities			
Purchase of short-term investments	(24,911)	(56,658)	(49,464)
Proceeds from the sale of short-term investments	44,228	29,751	76,552
business acquisitions, net of cash and cash equivalents acquired	13,475	(43,747)	(18,839)
Acquisition of a product line	—	(435)	(40)
Purchase of property, plant and equipment	(610)	(5,146)	(1,194)
Additions to intangible assets	(344)	(1,423)	(628)
	4,888	(77,385)	6,387
Net change in cash and cash equivalents	3,967	(25)	9,810
Effect of exchange rate changes on cash and cash equivalents	766	526	110
Cash and cash equivalents--Beginning of year	7,260	11,993	12,494
Cash and cash equivalents--End of year	11,993	12,494	22,414
Additional Information			
Interest paid	478	446	431
Income taxes paid	1,462	1,776	4,242

Source: Æterna Zentaris.

Risks

Some of the information in this report relates to future events or future business and financial performance. Such statements can be only predictions and the actual events or results may differ from those discussed due to, among other things, the risks described in Æterna Zentaris' reports on Forms 10-K, 10-Q, and 8-K. The content of this report with respect to Æterna Zentaris has been compiled primarily from information available to the public released by Æterna Zentaris, through news releases, and through SEC filings. Æterna Zentaris is solely responsible for the accuracy of that information. Information as to other companies has been prepared from publicly available information and has not been independently verified by Æterna Zentaris [Certain summaries of scientific activities and outcomes have been condensed to aid the reader in gaining a general understanding.] For more complete information about Æterna Zentaris, please refer to the Company's websites at www.aeterna.com and www.zentaris.com.

Competition

The biopharmaceutical industry is very competitive. Æterna Zentaris competes with other companies that develop products to treat the same diseases. Many of these companies have considerably greater resources than Æterna Zentaris and there is no guarantee that the products developed by other companies will not cause Æterna Zentaris' products and technologies to become less competitive.

No Guarantee of Development Success

The majority of Æterna Zentaris' products are currently in developmental stages, one of the riskiest stages for a company operating in the field of biotechnology. There is no guarantee that the research and development conducted by Æterna Zentaris will result in the creation of profitable products.

Government Regulation

The procedures involved in obtaining regulatory approval to market therapeutic agents from competent authorities are long and costly and may delay product development. Regulatory approval to market a product may be limited in its scope or it may be refused outright. Such an occurrence could be very detrimental to Æterna Zentaris' profitability. Obtaining approvals from the Health Protection Bureau (HPB), the U.S. Food and Drug Administration (FDA), and the European Medicines Evaluations Agency (EMEA) may take extended periods of time.

Patents and Technologies

The Company believes that its patent portfolio significantly contributes to the value and the success of its business. Æterna Zentaris' strategic approach is to build a portfolio that provides broad protection of technology, as well as a tiered patent claim structure to provide specific composition of matter, disease indication, and manufacturing process claims. The Company's policy is to file patent applications in all major markets in the world. The patent portfolio of the corporation and its subsidiaries comprises approximately 70 patent families. There is no guarantee that the company will obtain patents in the other countries in which patent applications have been or will be filed, or that it will develop other patentable products or processes.

Recent Events

05/11/2004—Announced plans to host an Investor and Analyst Day on Monday, May 17, 2004 from 1:15 p.m.–4:00 p.m. EDT at the St. Regis Hotel in New York City.

05/04/2004—Reported financial results for the first quarter ended March 31, 2004. Revenues for the first quarter 2004 were $58.4 million, an increase of 43% compared with $40.8 million for the same period in 2003. R&D expenses net of tax credits and grants decreased from $10.9 million in the first quarter of 2003 to $8.0 million in the first quarter of 2004, reflecting the realignment of the clinical development program initiated in December 2003, including the refocusing of the pipeline on perifosine and cetrorelix.

04/29/2004—Announced statistically significant positive results from a recently completed Phase II clinical program designed to evaluate cetrorelix, a LHRH antagonist, in three different indications: endometriosis, pre-surgical treatment of uterine myomas and BPH, which can benefit from a targeted and controlled decrease in sex hormones, including estrogen and testosterone.

