Turning scientific vision into hope for patients.

Product Development Candidates

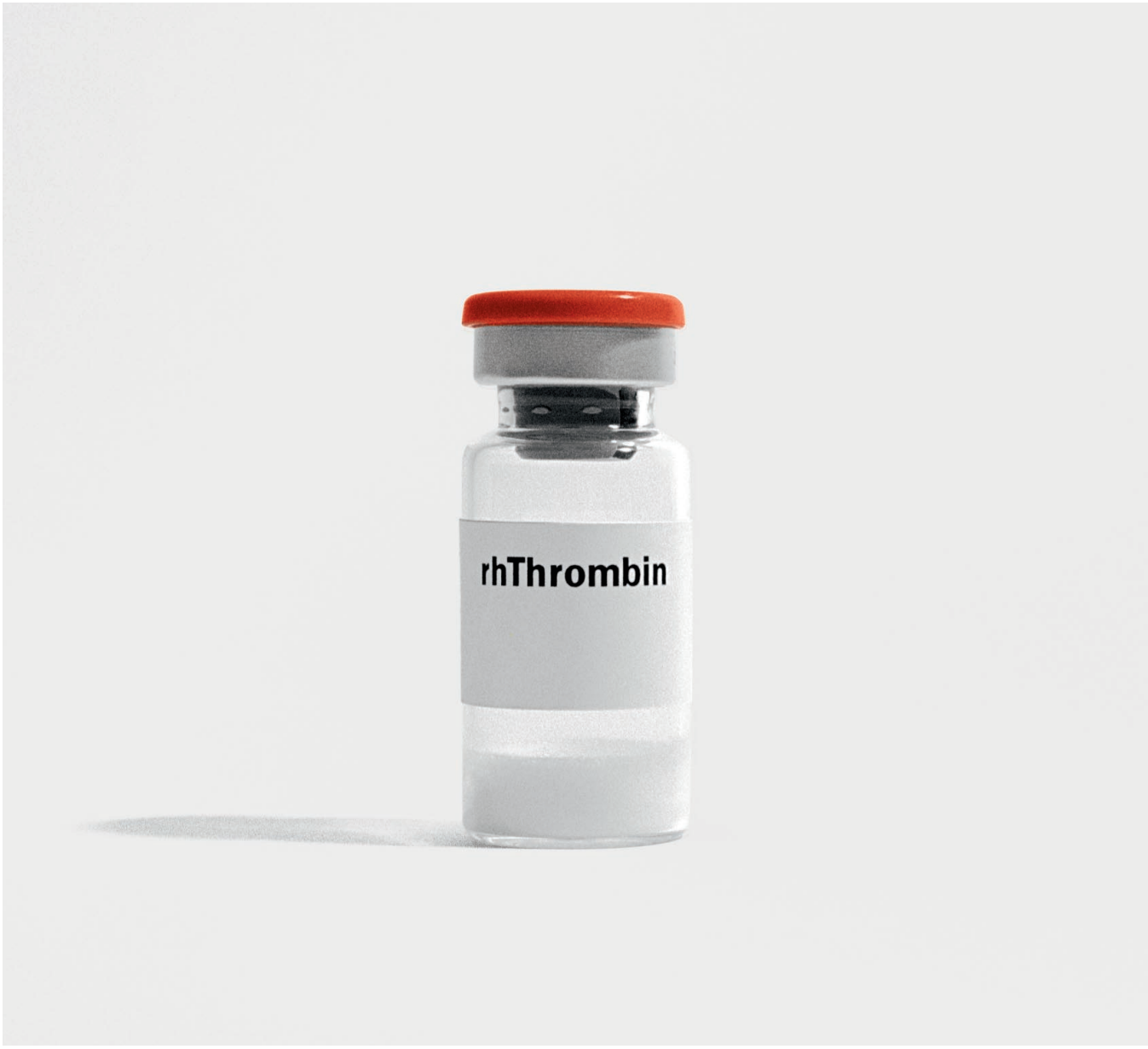
PRODUCT CANDIDATE	INDICATIONS	STAGE	PRODUCT RIGHTS
rhThrombin	Surgical hemostat	Phase 1/2	ZymoGenetics
rFactor XIII	Post-surgical bleeding	Phase 1	ZymoGenetics
TACI-Ig	Autoimmune diseases	Phase 1	ZymoGenetics/Serono
IL-21	Cancer	Phase 1	ZymoGenetics/Novo Nordisk

Marketed Products

ZymoGenetics contributed to the discovery or development of five recombinant protein products marketed by third parties, with our discoveries ranging from the initial identification of the gene coding for the protein to the development of manufacturing processes used to produce the therapeutic proteins.

MARKETED PRODUCT	INDICATIONS	MARKETED BY
Novolin® and NovoRapid® (Insulin)	Diabetes	Novo Nordisk A/S
NovoSeven® (Factor VIIa)	Hemophilia	Novo Nordisk A/S
Regranex® (Platelet-derived Growth Factor)	Non-healing diabetic ulcers	Ortho-McNeil Pharmaceuticals, Inc.
GlucaGen® (Glucagon)	GI motility inhibition & severe hypoglycemia	Novo Nordisk A/S & Bedford Labs and Eisai
Cleactor™ (tPA analog)	Myocardial infarction	Eisai

ZymoGenetics is a biopharmaceutical company focused on the discovery, development and commercialization of therapeutic proteins for the prevention or treatment of human diseases. The Company is developing a diverse pipeline of potential proprietary product candidates that are moving into and through clinical development. These span a wide array of clinical opportunities that include bleeding, autoimmune diseases and cancer.



Surgeons need a safe way to control bleeding during surgery.

Thrombin is a key enzyme involved in blood coagulation. Plasma-derived thrombin is used in surgical settings as a topical hemostat to stop bleeding. ZymoGenetics is developing recombinant human Thrombin (rhThrombin) as an alternative to bovine plasma-derived thrombin. In 2003, the Company initiated a Phase 1/2 clinical trial with rhThrombin to evaluate it as a stand-alone topical hemostat in spinal surgery. ZymoGenetics expects to conduct additional concurrent Phase 2 studies in other surgical indications in 2004 with the aim of obtaining a broad label for the product as a general hemostat.

CORPORATE TIMELINE OF EVENTS

1981

ZymoGenetics founded

1982

Collaboration with Novo Nordisk to develop recombinant human insulin

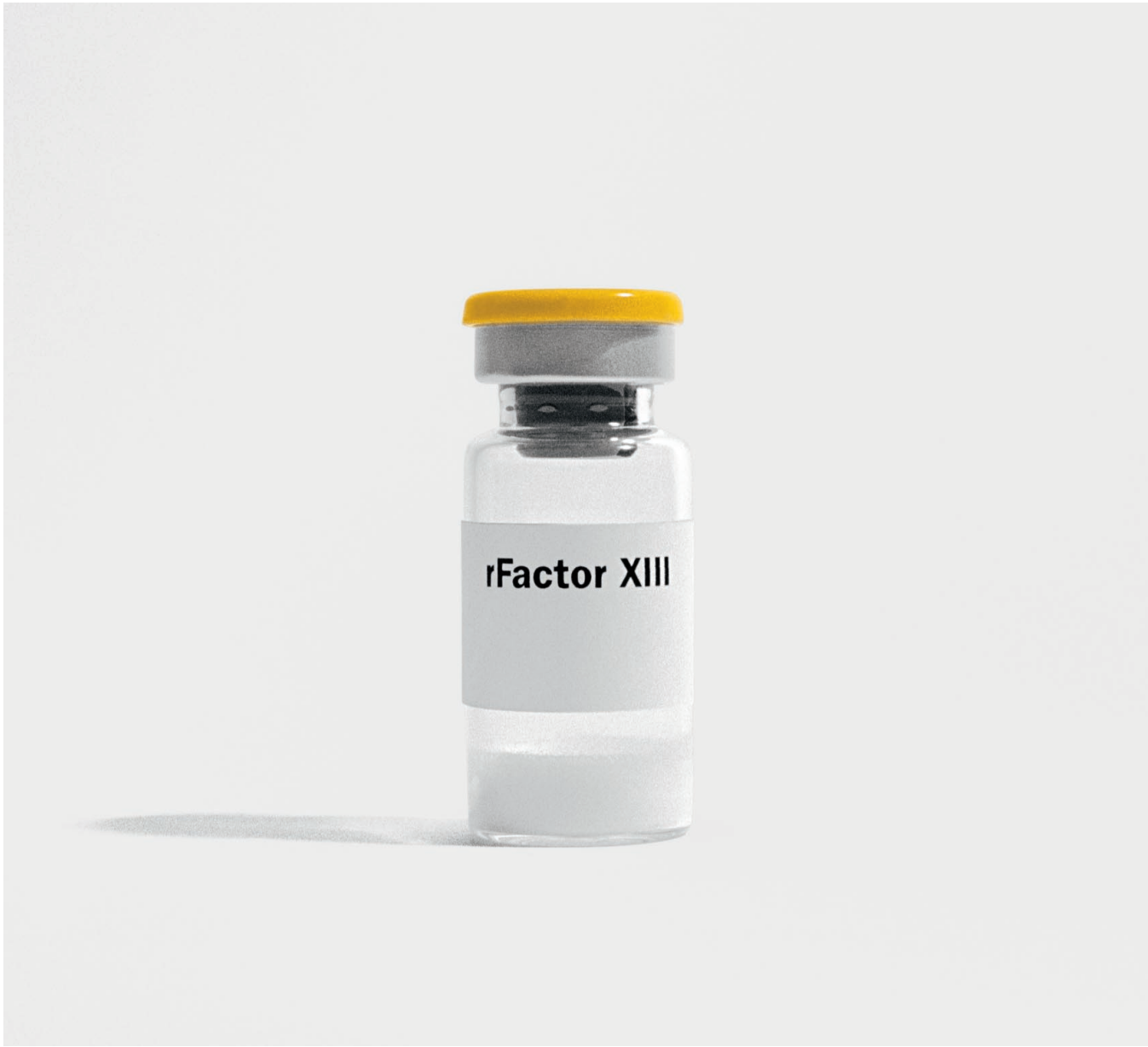
1986

Human Factor VIIa cloned by ZymoGenetics

1988

Company acquired by Novo Nordisk

Recombinant human insulin (Novolin®) marketed by Novo Nordisk (manufacturing process developed by ZymoGenetics)



Post-operative bleeding is a serious problem in need of a solution.

Factor XIII enhances clot strength by crosslinking fibrin strands within the clot. Recombinant human Factor XIII (rFactor XIII) is being developed for congenital and acquired Factor XIII deficiencies. In 2003, ZymoGenetics initiated and completed three Phase 1 clinical studies with rFactor XIII in healthy volunteers and in patients congenitally deficient for Factor XIII. In 2004, ZymoGenetics plans to initiate studies of rFactor XIII in patients undergoing cardiopulmonary bypass, a surgical procedure that has been associated with an acquired Factor XIII deficiency and post-operative bleeding. Also in 2004, ZymoGenetics plans to begin a pivotal clinical trial of rFactor XIII in congenitally deficient patients.

1991

First product (PDGF-BB) taken into clinical studies

1994

First to clone Thrombopoietin

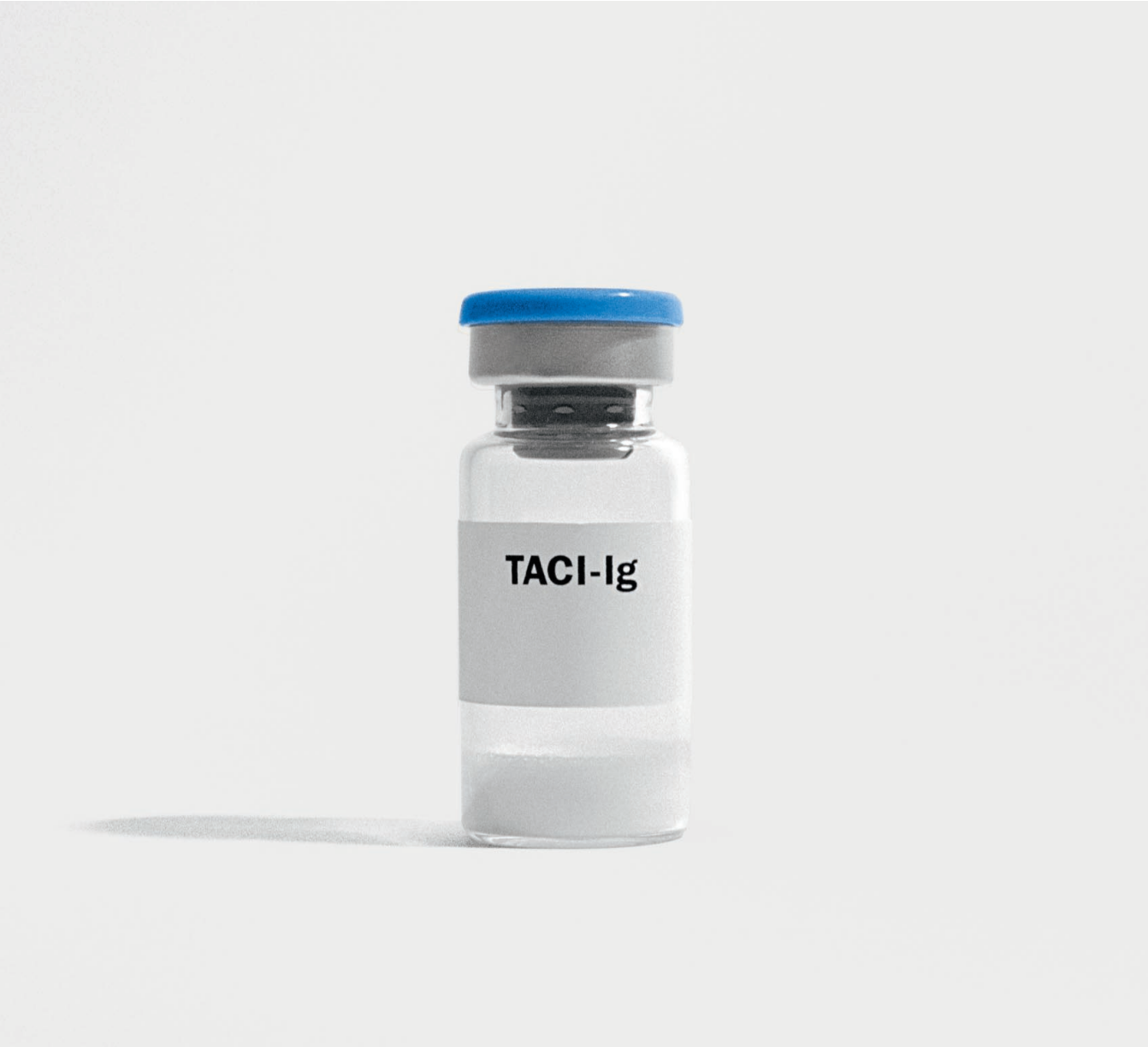
1996

Filed first bioinformatics-derived patent application

Factor VIIa (NovoSeven®) marketed by Novo Nordisk (licensed from ZymoGenetics)

1997

PDGF-BB (Regranex®) marketed by J&J (licensed from ZymoGenetics)



Lupus patients desperately need better treatments.

TACI is a cell-surface receptor for the cytokines BLyS and APRIL that are involved in regulation of B cells. Some autoimmune diseases are caused by hyperactive B cells that produce autoantibodies. TACI-Ig, a soluble fusion protein, is being developed by ZymoGenetics in collaboration with Serono S.A. for the autoimmune diseases systemic lupus erythematosus, rheumatoid arthritis and other potential indications such as B cell cancers. The Companies started clinical studies with TACI-Ig in healthy volunteers in 2003 and expect to initiate Phase 1 studies in the first half of 2004 in patients with systemic lupus erythematosus and later in 2004 in patients with rheumatoid arthritis.

CORPORATE TIMELINE OF EVENTS *(continued)*

1998

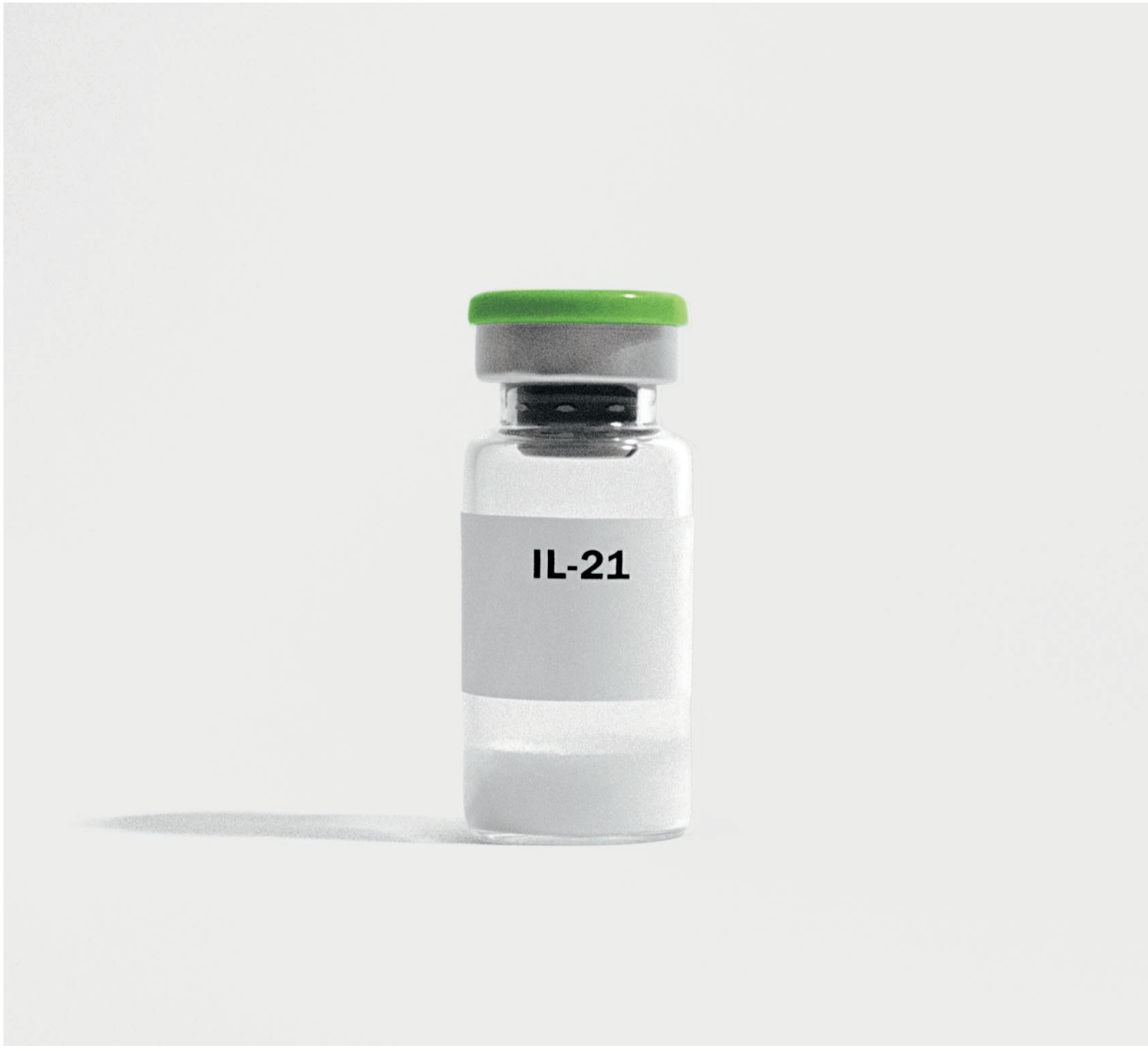
- TPA analog (Cleactor™) marketed by Eisai (licensed from ZymoGenetics)

2000

- ZymoGenetics reestablished as independent company
- Established License & Option Agreement with Novo Nordisk
- George Rathmann elected Chairman of the Board of Directors

2001

- Established co-development partnership for TACI-Ig with Serono S.A.



Cancer patients are still waiting for a cure.

Interleukin 21 (IL-21), a novel cytokine that activates cytotoxic T cells and natural killer cells, is being developed by ZymoGenetics for the treatment of cancer. In a number of preclinical models, IL-21 has been shown to have potent anti-tumor effects. IL-21 toxicology studies are complete, showing the drug to be tolerated at doses exceeding those that will be used in clinical trials. ZymoGenetics initiated IL-21 clinical development in 2004 for patients with metastatic renal cell carcinoma and metastatic melanoma.

2002

- Completed Initial Public Offering
- Completed sale-leaseback of corporate headquarters

2003

- Initiated clinical trials with rFactor XIII, TACI-Ig and rhThrombin
- Began facility expansion, including pilot-scale manufacturing facility
- Completed follow-on common stock offering

2004

- Initiated clinical development of IL-21 in cancer
- Plan to complete Phase 2 clinical trials of rhThrombin
- Expect to complete construction of pilot-scale manufacturing facility

Dear Fellow Shareholders We are proud of the progress our company made in 2003. We initiated clinical trials on three potential protein therapeutics, we further strengthened the company's finances, we continued to identify interesting proteins with future development potential, and we began construction of a pilot-scale manufacturing facility that will allow us to more rapidly move these future product candidates into clinical development.

Bruce L. A. Carter, Ph.D.
President and Chief Executive Officer

Early in the year we began the first human clinical trial of recombinant Factor XIII and by year's end we had completed and reported the results from three different clinical trials of rFactor XIII. All told, 65 individuals received rFactor XIII in these studies, some at doses producing circulating Factor XIII levels up to two and a half times normal levels. There were no serious adverse events, no development of antibodies to Factor XIII, and the drug appeared to be well tolerated in all observable respects.

Even more exciting were observations made specifically in patients with inherited Factor XIII deficiency. People with this deficiency form weak blood clots that are unstable and that can lead to re-bleeding problems. Blood samples taken from patients that were treated with rFactor XIII produced stronger and more stable blood clots, just as we had hypothesized. It is our hope that rFactor XIII will someday provide normal blood clotting not only for these congenitally deficient patients, but also for patients with significant bleeding or at risk for severe bleeding due to surgery or trauma.

Recombinant human Thrombin was the second of our blood clotting proteins to reach human clinical trials in 2003. Thrombin is commonly used today as a topical hemostatic agent in numerous surgical settings. But in the U.S. the currently marketed thrombin product is extracted from pooled cow blood. We believe that our rhThrombin will be an attractive, and potentially safer, alternative to the current bovine thrombin. With the initiation of clinical trials in late 2003, we have started down what we believe will be a relatively rapid clinical development path.

TACI-Ig is the first of our genomics-derived product candidates to reach human clinical trials. We firmly believe in genomics as an important opportunity for discovery. But it doesn't make drug discovery any easier; and it doesn't make drug development any faster. What it does is provide access to novel information that has enabled us to identify novel proteins with the potential to become drugs.

We approached genomics in a different way than everyone else. We searched only for proteins that could themselves become drugs. And we focused only on certain families of proteins that had previously been fruitful in yielding successful drugs or, at a minimum, potent biological activity. When you "take the road less traveled," you either fail embarrassingly or you end up with a distinct competitive advantage. Fortunately for our company, the latter is true, with the consequence that we have an intellectual property portfolio in the field of protein therapeutics that we believe stacks up favorably against that of any pharmaceutical or biotechnology company.

But back to TACI-Ig. We began human clinical testing in healthy volunteers in September in collaboration with our partner, Serono. We have been working together with Serono now for over two years, and their performance has been first rate. We see tremendous potential for TACI-Ig in treating autoimmune diseases that result from increased levels of autoantibodies produced from hyperactive B cells, such as systemic lupus erythematosus and rheumatoid arthritis. B cell cancers, including lymphoma, leukemia and multiple myeloma, may also be targets for treatment with TACI-Ig. And there is increasing evidence that B cells may play an important role in multiple sclerosis, leading one to envision a role for a drug that can suppress B cell autoimmunity. TACI-Ig, if it is successful, has the potential to be a huge drug.

We also made considerable progress on the second of our genomics-derived product candidates, Interleukin 21. We and others have demonstrated the anti-cancer properties of IL-21 in a number of different mouse models of cancer. But as we all know, history has shown most of these models to be poor predictors of activity in humans. Thus, we have moved rapidly over the course of the year to ready the program for the start of human clinical trials in the first half of 2004 in metastatic melanoma and renal cell carcinoma patients. Our toxicology studies are complete, showing the drug to be tolerated at doses exceeding those that will be administered in clinical trials. The drug for use in clinical testing has been manufactured. The FDA recently gave us clearance to proceed with IL-21 clinical trials, and we are very excited about the potential of IL-21 to help cancer patients.

Drug development is an inherently costly business. Financial strength is important to the prospects for success in this business. In 2003 we recognized an opportunity to add to our cash reserves and further reduce our financial risk. We acted on it, raising over $70 million in an equity offering, and allowing us to end the year with $300 million of cash and investments.

In this business time is money. To move our protein drug candidates rapidly from research into clinical development, we concluded that we needed to have the capability of manufacturing proteins in-house for use in clinical testing. Accordingly, we began a facility expansion that will include a pilot-scale manufacturing plant allowing us to produce proteins from mammalian or microbial cells in conformance with FDA regulations. As of today our project is on time, on budget and expected to come on-line in mid-2004.

SHAREHOLDER'S LETTER *(continued)*

It has been over three years now since our company became independent from Novo Nordisk. Reflecting back on that period of time, it is rewarding to see the progress we have made as an independent company. An important element of our success to date has been our focus and commitment to a strategy that has remained essentially unchanged. We believe in that strategy as much today as we did then. The following are the key elements.

> We focus solely on protein therapeutics, which we believe offer the potential to gain market exclusivity.

> We pursue protein discovery using a highly focused genomics-based approach, giving us an efficient method for identifying novel proteins with therapeutic potential.

> We balance our development risk with a portfolio of proprietary product candidates comprising both novel proteins with blockbuster potential and lower risk recombinant versions of proteins previously extracted from humans or animals.