04/21/2004—Announced today the initiation of a dose ranging study for its EP-1572 Growth Hormone Secretagogue (GHS), a novel, orally-available peptidomimetic agent which can directly stimulate growth hormone secretion from the pituitary gland. The study will evaluate the safety and pharmacokinetics/pharmacodynamics of the compound administered by oral route and its initiation triggers an undisclosed milestone payment to Æterna from its development partner Ardana Bioscience. Potential indications for EP-1572 include treatment of growth hormone deficiency disorders in adults and children (short stature), frailty of the elderly, as well as metabolic complications associated with critical illnesses, such as AIDS-associated cachexia, cancer, and trauma.

04/07/2004—Announced today that results of the recently completed Phase I trial evaluating Perifosine, the Company's novel, first-in-class, oral AKT inhibitor in combination with radiotherapy in patients with unresectable locally advanced tumors will be presented at the upcoming ASCO Annual Meeting.

04/02/2004—Announced that it's wholly owned subsidiary Zentaris and Ardana Bioscience have signed a new agreement for the LHRH antagonist Teverelix. Ardana acquired full global rights and is assigned the intellectual property relating to Teverelix and the underlying microcrystalline suspension technology. In return, Zentaris receives a substantial payment at signature, fixed annual guaranteed payments until 2006, as well as potential future income on sales of Teverelix. As part of the agreement, Zentaris will provide certain development services and supply clinical samples to Ardana.

03/31/2004—Reported positive preclinical results for the novel tubulin-inhibitor ZEN-014 at the American Association for Cancer Research (AACR) meeting in Orlando, Florida. ZEN-014 is a novel pyrazole derivative that was discovered by Zentaris. It represents a new class of small molecule tubulin binders with antiangiogenic properties which are assumed to be novel highly potent anticancer drugs with blockbuster potential.

03/29/2004—Announced that its Board of Directors has adopted a shareholder rights plan, which takes effect immediately. The objectives of the Rights Plan are to provide adequate time for the corporation's Board of Directors and shareholders to assess an unsolicited takeover bid for the corporation, to provide the Board of Directors with sufficient time to explore and develop alternatives for maximizing shareholder value if a takeover bid is made, and to provide shareholders with an equal opportunity to participate in a takeover bid.

03/11/2004—Presented the Company's product pipeline in oncology, endocrinology and infectious diseases at the Bio Square 2004 Conference in Basel, Switzerland. The presentation included a discussion of the recent addition to its portfolio of ghrelin antagonist compounds that could be promising agents for the management of obesity, as well as the addition of new targets as potential novel anticancer agents.

03/03/2004—Announced that its 62%-owned subsidiary, Atrium Biotechnologies Inc., has completed the acquisition of Pure Encapsulations Inc. (Pure) for approximately $50 million in cash. Based in the Boston area, Pure is a privately-held company focused mainly on the development, manufacturing and marketing of nutritional supplements for physicians and other healthcare professionals. With sales exceeding $25 million in 2003, Pure Encapsulations is among the leaders in this growing specialized sector which generates annual sales of over $1 billion in the United States.

02/27/2004—Announced fourth quarter and full year 2003 financial results. For the quarter, total revenue was $48.9 million, an increase of 75% versus $28.0 million in the year-ago period, driven by increased sales of branded pharmaceutical products, growing partnership revenues, and acquisitions made by the Company's subsidiary, Atrium Biotechnologies. For the year ended December 31, 2003, revenues increased by 64% to $166.4 million versus $101.2 million for the same period in 2002.

12/17/2003—Presented its updated plan on the clinical development of Neovastat®. This plan includes the continuation of the Phase III trial in NSCLC sponsored by the U.S. NCI with which Æterna has just renewed the agreement for a period of two years. Also, for strategic considerations, Æterna ceases all activities related to RCC, resulting in a workforce reduction. These actions are part of the Company's strategy aimed at reaching profitability for Æterna.

11/26/2003—Æterna's subsidiary, Atrium Biotechnologies, announced the acquisition of 100% of all issued and outstanding shares of Siricie S.A. for $2 million cash. Based in Paris, this profitable company is focused mainly in the development and marketing of active ingredients drawn from marine life for the cosmetics industry. In 2002, Siricie generated revenues of more than $2.5 million.

11/19/2003—Announced the appointment to its Board of Directors of Henri A. Roy, Chairman of the Board, President and General Manager of the Société générale de financement du Québec (SGF). Mr. Roy takes over the seat left vacant on Æterna's Board, after Francis Bellido's departure from the SGF last October. However, Mr. Bellido, now President and CEO of Biomundis, rejoins Æterna's Board, replacing Jean-Claude Gonneau, Managing Director SG Cowen, Europe SAS, who had been a board member since the Company's early beginnings in 1995.