> We intend to commercialize product candidates on our own, or with partner companies when appropriate, to reduce development costs, obtain access to infrastructure and specialized skills, and allow "more shots on goal," while maintaining active participation in product development and commercialization.

The year 2004 should be one of continued advancement for our company, with a number of important planned clinical milestones.

rhThrombin—we plan to complete the Phase 1 part of our ongoing spinal surgery clinical trial, move into and complete the Phase 2 spinal surgery trial, and initiate and complete Phase 2 studies in three other surgical settings, putting us in position to begin Phase 3 trials in 2005.

rFactor XIII—we plan to initiate our first clinical trial in patients with significant bleeding or at risk for severe bleeding due to surgery or trauma, such as those who have undergone cardiopulmonary bypass surgery, and begin a pivotal study in patients with congenital Factor XIII deficiency.

TACI-Ig—we plan to complete the analysis of the Phase 1 safety study in healthy volunteers, initiate a clinical trial in systemic lupus erythematosus patients in the first half of the year and initiate a clinical trial in rheumatoid arthritis patients.

IL-21—we plan to treat patients in a Phase 1 trial in metastatic melanoma and renal cell carcinoma patients in the first half of the year.

In addition, we hope to designate a fifth clinical development candidate from our portfolio of pre-development proteins and complete the construction of our ongoing facility expansion, including our pilot-scale manufacturing plant.

While our progress to date is gratifying, we recognize that we have a long way to go and a lot of work ahead of us. This is not an easy business by any means, and we understand the continued commitment and effort that will be necessary to reach our goals. Fortunately, we have an outstanding team of people who are highly motivated and working hard to help us get there. Together, we believe we have the potential to develop successful drugs that will improve many people's lives.

Sincerely,

Bruce L. A. Carter, Ph.D.
President and Chief Executive Officer

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

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15 (D) OF THE SECURITIES EXCHANGE ACT OF 1934**

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2003

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission File Number 0-33489

ZYMOGENETICS, INC.
(exact name of registrant as specified in its charter)

Washington	**91-1144498**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

1201 Eastlake Avenue East, Seattle, WA 98102
(Address of principal executive offices)

Registrant's telephone number, including area code (206) 442-6600

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

None

Securities registered pursuant to Section 12(g) of the Act:

Common Stock, no par value

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15 (d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive Proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendments to this Form 10-K. ☒

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Exchange Act).

Yes ☒ No ☐

The aggregate market value of the common equity held by non-affiliates computed by reference to the price at which the common equity was last sold as of June 30, 2003 was: $157,654,708.

Common stock outstanding at March 1, 2004: 52,749,422 shares.

DOCUMENTS INCORPORATED BY REFERENCE

(1) Portions of the Company's definitive Proxy Statement for the annual meeting of shareholders to be held on June 10, 2004, are incorporated by reference in Part III.

ZYMOGENETICS, INC.

ANNUAL REPORT ON FORM 10-K

For the Year Ended December 31, 2003

TABLE OF CONTENTS

PART I

Item 1. Business

This Annual Report on Form 10-K contains, in addition to historical information, forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that involve risks and uncertainties. This Act provides a "safe harbor" for forward-looking statements to encourage companies to provide prospective information about themselves so long as they identify these statements as forward looking and provide meaningful cautionary statements identifying important factors that could cause actual results to differ from the projected results. All statements other than statements of historical fact, including statements regarding industry prospects and future results of operations or financial position, made in this Annual Report are forward looking. We use words such as "anticipates," "believes," "expects," "future" and "intends" and similar expressions to identify forward-looking statements. Forward-looking statements reflect management's current expectations, plans or projections and are inherently uncertain. Our actual results could differ significantly from the results discussed in the forward-looking statements. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Factors that could cause or contribute to such differences include those discussed in "Important Factors That May Affect Our Business, Our Results of Operations and Our Stock Price" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," as well as those discussed elsewhere in this Annual Report on Form 10-K. We undertake no obligation to publicly release any revisions to these forward-looking statements that may be made to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events. Readers are urged, however, to review the factors set forth in reports that we file from time to time with the Securities and Exchange Commission.

Overview

Our company is focused on the discovery, development and commercialization of therapeutic proteins for the treatment of human disease. We have been active in the area of therapeutic proteins for over 20 years, since our incorporation in the state of Washington in 1981. For 12 years we were a wholly owned subsidiary of Novo Nordisk A/S, one of the world's largest producers of therapeutic proteins. We have contributed to the discovery or development of five recombinant protein products currently on the market, which had aggregate sales in 2003 in excess of $2 billion. In November 2000, as part of a restructuring by Novo Nordisk, we became an independent company in a transaction that included a $150 million private placement. In February 2002, we completed our initial public offering.

We have a growing pipeline of potential products that we expect to develop on our own or in collaboration with partners. Two of our most advanced internal product candidates, rhThrombin and rFactor XIII, are recombinant versions of proteins that are currently marketed in forms derived from human or cow blood. Our intent is to provide attractive, and potentially safer, alternatives to the currently marketed versions, building on our established expertise in recombinant protein production methods. Recombinant human thrombin (rhThrombin) is a topical hemostatic agent intended for the control of bleeding during surgical procedures. rFactor XIII is a protein involved in blood clotting that we are developing for the treatment of bleeding disorders, including bleeding complications following cardiopulmonary bypass surgery. We completed three Phase 1 clinical trials of rFactor XIII in 2003, and we began clinical trials of rhThrombin in December of 2003.

Our bioinformatics efforts, in combination with our biology expertise, have yielded numerous novel proteins with potential medical relevance. Our most advanced bioinformatics-derived product candidates are TACI-Ig and interleukin-21 (IL-21). TACI-Ig is a soluble receptor with potential applications for the treatment of autoimmune diseases, which we are developing in collaboration with Serono S.A., a leading global biotechnology company. IL-21 is a protein with potential applications for the treatment of cancer, which we are developing in North America and which Novo Nordisk is developing in the rest of the world. We began a Phase 1 clinical trial of TACI-Ig in September 2003 and we plan to begin clinical trials of IL-21 in the first half of 2004.

Early in our history, we built a core focus on protein chemistry and molecular and cellular biology. In the mid-1990's, we developed an advanced bioinformatics program that now represents the foundation of our discovery efforts. We were early to recognize the opportunity of genomics and were a pioneer in the use of bioinformatics tools to mine genomic databases. We focus our bioinformatics-based discovery efforts on the relatively small subset of genes that we believe have the highest probability of coding for proteins with therapeutic potential. Specifically, we focus on key protein categories that have members with proven therapeutic value or potent biological activity. We believe this approach increases our research efficiency and maximizes our chances of commercial success.

Our expertise in biology and protein chemistry strengthens our ability to determine the biological function and potential therapeutic utility of our protein candidates early in the discovery process. Determining biological function and therapeutic utility at an early stage improves our prospects of establishing patent priority by enabling us to file detailed patent applications covering both composition of matter and method of use claims. We have issued patents covering all four of our product candidates under development. In total, we have more than 270 issued or allowed United States patents and over 260 United States patent applications pending.

Business Strategy

Our corporate objective is to discover, develop and commercialize novel therapeutic proteins and other protein-based products derived from our proprietary portfolio of protein candidates. To achieve this objective, we plan to pursue the following key strategies:

- *Continue our focused approach to the discovery of therapeutic proteins.* We focus exclusively on therapeutic proteins. We use bioinformatics to identify the relatively small subset of genes that we believe have the highest probability of coding for proteins with therapeutic potential. Specifically, we focus on key protein categories that have members with demonstrated therapeutic potential or medically relevant biological activity. Once we have identified a protein candidate with relevant biological activity, we intend to develop the therapeutic protein directly, or, where appropriate, develop a monoclonal antibody or soluble receptor that targets the protein.
- *Pursue comprehensive intellectual property protection.* We intend to establish proprietary product opportunities by establishing patent priority for our gene and protein discoveries at the earliest possible time. Data generated from bioinformatics and exploratory biology enhances our patent applications. Our research teams work closely with our intellectual property department to prepare detailed patent applications on full-length genes and their corresponding proteins at an early stage in the discovery process. We augment initial filings with supporting data as it becomes available.
- *Leverage diverse biology expertise.* We have a world-class team of scientists who draw on a large number of biological assays and experimental systems to identify the biological functions of the genes and proteins we discover. Our comprehensive approach increases the likelihood of determining the medical relevance of these proteins.
- *Focus initially on lower-risk product candidates.* We intend to mitigate the risk of drug development by concentrating our initial product development efforts on product candidates that have a more favorable risk profile than more recently discovered proteins. Two of our most advanced internal product development candidates are rFactor XIII and rhThrombin, recombinant versions of proteins intended to replace currently marketed plasma-derived proteins.
- *Pursue a diversified commercialization strategy.* Because we expect to generate more product candidates than we have the capacity to develop on our own in the near term, we are pursuing a three-pronged commercialization strategy. We intend to internally develop and commercialize some product candidates where we believe the clinical trials and sales force requirements are manageable. We intend to partner with other companies to co-develop and co-promote product candidates in cases where we do not have access to the infrastructure required for development and commercialization. Finally, we intend to out-license other product candidates and intellectual property.

- *Conduct phased acquisition of manufacturing capabilities.* For our existing development candidates, we intend to use third-party contractors or collaborative partners to manufacture both clinical and commercial product. We began construction in 2003 of small-scale dedicated GMP manufacturing suites, which we intend to use as a source of clinical product supply beginning in late 2004. Over the long term, we may acquire larger-scale commercial manufacturing capabilities to allow us to control directly all critical elements of product development and commercialization.

Products and Product Pipeline

Our track record in the field of therapeutic proteins includes contributions to the discovery or development of five recombinant protein products currently being marketed by Novo Nordisk or other companies. Our current focus is the development of a pipeline of internal product candidates. We also have out-licensed several product candidates outside our areas of interest. The following table summarizes the marketed products and out-licensed product candidates, as well as our most advanced product candidates for internal development or co-development.

	Product/Product Candidate	Indication or Intended Use	Status	Stage of Development
Internal Candidates	rhThrombin	Surgical hemostat	Internal development	Phase 1/2
	rFactor XIII	Congenital Factor XIII deficiency; major cardiac surgery; other acquired Factor XIII deficiencies	Internal development	Phase 1
	TACI-Ig	Systemic lupus erythematosus; other autoimmune diseases	Co-development with Serono S.A.	Phase 1
	IL-21	Cancer; viral infections	Internal development in North America; Novo Nordisk outside North America	Pre-IND
Marketed Products	Novolin® and NovoRapid® (Insulin)	Diabetes	Out-licensed to Novo Nordisk	Marketed
	NovoSeven® (Factor VIIa)	Hemophilia	Out-licensed to Novo Nordisk	Marketed
	Regranex® (Platelet-derived Growth Factor)	Wound healing	Out-licensed to Johnson & Johnson	Marketed
	GlucaGen® (Glucagon)	Hypoglycemia; gastrointestinal motility inhibition	Out-licensed to Novo Nordisk	Marketed
	Cleactor™ (tPA Analog)	Myocardial infarction	Out-licensed to Eisai Co., Ltd.	Marketed
Out-Licensed Candidates	Platelet-derived Growth Factor	Periodontal disease	Out-licensed to BioMimetic Pharmaceuticals, Inc.	Pivotal
	Alpha 1-antitrypsin	Emphysema; atopic dermatitis	Out-licensed to Arriva Pharmaceuticals, Inc.	Phase 2

In the table above, Phase 1 refers to clinical trials designed primarily to determine safety and pharmacokinetics in human beings; Phase 2 refers to clinical trials in a limited patient population to evaluate preliminary efficacy, dosing and side effects; Phase 1/2 refers to a clinical trial designed to incorporate both

Phase 1 and Phase 2 objectives. Pivotal refers to clinical trials in a broad patient population with the intention of generating statistical evidence of efficacy and safety to support product approval. Pre-IND refers to the stage in which we have completed pre-development activities, have generated a commercial hypothesis for the product candidate and have begun the process leading to the filing of an investigational new drug (IND) application and the initiation of Phase 1 clinical trials.

Internal Product Candidates

We are developing several product candidates to treat a variety of serious diseases and medical conditions. We intend to develop and commercialize these product candidates on our own or in collaboration with other biotechnology or pharmaceutical companies.

rhThrombin

Thrombin is a specific blood-clotting enzyme that converts fibrinogen to fibrin. Fibrin is the primary protein contained in newly formed blood clots. Thrombin also promotes clot formation by activating Factor XIII, which cross-links the fibrin molecules and strengthens the newly forming clot.

Profuse bleeding is a serious complication of major surgeries. Surgeons try to limit bleeding during surgery to control blood loss, limit the use of transfused blood products and maintain visibility in the operating field. Thrombin is widely used to stop diffuse bleeding occurring during surgical procedures. It is generally sold as a freeze-dried powder, which is dissolved and absorbed onto a surgical sponge or gauze for topical application to wounds. Only bovine (cow) plasma-derived thrombin is available in the United States as a stand-alone product. Sales of bovine plasma-derived thrombin in the United States exceeded $140 million in 2003. It has been estimated that bovine plasma-derived thrombin is used in more than 500,000 surgical procedures annually in the United States.

We believe that there are several potentially important advantages to a recombinant human form of thrombin. A recombinant human form of thrombin would address concerns of viral contamination of plasma-derived products. It would also address concerns associated with products of bovine origin, including the potential risk of contamination with the pathogen that causes the human form of “mad cow” disease (vCJD). In addition, there is a risk of allergic reaction in patients sensitive to plasma products. Some patients develop antibodies to bovine plasma-derived thrombin or to Factor V or other protein impurities in the bovine plasma-derived product. In some cases, these antibodies can cross-react with analogous human proteins, creating a condition that is particularly difficult to manage and is potentially fatal in patients who develop severe bleeding conditions. Use of bovine plasma-derived thrombin in patients with antibodies to bovine clotting factors may result in abnormal clotting time, post-operative complications, clotting disorders and the resulting higher treatment costs.

We intend to develop rhThrombin as a preferred alternative to the currently marketed human and bovine plasma-derived thrombin products. As with plasma-derived thrombin, rhThrombin would be used in the clinical setting to control bleeding. Primary applications would include a wide range of surgeries, trauma and burn injuries. We believe the market for rhThrombin could be further expanded by developing line extensions in which rhThrombin is combined with other passive or active materials.

We have developed a patent-protected method that we believe will enable us to cost-effectively manufacture rhThrombin in a two-step process. First, recombinant human prethrombin-1 (“rhPrethrombin-1”) is produced in mammalian cells. Then, using an enzyme activation step, rhPrethrombin-1 is converted to rhThrombin. For the supply of Phase 1 and Phase 2 clinical trials, we have manufactured rhPrethrombin-1 internally, and a third-party manufacturer has performed the activation and purification of the resulting rhThrombin. In October 2003 we entered into a contract manufacturing agreement with Abbott Laboratories for the production of rhThrombin at commercial scale for late stage clinical studies and, assuming regulatory approval, commercial sale. In December 2003 we began a two-part Phase 1/2 clinical trial of rhThrombin in patients undergoing spinal surgery. Upon

completion of Part 1 of this clinical trial, we plan to initiate three Phase 2 clinical trials in liver resection, peripheral artery bypass and arterio venous graft formation surgeries.

We have obtained issuance of United States and foreign patents directed to certain recombinant human thrombin, methods of producing recombinant human thrombin from a genetically engineered precursor termed "prethrombin-1," and therapeutic use of the protein.

rFactor XIII

Factor XIII is a blood-clotting enzyme that functions by cross-linking fibrin molecules to each other and to other proteins in a newly formed blood clot, adding significant stability to the clot and protecting it from degradation by other proteins in circulation. Congenital Factor XIII deficiency, an inherited disorder, is a rare condition afflicting only a few hundred patients worldwide. These patients have a tendency to experience severe bleeding problems. Acquired Factor XIII deficiency, a transient drop in Factor XIII levels, is much more common, having been reported in several diseases and medical conditions. Acquired Factor XIII deficiency is also thought to be a major cause of bleeding and failure to heal after surgeries and clinical procedures of many types, including cardiopulmonary bypass surgery.

Human plasma-derived Factor XIII is produced by Aventis Behring GmbH and is marketed as Fibrogammin® P in Japan, Germany, Austria and South Africa. However, Fibrogammin® P is not approved for use in the United States and many European countries. Clinical studies have shown that normal levels of Factor XIII activity can be restored in patients with a congenital or acquired deficiency by intravenous administration of plasma-derived Factor XIII. Our market research indicates that physicians in some countries are currently using plasma-derived Factor XIII not only for the treatment of congenital Factor XIII deficiency, but for other medical conditions associated with acquired Factor XIII deficiency.

In patients undergoing cardiopulmonary bypass surgery, there is significant illness and death associated with post-operative bleeding. Multiple transfusions with plasma and other blood products are often used to compensate for blood loss, but there are adverse health risks and costs associated with these transfusions. In some cases, surgeries must be redone, at significant cost and risk to the patient, to address uncontrolled bleeding. Studies have indicated that levels of Factor XIII significantly decrease after cardiopulmonary bypass surgery. Published studies involving a small number of patients demonstrated that administration of human plasma-derived Factor XIII after cardiopulmonary bypass surgery led to a statistically significant decrease in chest tube drain volume compared to a control group, suggesting that Factor XIII treatment may reduce the need for blood transfusions in these patients. There are an estimated 700,000 major cardiac surgical procedures performed annually involving cardiopulmonary bypass surgery.

We believe that there are several important advantages to a recombinant human form of Factor XIII. Such a product would address concerns over viral contamination associated with plasma-derived products and could decrease or eliminate the potential allergic reactions associated with plasma-derived products, while helping to ensure a continuous and cost-effective product supply. A recombinant human form of Factor XIII could also reduce or eliminate the need for transfusions of plasma or other blood products in the treatment of Factor XIII deficiency.

We believe that rFactor XIII represents not only an effective alternative product for the existing plasma-derived product, but also an opportunity for addressing a potentially significant untapped market. We plan to develop rFactor XIII as a product for early intervention in patients experiencing post-operative bleeding, with the intent of reducing blood loss, transfusions, time in the intensive care unit and the frequency of re-operations. Although sales of plasma-derived Factor XIII have been relatively low to date, approval of a recombinant human form of Factor XIII in existing markets, as well as the introduction of a recombinant product in the United States and several major European countries, could facilitate significant expansion of the market and sales of Factor XIII. rFactor XIII is manufactured in yeast cells. The initial supply of rFactor XIII product for use in clinical testing has been manufactured for us by Avecia Limited.

We filed an IND application for rFactor XIII with the United States Food and Drug Administration, or FDA, in September 2002, and we conducted three Phase 1 clinical trials in both healthy subjects and congenitally deficient patients in 2003. In these clinical trials, rFactor XIII was administered to 65 individuals. rFactor XIII was well tolerated and no serious adverse events were observed. Side effects reported by individuals receiving rFactor XIII were similar to those reported by individuals receiving placebo. At the highest dose levels administered, circulating Factor XIII levels were raised to over 250% of normal levels. The half-life of rFactor XIII was observed to be nine to eleven days. In the trial involving patients having congenital Factor XIII deficiency, there were no serious adverse events and all subjects treated at therapeutic doses showed normalized blood clot strength and stability, as measured *in vitro,* for at least one month following administration of rFXIII, which is consistent with the established role of Factor XIII in hemostasis.

We plan to pursue cardiopulmonary bypass surgery as the first major acquired deficiency in our rFactor XIII clinical development program. We have filed an IND application with the FDA for an additional Phase 1 clinical trial in up to 50 patients undergoing bypass surgery. We are in the process of conducting an additional animal study requested by the FDA prior to beginning the trial. Our goal is to begin treating patients in this clinical trial in the first half of 2004.

We are the sole owner, joint owner or exclusive licensee of patents and patent applications relating to rFactor XIII, including patents and applications claiming: DNA sequences, expression vectors and host cells for producing, and methods of producing, rFactor XIII; Factor XIII formulations; methods of treating various diseases and conditions using Factor XIII; and methods for the purification of and purified forms of Factor XIII.

TACI-Ig

TACI is a member of the tumor necrosis factor receptor family of proteins. TACI-Ig is a soluble form of the TACI receptor that binds to two ligands, BLyS and APRIL, that are implicated in mounting B-cell mediated immune responses. When over-produced in transgenic animals, BLyS has been shown to lead to the development of autoimmune disease with symptoms resembling systemic lupus erythematosus. The aim of treatment with TACI-Ig is to neutralize the overactivity of these immune-stimulating ligands to prevent the activation of B cells and thus the production of harmful autoantibodies, which are antibodies to one's own cells.

We believe that TACI-Ig could represent a less toxic and more specific immunosuppressive agent than current therapies for the treatment of autoimmune diseases and other diseases for which the suppression of B-cell function and a decrease in autoantibody levels could have therapeutic benefit. Such diseases include systemic lupus erythematosus (SLE), rheumatoid arthritis, myasthenia gravis and multiple sclerosis. In an animal model of SLE, TACI-Ig has been shown to specifically inhibit the development of mature B cells and the development of antigen-induced antibody production. It has also been shown to inhibit the development of proteinuria, an indicator of kidney malfunction, and to prolong survival of the animals. In a collagen-induced model of rheumatoid arthritis, TACI-Ig has been shown to inhibit the incidence of disease. Taken together, these data indicate that TACI-Ig acts by inhibiting the production of mature B cells and decreasing autoantibody levels.

Based on positive data from animal models, SLE has been selected as the initial clinical indication for TACI-Ig. The cause of this disease remains unknown, but there is substantial evidence suggesting that B-cell hyperactivity resulting in the secretion of autoantibodies is fundamental to its development. Although estimates on prevalence vary widely, there are believed to be over 225,000 patients diagnosed with SLE in major markets. Of these, there are an estimated 100,000 such patients in the United States and a roughly equivalent number in major European countries. No new FDA-approved treatments for SLE have been introduced in the last 40 years. Current therapies, including immunosuppressives and corticosteroids, are not very effective and can have severe side effects. We believe that patients diagnosed with severe SLE would be candidates for treatment with TACI-Ig. Together with our partner, Serono, we plan to begin a Phase 1 clinical trial of TACI-Ig in SLE patients in the first half of 2004.

Rheumatoid arthritis has been selected as the second clinical indication for TACI-Ig. Rheumatoid arthritis is one of the most prevalent chronic inflammatory diseases, afflicting an estimated 1% of the population in industrialized countries, including over five million patients in North America, Europe and Japan. Although the underlying cause of rheumatoid arthritis is unknown, considerable data indicate a major role of B cells in this disease. Rheumatoid arthritis has been an attractive therapeutic area for drug development because of its large market size. As a consequence, a very large number of drugs are currently being developed. However, we believe that few of these product candidates target B cells specifically. Thus, TACI-Ig represents a novel mode of treatment that could alleviate the symptoms of rheumatoid arthritis associated with pathogenic B cells. Moreover, the specificity and mode of action of TACI-Ig strengthens its potential as an add-on therapy to existing drugs. Together with our partner, Serono, we plan to begin a Phase 1 clinical trial of TACI-Ig in rheumatoid arthritis patients in 2004.

In August 2001, we entered into a collaborative development and marketing agreement with Serono relating to TACI-Ig. Under our agreement, we will develop TACI-Ig jointly with Serono pursuant to a worldwide development plan. Serono has manufactured clinical grade materials in quantities adequate to supply initial clinical trials. Together with Serono, we initiated a Phase 1 clinical trial of TACI-Ig in healthy volunteers in September 2003, which we expect to complete in early 2004.

We own, have exclusively licensed, or have filed applications for, worldwide patent coverage for TACI-Ig and related technology. Our license with St. Jude's Children's Hospital of Memphis, Tennessee is central to our patent portfolio for TACI-Ig. St. Jude's owns the patents covering the TACI protein, related polypeptides, methods of production and antibodies. In addition, we have sole ownership of patents and patent applications that include claims to expression vectors, transformed cells used to produce TACI-Ig and methods of using TACI-Ig to treat various diseases and medical conditions.

IL-21

IL-21 is a protein belonging to a family of cytokines that modify the function of cells in the immune system. IL-21 shares both structural and genetic sequence similarity with interleukin-2 (IL-2), a cytokine approved as a therapy for malignant melanoma and renal cell carcinoma. We have shown that IL-21 regulates the proliferation and functional activity of several populations of immune cells, including cytotoxic T cells (CTL) and natural killer (NK) cells, both of which are thought to be critical in eliminating malignant or virally infected cells from the body.

Nonclinical studies have indicated that IL-21 is an effective therapy in a number of animal models of cancer. In an animal model of metastatic melanoma, IL-21 exhibited a high rate of tumor suppression. Animals in this model develop aggressive metastases to the lung, which can be readily measured. Treatment with IL-21 led to a significant reduction in the number of lung metastases relative to controls. IL-21 also was found to have potent inhibitory activity in other animal models of cancer. These models demonstrated that the *in vivo* effects of IL-21 were mediated through the activation of CTL and NK cells, which led to rejection of the tumors in the animal models.

In clinical practice, IL-2 is an effective therapy in approximately 5% to 8% of patients with malignant melanoma. Accompanying this low level of efficacy is a significant side effect profile that profoundly limits the utility of IL-2 in treating disease. These side effects can be so severe that many patients stop the therapy before completion of the treatment program. Therefore, it has been a high priority to assess the possible side effects of IL-21.

To assess the safety profile of IL-21, studies were conducted in mouse models to evaluate IL-21 in two aspects of known IL-2 toxicity: vascular leak and the release of inflammatory cytokines. In both areas, IL-21 exhibited a favorable toxicity profile compared to that observed with IL-2 treatment in these models. There was no increase in inflammatory cytokines in the blood stream with IL-21 treatment, and the levels of vascular leak were significantly lower than that observed using IL-2. Additionally, mice receiving IL-21 appeared normal and healthy.