11/05/2003—Announced third-quarter financial results. The Company reported total revenue of $37.8 million, an increase of 55% compared with $24.4 million in the third quarter 2002. Revenues from Cetrotide® for *in vitro* fertilization were substantially higher this quarter along with a solid performance from Atrium Biotechnologies, which acquired Chimiray-Interchemical in August of this year. The Company reported a loss per share of $0.20 compared to a loss per share of $0.15 in the comparable period for 2002.

10/02/2003—Announced that it had been named one of the 50 fastest growing technology companies in Canada by ranking 18th in the Fast 50 list.

09/24/2003—Reported results of a Phase III trial in RCC, a form of kidney cancer, evaluating Neovastat®, the Company's antiangiogenic compound. Results showed that the study, involving 305 patients refractory to immunotherapy, did not meet its primary endpoint of improving overall median survival time. However, significant survival advantage was observed in a subgroup of healthier patients with clear cell histology and only a single metastatic site. This 38 patient subgroup showed a median survival time of 26.3 months for those treated with Neovastat® compared to 12.6 months for patients receiving a placebo (p=0.0236).

08/06/2003—Æterna announced second-quarter financial results. The Company reported total revenues of $38.9 million, an increase of 66% compared with total revenues of $23.4 million for the second quarter 2002. The Company reported a loss per-share of $0.11, compared with a loss of $0.15 in the comparable period for 2002.

07/29/2003—Reported that results of a Phase III trial evaluating its drug Impavido® (miltefosine) for the treatment of cutaneous Leishmaniasis, a severe skin disease, showed that patients taking Impavido® had a 220% better cure rate compared with those in the placebo group. The average cure rate after treatment with Impavido® was 70%. This favorable data enables Æterna's subsidiary, Zentaris, which develops the drug, to immediately apply for a marketing authorization in South American countries where the cutaneous form of the disease is predominant.

06/18/2003—Announced the extension of the existing license agreement between its subsidiary Zentaris and Serono) for worldwide marketing rights, except in Japan, for Cetrotide®, a novel compound used for *in vitro* fertilization.

04/30/2003—Announced its first quarter financial results for the quarter ended March 31, 2003. The Company reported consolidated revenues of $Cdn 40.8 million and a net loss of $Cdn 4.8 million or $0.12 per share, versus revenues of $Cdn 25.3 million and a net loss of $Cdn 5.7 million, or $0.17 per share for the same period in 2002.

04/26/2003—Disclosed new scientific data on Neovastat®, which reinforces its antiangiogenic properties.

04/01/2003—Announced that it had entered into a term loan facility with two strategic investors**—**SGF Sante Inc. and Solidarity Fund QFL. The term loan is in a principal amount of $Cdn 25 million ($12.5 million per investor), matures on March 31, 2006, and bears interest at an annual rate of 12%. Æterna also announced the merger of its subsidiaries Æterna GmbH and Zentaris AG, thus completing the integration of Zentaris AG, which was acquired in December 2002.

03/26/2003—Announced that it had signed an agreement with Korean based LG Life Sciences Ltd., an affiliate of the LG Group, for marketing Neovastat® in Korea. The agreement provides Æterna with upfront and milestone payments, as well as a return on manufacturing and sales of Neovastat®.

02/27/2003—Æterna's subsidiary, Zentaris, commenced distribution of Impavido® in India, the first oral drug against visceral leishmaniasis in the Indian market.

02/20/2003—Reported financial results for 2002. The year was marked by record sales and net earnings for its Atrium subsidiary and the acquisition of Zentaris AG.

02/14/2003—Announced that Baxter Healthcare S.A. has made another payment in a series of milestone payments to its subsidiary Zentaris AG, for further assessment of the compound D-63153, a LHRH antagonist currently being assessed in a Phase II clinical trial for prostate cancer. The milestone payment is part of the ongoing agreement between the two companies.

01/28/2003—Dr. Éric Dupont announced the following executive appointments**—**Gilles Gagnon, President and Chief Operating Officer of the Company was promoted to President and Chief Executive Officer, and Dr. Jürgen Engel, current Chief Executive Officer of Zentaris AG, was appointed Executive Vice President, Global Research and Development and Chief Operating Officer. Furthermore, Dr. Engel was appointed to Æterna's Board of Directors. Dr. Dupont assumed the role of Executive Chairman on a full-time basis, overseeing strategic planning of Company activities as well as focusing on acquisitions, which is an important element of Æterna's growth strategy.