We intend to pursue malignant melanoma and renal cell carcinoma, the two approved indications for IL-2, as initial indications for IL-21. There are approximately 80,000 new cases of melanoma per year worldwide with approximately 50% of these cases occurring in North America. Melanoma is the cause of 8,000 deaths per year in North America. There are over 100,000 cases of renal cell carcinoma worldwide. There is a demonstrated need for new and improved therapies for both types of cancer. Subject to the outcome of the initial clinical studies, we intend to expand the IL-21 clinical program into additional cancer indications and, potentially, into the treatment of viral diseases.

Pursuant to an Option and License Agreement, Novo Nordisk has licensed the rights to IL-21 outside North America and we have retained all rights within North America. In December 2002, we entered into a collaborative preclinical development agreement with Novo Nordisk. Under our agreement, we are sharing all costs of the IL-21 preclinical development program with Novo Nordisk through the filing of an IND application in the United States. We plan to file an IND application and begin clinical development of IL-21 in the first half of 2004.

We own issued patents for IL-21 polypeptides, polynucleotides and methods of using IL-21 to stimulate immune responses, particularly in tumor-bearing subjects. We have filed patent applications for IL-21 antibodies, additional compositions and other methods of using IL-21 for the treatment of disease. We have also filed patent applications relating to IL-21 directed to methods for expressing and purifying recombinant IL-21, methods of treating specific oncological and viral diseases, and antagonist ligands.

Currently Marketed Products

We have participated in the discovery or development of five recombinant protein products marketed by other companies.

- Novolin® and NovoRapid® (insulin), recombinant human insulin products marketed by Novo Nordisk worldwide for the treatment of diabetes. In collaboration with Novo Nordisk, we developed a process for the production of recombinant human insulin in yeast that is used by Novo Nordisk.
- NovoSeven® (Factor VIIa), a protein involved in the generation of blood clots, marketed worldwide by Novo Nordisk for the treatment of hemophilia patients. We cloned the gene that codes for human Factor VII and developed a process for the production of activated recombinant human Factor VII, or Factor VIIa, which led to the establishment of the manufacturing process that Novo Nordisk currently uses to produce this protein.
- Regranex® (platelet-derived growth factor), a growth factor marketed by Ortho-McNeil Pharmaceuticals, Inc., a Johnson & Johnson company, for the treatment of non-healing diabetic ulcers. We cloned the gene that codes for platelet-derived growth factor and demonstrated the importance of this protein in stimulating wound healing.
- GlucaGen® (glucagon), a protein marketed by Novo Nordisk, Bedford Laboratories and Eisai Co., Ltd. for use as an aid for gastrointestinal motility inhibition and for the treatment of severe hypoglycemia in diabetic patients treated with insulin. In collaboration with Novo Nordisk, we developed a process for the production of this protein that is currently used by Novo Nordisk in the manufacture of GlucaGen.
- Cleactor™ (tPA analog), a modified form of the protein tissue plasminogen activator, marketed in Japan by Eisai for the treatment of myocardial infarction, or heart attacks. In collaboration with Eisai, we developed this modified protein, which has enhanced properties that allow it to be given as a single injection.

We earn royalties on sales of all these products except for NovoSeven and NovoRapid, for which we received a one-time payment to satisfy future royalty obligations. In the aggregate, we earned royalties of $9.4 million for the year ended December 31, 2003.

Discovery and Research Process

We have developed a fully integrated therapeutic protein discovery and research program that draws upon a broad range of skills and technologies, including DNA sequencing, bioinformatics, molecular and cellular biology, animal biology, protein chemistry, intellectual property protection, pharmacology, medical and regulatory affairs, drug formulation, manufacturing and strategic market research. We believe that this comprehensive program gives us a competitive advantage over many other biotechnology companies. While many of these companies were founded on the use of high-throughput DNA sequencing and bioinformatics to identify gene sequences of interest, we built our bioinformatics capabilities on top of our pre-existing strengths in molecular biology, protein chemistry and animal biology. As a result, we have been successful in characterizing important biological properties of our lead product candidates.

Bioinformatics

We have focused our discovery efforts on identifying the relatively small subset of genes that we believe have the highest probability of coding for proteins with therapeutic potential. We have defined what we consider to be the key protein categories according to structural similarity, sequence similarity and functional activity. These categories have known members with demonstrated therapeutic potential or potent biological activity, and most recombinant human proteins currently marketed as drugs are members of these categories. We believe that newly discovered proteins within these categories are likely to have important novel biological activity, and therefore may have potential as therapeutic products.

The foundation of our bioinformatics platform is our DNA sequence databases of millions of EST sequence entries and billions of nucleotide sequences derived from genomic sequences. In 1995, we became the first subscriber to gain direct in-house access to and analyze Incyte Genomics' LifeSeq database of ESTs. Since that time, we have built our internal sequence database from a number of sources, including:

- private databases, including Incyte Genomics' LifeSeq database;
- public EST and DNA sequences;
- our own internal EST sequences, where we have eliminated transcripts of highly expressed genes to concentrate on sequences of rarely expressed genes; and
- genomic sequences published by the Human Genome Project.

To discover novel gene sequences within the sequence databases, we have developed sensitive proprietary search algorithms based on protein motifs, which can include sequence homologies and predicted protein structure similarities. We have developed sophisticated threading algorithms that allow us to use distant and apparently unrelated elements in sequences to identify pre-defined three-dimensional structures contained within certain key protein categories. These algorithms are tailored to the specific category of proteins under consideration, as the optimal search strategy for novel gene sequences depends on characteristics unique to each protein category.

Exploratory Biology

We use a diverse set of tools to identify the biological functions of the genes and proteins we discover. Throughout our exploratory biology effort, we use a variety of in-house approaches, including physiological screens of mice in which the gene of interest has either been genetically over-expressed from birth, otherwise known as transgenic mice, or temporarily over-expressed in adult mice using an adenovirus containing the gene. We also conduct screens of mice in which the gene of interest has been eliminated from birth, otherwise known as knockout mice. In addition, we conduct analyses of disease models using a variety of laboratory tests, or assays, to detect changes in behavior, physiology and biochemistry. We also use hundreds of in-house assays to investigate biological activities of our novel proteins. To obtain additional information, our scientists either adapt or create *in vivo* laboratory models that mimic human diseases to determine the cause of disease and response to

treatment. For certain ligands, we can also apply laboratory techniques to clone the receptors for the ligand present in a tissue or cell. In addition to providing a marker for tissues that should respond to the protein, the receptors themselves can have therapeutic potential. We also rely on an external network of collaborators to investigate biology and conduct additional tests that we do not perform in-house.

Within our exploratory biology operation, there are several stages of activity through which we identify a protein's function, determine whether the protein plays a role in disease and determine whether it has commercial potential. A protein begins in the exploratory stage, in which experiments are performed to support the development of a biological hypothesis as to the protein's function. Once a biological hypothesis is developed, the protein moves to the validation stage, in which more extensive experiments are performed to confirm the biological hypothesis for the protein and to establish a medical hypothesis. A medical hypothesis involves the identification of specific diseases or conditions for which we believe the protein would have therapeutic importance. In cases where a protein demonstrates beneficial biological effects, it becomes a product candidate. Where a protein has been found to have detrimental effects, we attempt to generate a monoclonal antibody or soluble receptor to inhibit the activity of the protein. In those cases, a resulting monoclonal antibody or soluble receptor becomes the product candidate. Once a product candidate is identified, it moves to the pre-development stage, at which time it is tested in specific animal models of diseases. At the pre-development stage, we not only learn which diseases or conditions show promise for treatment, but also obtain information about dosing and systemic effects of the product candidate. Assuming positive results, both in terms of efficacy and toxicology, we may develop a commercial hypothesis for the product candidate. A commercial hypothesis requires the identification of a market opportunity and a preliminary determination that it will be economically feasible to manufacture the product candidate and administer it to patients.

Collaborative Relationships

Novo Nordisk Option Agreement

As part of our separation from Novo Nordisk, we granted Novo Nordisk options to license certain rights to potential therapeutic proteins pursuant to an option agreement. Under this agreement, we retain exclusive rights to these proteins in North America, and Novo Nordisk may obtain exclusive rights in the rest of the world. However, Novo Nordisk has the option to obtain exclusive worldwide rights to any licensed protein that acts to generate, expand or prevent the death of insulin-producing beta cells, which are involved in diabetes, a core business focus of Novo Nordisk. The option agreement also provides that:

- over a four-year period beginning November 10, 2000, Novo Nordisk will pay us a fee of $7.5 million per year for the option rights under the agreement;
- during this four-year period, Novo Nordisk may, for specified license payments, license up to the greater of eight proteins or 25% of all proteins discovered by us after August 25, 1995 and for which a hypothesis as to medical utility is generated, except for beta-cell-related proteins, of which Novo Nordisk may license an unlimited number; and
- Novo Nordisk may extend the option agreement for two years, during which time it is required to pay us a fee of $7.5 million per year for the right to license four additional proteins.

Under the option agreement, we must promptly disclose to Novo Nordisk each protein for which we develop a hypothesis as to medical utility, together with information known to us about the protein, such as gene sequence and similarity, exploratory data and relevant patent filings. Novo Nordisk then has 60 days to decide on three possible courses of action:

- exercise one of its options to license the protein;
- decline to exercise one of its options, thereby forgoing any and all future rights to the protein; or
- extend its option on the particular protein by paying a $500,000 extension fee and agreeing to pay half of our research and development costs to advance the protein to the status of a preclinical lead.

Upon the exercise of an option by Novo Nordisk, we will negotiate an exclusive license agreement to commercialize the protein containing certain predetermined terms, including up-front payments, milestone payments and royalty terms. The option agreement provides that up-front and milestone payments for each non-beta-cell-related protein licensed may total up to approximately $20 million, regardless of the point at which the protein is licensed. Up-front and milestone payments for beta-cell proteins licensed may total up to approximately $28 million. Royalty rates are lowest if an option to license a protein is exercised at the medical utility hypothesis stage and will increase substantially each time the option is extended. Royalty obligations end on the expiration date of the last-to-expire patent on the licensed protein or, if the product is not based on a patented protein, 12 years from the date of the first sale of the product. Royalty obligations may be reduced if Novo Nordisk is required to license third-party patented technology to utilize the licensed protein or if a generic product that is identical to a patented product achieves certain levels of market share.

If Novo Nordisk extends its option on a protein, then when the protein reaches the status of a preclinical lead meeting certain criteria, Novo Nordisk may exercise the option, extend the option or decline to exercise the option, in which case it forgoes any and all future rights to the protein. If Novo Nordisk elects to extend the option at the preclinical lead stage, it must pay us a $1.0 million extension fee and agree to pay two-thirds of our research and development costs to advance the protein through the completion of Phase 2 clinical trials. Upon completion of Phase 2 clinical trials, Novo Nordisk has one final opportunity to license the protein.

If, at any of Novo Nordisk's decision points, we decide that we do not wish to move forward in the development of a particular protein, then we have the right to terminate our participation in the development of the protein. In that case Novo Nordisk has the right to continue the research and development on its own, and maintains its right to license the protein under the option agreement.

To date, Novo Nordisk has licensed the rights to develop IL-21, IL-20 and IL-20 receptor outside North America pursuant to this agreement.

In December 2002, we announced that we had signed a collaborative agreement with Novo Nordisk for the preclinical development of IL-21. Under the terms of the agreement, we and Novo Nordisk are collaborating on all research and development activities leading up to the filing of an IND application in the United States. Novo Nordisk reimbursed us for a portion of our costs incurred prior to the agreement, and the two companies will equally share all costs of the program going forward. As of December 31, 2003, we have received or accrued $8.9 million under the agreement.

Serono S.A.

In August 2001, we entered into a collaborative development and marketing agreement with Ares Trading S.A., a wholly owned subsidiary of Serono S.A., focused on two preclinical product candidates derived from our discovery research. These two candidates are based on cellular receptors, designated TACI and BCMA, that are involved in the regulation of the human immune system. During the term of the agreement, we and Serono will work together exclusively to develop biopharmaceutical products based on the two receptors for the treatment of autoimmune diseases such as systemic lupus erythematosus and rheumatoid arthritis.

We share research and development expenses worldwide with the exception of Japan, where Serono covers all expenses. The research and development activities are governed by a steering committee made up of an equal number of representatives from each company. Serono is responsible for manufacturing all products for both clinical trials and commercial sale. We retain an option to co-promote the sale of products with Serono in North America, which we can exercise provided that we fund our share of the research and development expenses and meet certain sales force and marketing requirements. If we exercise the co-promotion option, we will share commercialization expenses and profits in North America equally with Serono and Serono will have exclusive rights to market and sell products in the rest of the world, for which we will be entitled to receive royalties. In the event of certain changes in control of our company, we could lose our right to co-promote products in North America.

Either company may terminate its co-development and co-funding obligations upon 90 days' notice until the start of Phase 2 clinical trials, after which time 180 days' notice is required. If we were to terminate our co-development and co-funding obligations, Serono would take control of all research and development, we would forgo our co-promotion rights in North America, we would be entitled to receive royalties on any product sales in North America in lieu of sharing in the profits from the sale of products and Serono would continue to be obligated to make any milestone payments. If Serono were to terminate its co-development and co-funding obligations, all rights in any products would revert to us, and we could take control and fund all costs of the research and development, subject to negotiation of commercially reasonable financial consideration to be paid to Serono. Furthermore, if clinical trials had begun prior to Serono's termination, Serono would be obligated to manufacture product for use in clinical testing for up to one year from the termination date.

We granted Serono an exclusive license to our intellectual property relating to TACI, BCMA and certain other related technologies to make, use, have made, sell, offer to sell and import products based on TACI and BCMA. Serono is required to pay royalties on sales, which may vary based on annual sales volume and the degree of patent protection provided by the licensed intellectual property. Royalty payments may be reduced if Serono is required to license additional intellectual property from one or more third parties in order to commercialize a product or, in certain circumstances, if a product suffers from competition. Royalty obligations under the agreement continue on a country-by-country basis until the date on which no valid patent claims relating to a product exist or, if the product is not covered by a valid patent claim, 15 years from the date of first sale of the product.

The term of the agreement began on August 30, 2001 and will continue for as long as a TACI or BCMA product is the subject of an active development project or there is an obligation to pay royalties under the agreement. The agreement provides for an initial fee and milestone payments to be paid by Serono in connection with the development and approval of products, up to an aggregate of $52.5 million.

Out-licensed Product Candidates

In addition to the five products currently on the market, we have contributed to the discovery and development of several product candidates that we have out-licensed to third parties in return for milestone payments and royalties:

- Platelet-derived growth factor, a growth factor that stimulates the growth of a variety of cell types. We have out-licensed this growth factor to BioMimetic Pharmaceuticals, Inc. (BMPI), originally for the treatment of periodontal disease and bone defects of the head and face, and more recently for the treatment of all other bone defects. BMPI has completed a pivotal study of platelet-derived growth factor in periodontal disease.
- Platelet-derived growth factor receptor antibody, an antibody that blocks the binding of platelet-derived growth factor to its beta receptor, which we have out-licensed to Celltech Group plc. Celltech completed a Phase 2 proof-of-concept study in cancer and indicated that they intend to partner the product candidate with a company possessing significant oncology development experience. More recently, in March 2004, Celltech announced its discontinuation of the program.
- Alpha 1-antitrypsin, a protease inhibitor, which we have out-licensed to Arriva Pharmaceuticals, Inc. and which is being developed for the treatment of respiratory diseases and dermatological conditions, including atopic dermatitis. Arriva has initiated Phase 2 clinical trials of Alpha 1-antitrypsin.

Other Collaborations

We recognize external collaborations as an important aspect of our success in analyzing and characterizing protein function. Where possible, we establish collaborations with experts in the field who have a depth of knowledge on a select protein, protein category or disease state that is related to the understanding of our gene and protein discoveries. These collaborations serve to accelerate the rate at which we can assess the biological

functions of proteins and confirm medical hypotheses. In addition, throughout our history, we have collaborated actively with the University of Washington, a leading biomedical research institution, to explore the biological function of proteins. The University's significant resources and expertise, together with its geographic proximity to us, have made it a valuable partner on a number of our projects.

Manufacturing

Currently, we have internal capabilities to manufacture products at up to 100-liter scale using various production systems, including yeast, E. coli and mammalian cells. Generally, we have used these facilities for process development and the manufacture of product for nonclinical studies supporting our research and development programs. Recently, we converted certain of these facilities for the manufacture of prethrombin in compliance with GMP regulations. We began construction in 2003 of an expanded research and development facility that will include additional small-scale GMP manufacturing suites to be used to supply product for toxicology studies and clinical trials. Until these dedicated suites are available in late 2004, we intend to utilize third-party contract manufacturers or to rely on co-development partners for the manufacture of clinical-grade product.

For rFactor XIII, which is made in yeast, large-scale manufacturing of preclinical and clinical grade product is being performed by Avecia Limited. We have entered into a contract manufacturing agreement with Abbott Laboratories for the commercial scale production of rhThrombin, which is made in mammalian cells. Serono will manufacture TACI-Ig, which is made in mammalian cells, under the terms of our collaborative development and marketing agreement. Avecia Limited has manufactured our initial clinical supply of IL-21, which is manufactured in E. coli.

Some of the inventions licensed to us were initially developed at universities or other not-for-profit institutions with funding support from an agency of the United States government. In accordance with federal law, we or our licensees may be required to manufacture products covered by patents in those inventions in the United States, unless we can obtain a waiver from the government on the basis that such domestic manufacture is not commercially feasible.

Commercialization

We have developed the following three-pronged strategy for the development and commercialization of our product candidates:

Internal development. We intend to independently develop products for North America that we believe can be successfully developed with our current infrastructure, as well as additions made to our infrastructure over the next few years. To qualify for internal development, product candidates must satisfy a number of criteria. Formulation, development and manufacturing of these products must initially be feasible through the use of contract providers. The anticipated clinical trials must be of a reasonable size and with fairly well-defined endpoints and guidelines. Finally, the clinical indication and target market must be accessible with a relatively small sales force. We believe that certain of our product candidates, including rhThrombin, rFactor XIII and IL-21, meet these criteria.

Co-development. We intend to develop certain product candidates jointly with other companies. In these arrangements, we would expect to pay a share of the research and development costs, retain rights to co-promote or co-market the potential products, and share in the profits from selling the potential products. Our criteria for selecting product candidates for co-development include our level of internal expertise related to the field, manufacturing requirements, clinical trial size and complexity, target market size and investment considerations. If we determine that it is desirable to invest our capital in a development program for a product candidate, but we do not believe that we can internally meet the development requirements, we will seek a co-development partner. TACI-Ig meets the criteria for co-development, and we have entered into a collaborative development and marketing agreement with Serono to co-develop this product candidate.

Out-licensing. We intend to derive value from other product candidates through out-licensing to other biotechnology or pharmaceutical companies. From out-licensing transactions, we would expect to earn up-front license fees, milestone payments and royalties on sales. We would expect no ongoing participation, financial or otherwise, in development activities of these licensed products.

Patents and Proprietary Rights

We intend to seek appropriate patent protection for our proprietary technologies by filing patent applications in the United States. We have more than 270 issued or allowed United States patents, and over 260 pending United States patent applications. When appropriate, we also seek foreign patent protection and to date have more than 500 issued or allowed foreign patents.

Our success will depend in large part on our ability to:

- obtain patent and other proprietary protection for the genes and proteins we discover;
- enforce and defend patents once obtained;
- operate without infringing the patents and proprietary rights of third parties; and
- preserve our trade secrets.

Our patents and patent applications are directed to composition of matter, methods of use and enabling technologies. Although we believe our patents and patent applications provide a competitive advantage, the patent protection available for genes and therapeutic protein-based products is highly uncertain and involves complex legal and factual questions. No clear policy has emerged regarding the breadth of patents in this area. There have been, and continue to be, intensive discussions concerning the scope of patent protection for partial gene sequences, full-length genes and their corresponding proteins. Also, there is substantial uncertainty regarding patent protection for genes without known function or correlation with specific diseases. Social and political opposition to patents on genes may lead to narrower patent protection for genes and their corresponding proteins. Patent protection relating to genes and therapeutic protein-based products is also subject to a great deal of uncertainty outside the United States, and patent laws are currently undergoing review and revision in many countries. Changes in, or different interpretations of, patent laws in the United States and other countries may result in our inability to obtain patents covering the genes or proteins we discover or to enforce patents that have been issued to us, and may allow others to use our discoveries to develop and commercialize therapeutic protein-based products.

We apply for patents covering our discoveries and technologies as we deem appropriate. However, we may fail to apply for patents on important discoveries or technologies in a timely fashion or at all. Also, our pending patent applications may not result in the issuance of any patents. These applications may not be sufficient to meet the statutory requirements for patentability, and therefore we may be unable to obtain enforceable patents covering the related discoveries or technologies we may want to commercialize. In addition, because patent applications in the United States until recently have been maintained in secrecy until a patent issues, other parties may have filed patent applications on genes or their corresponding proteins before we filed applications covering the same genes or proteins, and we may not be the first to discover these genes or proteins. Any patent applications filed by third parties may prevail over our patent applications or may result in patents that issue alongside patents issued to us, leading to uncertainty over the scope of the patents or the freedom to practice the claimed inventions.

Although we have a number of issued patents, the discoveries or technologies covered by these patents may not have any therapeutic or commercial value. Also, issued patents may not provide commercially meaningful protection against competitors. Other parties may be able to design around our issued patents or independently develop products having effects similar or identical to our patented product candidates. Some companies are currently attempting to develop therapeutic protein-based products substantially equivalent to products patented

by other parties by altering the amino acid sequence within the therapeutic protein-based product and declaring the altered product a new product. It may be easier to develop substantially equivalent versions of therapeutic protein-based products such as monoclonal antibodies and soluble receptors than it is to develop substantially equivalent versions of the proteins with which they interact because there is often more than one antibody or receptor that has the same therapeutic effect. Consequently, any existing or future patents we have that cover monoclonal antibodies or soluble receptors may not provide any meaningful protection against competitors. In addition, the scope of our patents is subject to considerable uncertainty and competitors or other parties may obtain similar patents of uncertain scope. For example, other parties may discover uses for genes or proteins different from the uses covered in our patents, and these other uses may be separately patentable. If another party holds a patent on the use of a gene or protein, then even if we hold the patent covering the composition of matter of the gene or protein itself, that other party could prevent us from selling any product directed to such use. Also, other parties may have patents covering the composition of matter of genes or proteins for which we have patents covering only methods of use of these genes or proteins. Furthermore, the patents we hold relating to recombinant human proteins, such as our patents covering rhThrombin or rFactor XIII, may not prevent competitors from developing, manufacturing or selling other versions of these proteins. Moreover, although we hold patents relating to the manufacture of recombinant human thrombin, we have limited composition of matter patent protection covering thrombin. Accordingly, we may not be able to prevent other parties from commercializing competing forms of recombinant human thrombin.

Third parties may infringe our patents or may initiate proceedings challenging the validity or enforceability of our patents. The issuance of a patent is not conclusive as to its validity or enforceability. Challenges raised in patent infringement litigation we initiate or in proceedings initiated by third parties may result in determinations that our patents have not been infringed or that they are invalid, unenforceable or otherwise subject to limitations. In the event of any such determinations, third parties may be able to use the discoveries or technologies claimed in our patents without paying licensing fees or royalties to us, which could significantly diminish the value of these discoveries or technologies. Also, as a result of such determinations we may be enjoined from pursuing research, development or commercialization of potential products or may be required to obtain licenses, if available, to the third-party patents or to develop or obtain alternative technology. Responding to challenges initiated by third parties may require significant expenditures and divert the attention of our management and key personnel from other business concerns. In addition, enforcing our patents against third parties may require significant expenditures regardless of the outcome of such efforts.

In addition, third parties may independently develop intellectual property similar to our patented intellectual property, which could result in, among other things, interference proceedings in the United States Patent and Trademark Office to determine priority of invention. An interference proceeding is an administrative proceeding to determine which party was first to invent the contested subject matter. Responding to interference proceedings or other challenges initiated by third parties may require significant expenditures and divert the attention of our management and key personnel from other business concerns.

Third parties may claim that our potential products or related technologies infringe their patents. Patent litigation is very common in the biopharmaceutical industry, and the risk of infringement claims is likely to increase as the industry expands and as other companies obtain more patents and increase their efforts to discover genes through automated means and to develop proteins. Any patent infringement claims that might be brought against us may cause us to incur significant expenses, divert the attention of our management and key personnel from other business concerns and, if successfully asserted against us, require us to pay substantial damages. In addition, as a result of a patent infringement suit, we may be forced to stop or delay developing, manufacturing or selling potential products that are claimed to infringe a patent covering a third party's intellectual property unless that party grants us rights to use its intellectual property. We may be unable to obtain these rights on terms acceptable to us, if at all. Even if we are able to obtain rights to a third party's patented intellectual property, these rights may be nonexclusive, thereby giving our competitors access to the same intellectual property. Ultimately, we may be unable to commercialize our potential products or may have to cease some of our business operations as a result of patent infringement claims.

In addition to our patented intellectual property, we also rely on unpatented technology, trade secrets and confidential information, including our genetic sequence database and our bioinformatics algorithms. Our policy is to require our employees, consultants and advisors to execute a confidentiality and proprietary information agreement before beginning their employment, consulting or advisory relationship with us. These agreements generally provide that the individual must keep confidential and not disclose to other parties any confidential information developed or learned by the individual during the course of the individual's relationship with us except in limited circumstances. These agreements also generally provide that we shall own all inventions conceived by the individual in the course of rendering services to us. The agreements may not provide effective protection of our technology or confidential information or, in the event of unauthorized use or disclosure, may not provide adequate remedies.

As part of our business strategy, we work with third parties in our research and development activities. Accordingly, disputes may arise about inventorship and corresponding rights to know-how and inventions resulting from the joint creation or use of intellectual property by us and our corporate partners, licensors, scientific collaborators and consultants. In addition, other parties may circumvent any proprietary protection we do have. These parties may independently develop equivalent technologies or independently gain access to and disclose substantially equivalent information, and confidentially agreements and material transfer agreements we have entered into with them may not provide us with effective protection.