01/13/2003—Reported on its new product pipeline and clinical development strategy following Zentaris' acquisition. Its main focus is in oncology and endocrinology, with a dozen products ranging from preclinical development to market approval.

01/08/2003—Æterna-subsidiary Zentaris signed product partnership for a novel platinum cancer drug in China. A collaboration with Hainan Chang International Pharmaceutical formed basis for further moves in fast-growing market.

12/30/2002—Announced that it has concluded a definitive sales and purchase agreement with Degussa AG to acquire all the outstanding shares of Zentaris AG for €50 million ($Cdn 81.5 million).

Potential Milestones Within Next 12 Months

Oncology

- Perifosine—Preliminary Phase II data from multiple N.A. trials 2H04
- Perifosine—Phase I data in combination with radiotherapy (ASCO)
- Perifosine—Data presentations at major conferences
- Teverelix—Phase I data in prostate cancer 2Q04
- Advance preclinical pipeline—Initiate one or more Phase I trials

Endocrine Therapy

- Cetrorelix—Initiation of Phase III studies in endometriosis, uterus myoma, or BPH
- Cetrotide®—Market approval in Japan for *in vitro* fertilization 2H04

Products and Profits

- Impavido®—Approval and launch in certain territories
- Atrium Biotechnologies—Continued growth through acquisition strategy

Glossary of Lesser-Known Terms

adenocarcinoma—Cancer that begins in cells that line certain internal organs and that have glandular (secretory) properties.

anemia—Having less than the normal number of red blood cells or less hemoglobin than normal in the blood.

angiogenesis—Blood vessel formation. Tumor angiogenesis is the growth of blood vessels from surrounding tissue to a solid tumor. This is caused by the release of chemicals by the tumor.

angiogenesis inhibitor—A substance that may prevent the formation of blood vessels. In anti-cancer therapy, an angiogenesis inhibitor prevents the growth of blood vessels from surrounding tissue to a solid tumor.

antiangiogenic—Drugs that include angiostatin and endostatin, halt the process of developing new blood vessels (angiogenesis). Angiostatin is a piece of a larger and very common protein, plasminogen, which the body uses in blood clotting. Endostatin is a piece of a different protein, collagen 18, which is in all blood vessels. Both angiostatin and endostatin are normally secreted by tumors. It is hoped that they will provide the basis for a new class of agents to treat cancer.

antineoplastic agents—Agents inhibiting or preventing growth of neoplasms, checking the maturation and proliferation of malignant cells.

apoptosis—Programmed cell death.

assisted reproductive technologies (ART)—All treatments or procedures that include the handling of human oocytes or embryos. That is, all procedures which result from the removal of oocytes from the ovary. This would include *in vitro* fertilization (IVF), gamete intrafallopian transfer (GIFT), frozen embryo transfer (FET), and related procedures.

benign prostatic hyperplasia (BPH)—Nonmalignant (noncancerous) enlargement of the prostate gland, a common occurrence in older men. It is also known as benign prostatic hypertrophy (BPH) and as nodular hyperplasia of the prostate.

cancer—Disease in which abnormal cells divide without control. Cancer cells can invade nearby tissue and spread through the blood stream and lymphatic system to other parts of the body.

carboplatin—An injectable chemotherapy drug used to treat carcinoma.

carcinoma—Cancer that begins in the epithelium, the cells that line or cover an organ. Carcinomas tend to infiltrate adjacent tissues and metastasize to distant organs.

cisplatin—An anticancer drug that belongs to the family of drugs called platinum compounds.

clinical trial—A research study that evaluates the effectiveness of new interventions in people. Each study is designed to evaluate new methods of screening, prevention, diagnosis, or treatment of a disease.

cutaneous leishmaniasis—Skin disease mainly found on the head, neck, and arms. Its symptoms are either in the form of dry lumps or seeping cutaneous sores. The initially lumpy skin lesions open by themselves after weeks or months. Spontaneous, if somewhat delayed, healing can occur, leaving scars.

cytotoxic—Cell killing.

diabetes—A life-long disease characterized by the body's inability to produce or properly use insulin. Insulin is a natural hormone produced by the pancreas, which is responsible for converting sugar, starches, and other food into energy that the body relies upon for daily life. There are two forms of diabetes: Type 1 and Type 2.

dysuria—Pain during urination, or difficulty urinating.

endometriosis—Growth of cells similar to those that form the inside of the uterus (endometrial cells) outside of the uterus. Endometrial cells are the same cells that are shed each month during menstruation. When endometrial cells grow outside the uterus, endometriosis results.

endothelial cell—Main type of cell found in the inside lining of blood vessels, lymph vessels, and the heart.

follicle stimulating hormone (FSH)—Hormone produced by the pituitary gland that controls estrogen production by the ovaries.

hematotoxicity—Toxicity for normal blood cells.

intramural myoma—Within the uterine wall.