Government Regulation

Regulation by government authorities in the United States, Europe, Japan and other countries is a significant consideration in our ongoing research and product development activities and in the manufacture and marketing of our potential products. The FDA and comparable regulatory bodies in other countries currently regulate therapeutic proteins and related pharmaceutical products as biologics. Biologics are subject to extensive pre- and post-market regulation by the FDA, including regulations that govern the collection, testing, manufacture, safety, efficacy, potency, labeling, storage, record keeping, advertising, promotion, sale and distribution of the products. The time required for completing testing and obtaining approvals of our product candidates is uncertain but will take several years. Any delay in testing may hinder product development. In addition, we may encounter delays in product development or rejections of product applications due to changes in FDA or foreign regulatory policies during the period of product development and testing. Failure to comply with regulatory requirements may subject us to, among other things, civil penalties and criminal prosecution; restrictions on product development and production; suspension, delay or withdrawal of approvals; and the seizure or recall of products. The lengthy process of obtaining regulatory approvals and ensuring compliance with appropriate statutes and regulations requires the expenditure of substantial resources. Any delay or failure, by us or our corporate partners, to obtain regulatory approvals could adversely affect our ability to commercialize product candidates, receive royalty payments and generate sales revenue.

The nature and extent of the governmental pre-market review process for our potential products will vary, depending on the regulatory categorization of particular products. The necessary steps before a new biological product may be marketed in the United States ordinarily include:

- nonclinical laboratory and animal tests;
- compliance with product manufacturing requirements including, but not limited to, current GMP regulations;
- submission to the FDA of an investigational new drug (IND) application, which must become effective before clinical trials may commence;
- completion of adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of a biologics license application; and
- FDA review and approval of the biologics license application prior to any commercial sale or shipment of the product.

Nonclinical tests include laboratory evaluation of the product, as well as animal studies to assess the potential safety concerns and efficacy of the product. Nonclinical safety tests must be conducted by laboratories that comply with current Good Laboratory Practices regulations. The results of nonclinical tests, together with extensive manufacturing information, analytical data and proposed clinical trial protocols, are submitted to the FDA as part of an investigational new drug (IND) application, which must become effective before the initiation of clinical trials. The IND application will automatically become effective 30 days after receipt by the FDA unless the FDA indicates prior to the end of such 30-day period that the application does not contain sufficient information to permit initiation of the clinical studies. If the FDA raises any concerns related to the clinical program, it is possible that these concerns will not be resolved quickly, if at all. In addition, the FDA may impose a clinical hold on a proposed or ongoing clinical trial if, for example, safety concerns arise, in which case the trial cannot commence or recommence without FDA authorization under terms sanctioned by the agency.

Clinical trials involve the administration of the product to healthy volunteers or to patients under the supervision of a qualified principal investigator. Clinical trials are conducted in accordance with current Good Clinical Practices regulations under protocols that detail the objectives of the trial, inclusion and exclusion criteria, the parameters to be used to monitor safety and the efficacy criteria to be evaluated. Protocols for each phase of the clinical trials are submitted to the FDA as an amendment to the IND application. Further, each clinical trial must be reviewed and approved by an independent institutional review board at each institution. The institutional review board will consider, among other things, ethical factors, the safety of human subjects and the possibility of liability of the institution conducting the trial. An institutional review board may require changes in a protocol, and the submission of an investigational new drug application does not guarantee that a trial will be initiated or completed.

Clinical trials generally are conducted in three sequential phases that may overlap. In Phase 1, the initial product is administered to healthy human subjects or patients, or both, to assess safety, metabolism, pharmacokinetics and pharmacological actions associated with increasing doses. Phase 2 usually involves trials in a limited patient population to evaluate the efficacy of the potential product for specific, targeted indications, to determine dosage tolerance and optimum dosage, and to further identify possible adverse reactions and safety risks. If a compound appears to be effective and to have an acceptable safety profile in Phase 2 evaluations, Phase 3 trials may be undertaken to evaluate further clinical efficacy in comparison to standard therapies, generally within a broader patient population at geographically dispersed clinical sites. Phase 3 protocols are reviewed with the FDA to establish endpoints and data handling parameters. Phase 1, Phase 2 or Phase 3 testing may not be completed successfully within any specific period of time, if at all, with respect to any of our potential products. Furthermore, we, an institutional review board, the FDA or other regulatory bodies may suspend a clinical trial at any time for various reasons, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

The results of pharmaceutical development, nonclinical studies and clinical trials are submitted to the FDA in the form of a biologics license application for approval of the manufacture, marketing and commercial shipment of the biological product. The biologics license application contains extensive manufacturing information, and each manufacturing facility must be inspected and approved by the FDA before a biologics license application can be approved. The testing and approval process is likely to require substantial time, effort and resources, and necessary approvals may not be granted on a timely basis, if at all. The FDA may deny a biologics license application if applicable regulatory criteria or clinical endpoints have not been met. The FDA may also require additional testing of the product or other information, or require post-market testing and surveillance to monitor the safety or efficacy of the product. In addition, after marketing approval is granted, the FDA may require post-marketing clinical trials, which typically entail extensive patient monitoring and may result in restricted marketing of an approved product for an extended period of time.

Some of our product candidates may qualify as orphan drugs under the Orphan Drug Act of 1983. This act generally provides incentives to manufacturers who undertake development and marketing of products to treat relatively rare diseases, defined as those diseases that affect fewer than 200,000 persons annually in the United States. A drug that receives orphan drug designation by the FDA and is the first product to receive FDA marketing

approval for its product claim is entitled to various advantages, including a seven-year exclusive marketing period in the United States for that product claim. However, any new orphan drug that is under review by the FDA for the same or similar product claim will not be precluded from sale in the United States during the seven-year exclusivity period of the approved orphan drug, if the new product is significantly different or clinically superior to the approved orphan drug. It is possible that none of our product candidates will be designated as an orphan drug by the FDA. Also, if one of our products receives orphan drug designation, that may not have a positive effect on our revenues.

To manufacture and sell our potential products, a domestic or foreign drug manufacturing facility must pass an FDA inspection of the facility. The facilities are inspected for compliance with applicable requirements, including current Good Manufacturing Practice (cGMP) guidelines and must submit to continued periodic inspection by the FDA. In addition, the FDA imposes a number of complex regulations on entities that advertise and promote biologics, including, among others, standards and regulations for direct-to-consumer advertising, off-label promotions, industry-sponsored scientific and educational activities, and promotional activities involving the Internet. The FDA has very broad enforcement authority under the Federal Food, Drug and Cosmetic Act, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing us to correct deviations from FDA standards, a requirement that future advertising and promotional materials be pre-cleared by the FDA, and civil and criminal penalties.

FDA marketing approval is only applicable in the U.S. Marketing approval in foreign countries is subject to the regulations of those countries. The approval procedures vary among countries and can involve additional testing. The time required to obtain approval may differ from that required for FDA approval. Although there are some centralized procedures for filings in the European Union countries, in general each country has its own procedures and requirements, and compliance with these procedures and requirements may be expensive and time-consuming. Accordingly, there may be substantial delays in obtaining required approvals from foreign regulatory authorities after the relevant applications are filed, if we ultimately receive any approvals at all.

We are also subject to various federal, state and local laws, regulations and recommendations relating to safe working conditions, laboratory and manufacturing practices, the experimental use of animals, and the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our work. Government regulations that might result from future legislation or administrative action, including additions or changes to environmental laws, may materially affect our business operations and revenues.

Competition

We compete with others to identify, establish uses for and patent as many genes and their corresponding proteins as possible and to commercialize the products we develop from these genes and proteins. We face competition from other entities using sophisticated bioinformatics technologies to discover genes, including Genentech, Inc., Human Genome Sciences, Inc., Curagen, Inc. and Amgen Inc. We also face competition from entities using more traditional methods to discover genes related to particular diseases, including other large biotechnology and pharmaceutical companies. We expect that competition in our field will continue to be intense.

Research to identify genes is also being conducted by various institutes and government-financed entities in the United States and in foreign countries, including France, Germany, Japan and the United Kingdom, as well as by numerous smaller laboratories associated with universities or other not-for-profit entities. In addition, a number of pharmaceutical and biotechnology companies and government-financed programs are engaged or have announced their intention to engage in areas of research similar to or competitive with our focus on gene discovery, and other entities are likely to enter the field.

We believe the principal competitive factors affecting our markets are:

- rights to develop and commercialize therapeutic protein-based products, including appropriate patent and proprietary rights;
- safety and effectiveness of therapeutic protein-based products;
- the timing and scope of regulatory approvals;
- the cost and availability of these products;
- the availability of appropriate third-party reimbursement programs; and
- the availability of alternative therapeutic products or treatments.

Although we believe that we are well positioned to compete adequately with respect to these factors in the future, our future success is currently difficult to predict because we are an early stage company; many of our internal product candidates have yet to undergo clinical trials. Also, although we believe that our bioinformatics technologies and exploratory biology capabilities provide us with a competitive advantage, any of the companies or other entities we compete with may discover and establish a patent position in one or more genes or proteins that we have identified and designated or considered designating as a product candidate. In addition, any potential products based on genes or proteins we identify will face competition both from companies developing gene- or protein-based products and from companies developing other forms of treatment for diseases that may be caused by, or related to, the genes or proteins we identify. Furthermore, our potential products, if approved and commercialized, may compete against well-established existing therapeutic protein-based products, many of which may be currently reimbursed by government health administration authorities, private health insurers and health maintenance organizations. Also, health care professionals and consumers may prefer existing or newly developed products to any product we develop.

Employees

As of December 31, 2003, we had 360 full-time employees, approximately 290 of whom are dedicated to research and development. Each of our employees has signed a confidentiality agreement, and no employees are covered by a collective bargaining agreement. We have never experienced employment-related work stoppages and consider our employee relations to be good.

Important Factors That May Affect Our Business, Our Results of Operations and Our Stock Price

Risks Related to Our Business

We have limited experience in developing products.

We have not yet developed or commercialized any products on our own. Our contributions to the discovery or development of certain therapeutic proteins currently on the market do not indicate that we will be able to successfully develop products alone. Our work relating to these marketed products generally did not include clinical trials or manufacturing, and we did not participate in marketing or other late-stage development or commercialization activities. We have limited experience with product development activities and may not be successful in developing or commercializing any products.

Any failure or delay in commencing or completing clinical trials for product candidates could severely harm our business.

The successful commercialization of any product candidates will depend on regulatory approval in each market in which our collaborators, our licensees or we intend to market the product candidates. Each of our product candidates must undergo extensive nonclinical studies and clinical trials as a condition to regulatory approval. Nonclinical studies and clinical trials are time-consuming and expensive and together take several

years to complete, and to date we have not completed the clinical testing of any product candidate on our own. The commencement and completion of clinical trials for our product candidates may be delayed by many factors, including:

- our inability or the inability of our collaborators or licensees to manufacture or obtain from third parties materials sufficient for use in nonclinical studies and clinical trials;
- delays in patient enrollment and variability in the number and types of patients available for clinical trials;
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data;
- ineffectiveness of product candidates during the clinical trials;
- unforeseen safety issues or side effects; and
- governmental or regulatory delays.

It is possible that none of our product candidates, whether developed on our own, with collaborators or by licensees, will complete clinical trials in any of the markets in which we, our collaborators or licensees intend to sell those product candidates. Accordingly, our collaborators, our licensees or we may not receive the regulatory approvals needed to market our product candidates in any markets. Any failure or delay in commencing or completing clinical trials or obtaining regulatory approvals for our product candidates could severely harm our business.

Clinical trials may fail to demonstrate the safety and effectiveness of our product candidates, which could prevent or significantly delay their regulatory approval.

Clinical trials involving our product candidates may reveal that those candidates are ineffective, have unacceptable toxicity or have other unacceptable side effects. In addition, data obtained from tests are susceptible to varying interpretations, which may delay, limit or prevent regulatory approval. Likewise, the results of preliminary studies do not predict clinical success, and larger and later-stage clinical trials may not produce the same results as earlier-stage trials. Frequently, product candidates that have shown promising results in early clinical trials have subsequently suffered significant setbacks in later clinical trials. In addition, clinical trials of potential products often reveal that it is not practical or feasible to continue development efforts for these product candidates. For example, in 2004, Celltech Group plc discontinued development of platelet-derived growth factor receptor antibody, a product candidate that Celltech licensed from us. Celltech concluded that the Phase 2 clinical trial results did not justify further development of the product candidate.

We may be unable to satisfy the rigorous government regulations relating to the development and commercialization of our product candidates.

Any failure to receive the regulatory approvals necessary to commercialize our product candidates could severely harm our business. Our product candidates are subject to extensive and rigorous government regulation. The FDA regulates, among other things, the collection, testing, manufacturing, safety, efficacy, potency, labeling, storage, record keeping, advertising, promotion, sale and distribution of therapeutic products. If our potential products are marketed abroad, they will also be subject to extensive regulation by foreign governments. None of our product candidates has been approved for sale in the United States or any foreign market, and we have only limited experience in filing and pursuing applications necessary to gain regulatory approvals.