***in vitro*—**In the laboratory (outside the body). The opposite of in vivo (in the body).

***in vivo*—**In the body. The opposite of in vitro (outside the body).

luteinizing hormone (LH)—A protein hormone produced by the pituitary gland that triggers ovulation and supports the production of estrogen and progesterone after ovulation in the second half of the menstrual cycle. Because large amounts of LH are released prior to ovulation, it can be detected in urine and used to predict ovulation. Detection of LH in urine is the basis of commercially available ovulation predictor kits. Because LH is metabolized too rapidly to be effective when administered by injection, a similar but more potent hormone, human chorionic gonadotropin (hCG), is used by fertility specialists to induce ovulation.

luteinizing hormone releasing hormone (LHRH)—A peptide hormone of the hypothalamus, which controls female and male sexual hormones by releasing LH.

melanoma—A malignant tumor that develops from melanocytes, melanin producing cells in the skin.

neurotoxicity—Poisonous to nerves or nerve tissue.

nocturia—Excessive urinating at night.

non-small cell lung cancer (NSCLC)—Cancer of the lung, which is not of the small cell carcinoma (oat cell carcinoma) type. The term "non-small cell lung cancer" applies to the various types of bronchogenic carcinomas (those arising from the lining of the bronchi), which include **adenocarcinoma**, squamous cell carcinoma, and large cell undifferentiated carcinoma. The distinctions between small and non-small cell lung cancer is made by looking at the tumor under the microscope and is important for proper treatment. Surgery is the treatment of choice for the early stage of non-small cell lung cancer.

osteoporosis—A disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures, especially of the hip, spine, and wrist.

prostate specific antigen (PSA)—Test used to screen for cancer of the prostate and to monitor treatment.

radiation therapy—The use of high-energy radiation from X-rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy) or from materials (radioisotopes) that produce radiation that are placed in or near a tumor or in the area where cancer cells are found (internal radiation therapy, implant radiation, or

brachytherapy). Systemic radiation therapy involves giving a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Also called radiotherapy.

renal cell carcinoma (RCC)—Cancer that develops in the lining of the renal tubules, which filter the blood and produce urine.

sarcoma—A cancer of the bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue.

submucous myoma—A relatively common cause of abnormal uterine bleeding. Vascular changes and endometrial surface changes caused by even small myomas may cause significant abnormalities in menstrual flow. Some of these lesions may be small enough to be missed or ignored during a pelvic exam and even sonography.

subserious myoma—Uterine myoma located below the peritoneal covering of the uterus and grow towards the intestinal cavity.

Thrombocytopenia—A decrease in the number of platelets in the blood, potentially resulting in increased bleeding and poor clotting function.

tubulogenesis—Formation of blood vessels.

uterus myoma—Benign tumor of the uterine muscles. If the entire uterine wall is penetrated by myoma, one refers to uterus myomatosus.

vascular endothelial growth factor (VEGF)—Substance made by cells that stimulates new blood vessel formation, a mitogen for vascular endothelial (vessel lining) cells. VEGF is a polypeptide structurally related to platelet-derived growth factor (PDGF). The gene for VEGF is on chromosome 6p12.

visceral leishmaniasis—Parasitic infectious disease transmitted by the sandfly and occurs when a parasite enters the patient's immune system via the blood stream, multiplies, and again via the blood stream, attacks primarily the spleen, liver, lymph nodes, and bone marrow. Symptoms of this disease include fevers lasting many weeks, swelling of the spleen and liver, deficiencies of the blood forming system, bleeding of mucous membranes and severe weight loss. If untreated, after infection, this disease can result in death between six months and two years.

Zollinger Ellison Syndrome (ZES)—A rare disorder that causes tumors in the pancreas and duodenum and ulcers in the stomach and duodenum.

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