The regulatory review and approval process, which includes nonclinical studies and clinical trials of each product candidate, is lengthy, expensive and uncertain. Securing FDA approval requires the submission of extensive nonclinical and clinical data and supporting information to the FDA for each indication to establish the product candidate's safety and effectiveness. The approval process typically takes many years to complete and may involve ongoing requirements for post-marketing studies. In addition, we may not achieve FDA approval of

a product candidate even if we have met our internal safety and efficacy criteria and completed clinical trials. Also, any FDA or other regulatory approval of our product candidates, once obtained, may be withdrawn. Government regulation may result in:

- prohibitions or significant delays in the marketing of potential products;
- discontinuation of marketing of potential products; and
- limitations of the indicated uses for which potential products may be marketed.

If we fail to comply with the laws and regulations pertaining to our business, we may be subject to sanctions, including the temporary or permanent suspension of operations, product recalls, marketing restrictions and civil and criminal penalties.

Because we currently do not have the capability to manufacture materials for clinical trials or for commercial sale, we will have to rely on third parties to manufacture our potential products, and we may be unable to obtain required quantities in a timely manner or on acceptable terms, if at all.

We currently do not have the manufacturing facilities necessary to produce materials for clinical trials or commercial sale, and we have only limited capabilities to produce materials for nonclinical studies. We intend to rely on collaborators and third-party contract manufacturers and suppliers to produce or provide the quantities of drug materials needed for nonclinical studies, clinical trials and commercialization of our potential products. We will have to rely on these manufacturers and suppliers to deliver materials on a timely basis and to comply with regulatory requirements, including current GMP regulations enforced by the FDA through its facilities inspection program. These manufacturers and suppliers may not be able to meet our needs with respect to timing, quantity or quality of materials, and may fail to satisfy applicable regulatory requirements with respect to the manufacturing of these materials. In addition, agreements that we have entered into with third-party contract manufacturers in the past contain, and any contracts that we enter into with third-party contract manufacturers in the future may contain, limitations on the quantities of drug materials that such manufacturers will produce, and we may not be able to increase or decrease the supply of drug materials based on unanticipated changes in demand. If we are unable to contract for a sufficient supply of needed materials on acceptable terms, or if we encounter delays in the delivery of materials from, or difficulties in our relationships with, manufacturers, our IND-enabling nonclinical studies and clinical trials may be delayed. Delays in nonclinical studies could postpone the filing of IND applications or the initiation of clinical trials, and delays in clinical trials could postpone the subsequent submission of product candidates for regulatory approval and market introduction.

We may not be successful in developing internal manufacturing capabilities or complying with applicable manufacturing regulations.

We are in the process of expanding our facilities to include dedicated small-scale GMP manufacturing suites for the production of therapeutic proteins for use in nonclinical and clinical testing. We may be unable to establish the internal manufacturing capabilities necessary to develop our potential products. Therapeutic proteins are often more difficult and expensive to manufacture than other classes of drugs, and the manufacture of therapeutic proteins may not be commercially feasible. Also, we will be required to adhere to rigorous GMP regulations in the manufacture of therapeutic proteins. Assuming we successfully complete construction of our planned small-scale GMP manufacturing suites, we will need to hire and train employees to staff them. These initial manufacturing suites will not provide us with the capability to produce drug materials for commercial sale. To develop this capability we would need to acquire larger manufacturing facilities. If any of our future facilities cannot pass a pre-approval plant inspection, the FDA marketing approval of our product candidates may not be granted. In complying with these regulations and any applicable foreign regulatory requirements, we will be obligated to expend time, money and effort in production, record keeping and quality assurance to assure that our potential products meet applicable specifications and other requirements. Any failure to comply with these requirements may subject us to regulatory sanctions and delay or interrupt our development and commercialization efforts.

In addition, some of the inventions licensed to us were initially developed at universities or other not-for-profit institutions with funding support from an agency of the United States government. In accordance with federal law, our licensees or we may be required to manufacture products covered by patents in those inventions in the United States, unless we can obtain a waiver from the government on the basis that such domestic manufacture is not commercially feasible. We have not attempted to secure any such waivers from the government, and do not know if they would be available if sought. If we are not able to obtain such waivers on a timely basis, we might be forced to seek manufacturing arrangements at higher prices, or on otherwise less favorable terms, than might be available to us in the absence of this domestic manufacturing requirement.

Because we will depend on third parties to conduct laboratory tests and clinical trials, we may encounter delays in or lose some control over our efforts to develop product candidates.

We will rely on third parties to design and conduct laboratory tests and clinical trials for us. If we are unable to obtain these services on acceptable terms, we may not be able to complete our product development efforts in a timely manner. Also, because we will rely on third parties for laboratory tests and clinical trials, we may lose some control over these activities or be unable to manage them appropriately, or may become too dependent on these parties. These third parties may not complete the tests or trials on schedule or when we request, and the tests or trials may be methodologically flawed or otherwise defective. Any delays or difficulties associated with third-party laboratory tests or clinical trials may delay the development of our product candidates.

Because we currently have no sales or marketing capabilities, we may be unable to successfully commercialize our potential products.

We currently have no direct sales capabilities or marketing capabilities. We expect that in the future we will rely on collaborators or other third parties to market products that we may develop. These third parties may not be successful in marketing our potential products, and we will have little or no control over their marketing efforts. In addition, we may co-promote our potential products or retain marketing rights in North America to these products. If we decide to market products directly, we will need to incur significant additional expenses and commit significant additional management resources to develop effective sales and marketing capabilities. We may not be able to establish these capabilities despite these additional expenditures. In addition, co-promotion or other marketing arrangements with third parties to commercialize potential products could significantly limit the revenues we derive from these products.

Our bioinformatics-based discovery strategy is unproven, and we may not be able to discover any genes or proteins of commercial value.

We do not know whether our bioinformatics-based therapeutic protein discovery strategy will yield commercially valuable products because we are in the early stages of development. For most of our corporate existence, we relied on exploratory biology to study particular diseases and medical conditions and to find potential treatments. We shifted our emphasis to bioinformatics-based discovery relatively recently. Bioinformatics is the use of high-powered computers, software and analytical tools to interpret DNA sequence data and to assist in identifying those genes and proteins that are likely to play a meaningful role in human health. We use bioinformatics to discover genes and their corresponding proteins in genomic databases, with the goal of developing therapeutic protein-based products based on these discoveries. We have focused our efforts on certain key protein categories, some of which have yielded successful products in the past. Prior successes of other companies in commercializing protein-based products derived from these categories provide no indication that we will be able to establish the medical utility of any therapeutic proteins within these categories beyond those that have already been identified. In addition, some of the protein categories we concentrate on have not yielded any successful therapeutic protein products or late-stage clinical trial candidates. Research and development efforts we expend on these categories may prove ineffective and may detract from our efforts to discover and develop therapeutic proteins within those categories that have shown more promise. Also, by focusing on specific categories of proteins, we may overlook other therapeutic proteins not contained in these

categories that ultimately will be successfully commercialized by others. We have only recently begun clinical testing of our first product candidates discovered through our bioinformatics-based efforts, and we are not aware of any other company that has successfully commercialized products derived from bioinformatics-based research. Our bioinformatics-based strategy may not result in the successful development or commercialization of any products.

The availability of novel genomic data continues to decrease, which negatively affects our ability to discover entirely novel therapeutic proteins.

We have relied on the generation of new genomic data for the discovery of novel genes and proteins. Because the flow of genomic data has slowed, it has become increasingly difficult for us to discover novel genes through the analysis of this data. This decrease in the rate of generation of novel sequence data has impaired our ability to discover entirely novel therapeutic proteins, and we will need to continue to develop approaches to find difficult-to-recognize proteins in order to discover novel proteins.

Our patent applications may not result in issued patents, and our competitors may commercialize the discoveries we attempt to patent.

Our pending patent applications covering genes and their corresponding proteins may not result in the issuance of any patents. These applications may not be sufficient to meet the statutory requirements for patentability, and therefore we may be unable to obtain enforceable patents covering the related therapeutic protein-based product candidates we may want to commercialize. In addition, other parties have filed or may file patent applications that cover genes, proteins or related discoveries or technologies similar or identical to those covered in our patent applications. Because patent applications in the United States until recently have been maintained in secrecy until a patent issues, other parties may have filed patent applications on genes or their corresponding proteins before we filed applications covering the same genes or proteins, and we may not be the first to discover these genes or proteins. Any patent applications filed by third parties may prevail over our patent applications or may result in patents that issue alongside patents issued to us, leading to uncertainty over the scope of the patents or the freedom to practice with respect to the claimed inventions.

Third parties may infringe our patents or challenge their validity or enforceability.

Third parties may infringe our patents or may initiate proceedings challenging the scope, validity or enforceability of our patents. The issuance of a patent is not conclusive as to its scope, validity or enforceability. Challenges raised in patent infringement litigation we initiate or in proceedings initiated by third parties may result in determinations that our patents have not been infringed or that they are invalid, unenforceable or otherwise subject to limitations. In the event of any such determinations, third parties may be able to use the discoveries or technologies claimed or described in our patents without paying licensing fees or royalties to us, which could significantly diminish the value of our intellectual property. In addition, enforcing our patents against third parties may require significant expenditures regardless of the outcome of such efforts.

Furthermore, third parties may independently develop intellectual property similar to our patented intellectual property, which could result in, among other things, interference proceedings in the United States Patent and Trademark Office to determine priority of discovery or invention. Interference proceedings could result in the loss of or significant limitations on patent protection for our discoveries or technologies. Responding to interference proceedings or other challenges initiated by third parties may require significant expenditures and divert the attention of our management and key personnel from other business concerns.

We may be subject to patent infringement claims, which could result in substantial costs and liability and prevent us from commercializing our potential products.

Third parties may claim that our potential products or related technologies infringe their patents. Patent litigation is very common in the biopharmaceutical industry, and the risk of infringement claims is likely to

increase as the industry expands and as other companies obtain more patents and increase their efforts to discover genes through automated means and to develop proteins. Any patent infringement claims or similar legal impediments that might be brought against us may cause us to incur significant expenses, divert the attention of our management and key personnel from other business concerns and, if successfully asserted against us, require us to pay substantial damages. In addition, as a result of a patent infringement suit, we may be forced to stop or delay developing, manufacturing or selling potential products that are claimed to infringe a patent covering a third party's intellectual property unless that party grants us rights to use its intellectual property. We may be unable to obtain these rights on terms acceptable to us, if at all. Even if we are able to obtain rights to a third party's patented intellectual property, these rights may be non-exclusive, and therefore our competitors may be able to obtain access to the same intellectual property. Ultimately, we may be unable to commercialize our potential products or may have to cease some of our business operations as a result of patent infringement claims, which could severely harm our business.

Issued patents may not provide us with any competitive advantage or provide meaningful protection against competitors.

Issued patents may not provide us with any competitive advantage. Although we have a number of issued patents, the discoveries or technologies covered by these patents may not have any value. In addition, issued patents may not provide commercially meaningful protection against competitors. Other parties may be able to design around our issued patents or independently develop products having effects similar or identical to our patented product candidates. Some companies are currently attempting to develop therapeutic protein-based products substantially equivalent to products patented by other parties by altering the amino acid sequence within the therapeutic protein-based product and declaring the altered product a new product. It may be easier to develop substantially equivalent versions of therapeutic protein-based products such as monoclonal antibodies and soluble receptors than it is to develop substantially equivalent versions of the proteins with which they interact because there is often more than one antibody or receptor that has the same therapeutic effect. Consequently, any existing or future patents we have that cover monoclonal antibodies or soluble receptors may not provide any meaningful protection against competitors. In addition, the scope of our patents is subject to considerable uncertainty and competitors or other parties may obtain similar patents of uncertain scope. For example, other parties may discover uses for genes or proteins different from the uses covered in our patents, and these other uses may be separately patentable. If another party holds a patent on the use or manufacture of a gene or protein, then even if we hold the patent covering the composition of matter of the gene or protein itself, that other party could prevent us from selling any product directed to such use or using the manufacturing method covered by the other party's patent. Also, other parties may have patents covering the composition of matter of genes or proteins for which we have patents covering only methods of use or methods of manufacture of these genes or proteins. Furthermore, the patents we hold relating to recombinant human proteins, such as our patents covering rhThrombin or rFactor XIII, may not prevent competitors from developing, manufacturing or selling other versions of these proteins. Moreover, although we hold patents relating to the manufacture of recombinant human thrombin, we have limited composition of matter patent protection covering thrombin. Accordingly, we may not be able to prevent other parties from commercializing competing forms of recombinant human thrombin or thrombin made through different manufacturing methods.

The patent field relating to therapeutic protein-based products is subject to a great deal of uncertainty, and if patent laws or the interpretation of patent laws change, our competitors may be able to develop and commercialize products based on proteins that we discovered.

The patent protection available for genes, proteins and therapeutic protein-based products is highly uncertain and involves complex legal and factual questions that determine who has the right to develop a particular product. No consistent case law has emerged regarding the breadth of patents in this area. There have been, and continue to be, policy discussions concerning the scope of patent protection that should be awarded to genes and their corresponding proteins. Social and political opposition to patents on genes may lead to narrower patent protection for genes and their corresponding proteins. Patent protection relating to genes and therapeutic

protein-based products is also subject to a great deal of uncertainty outside the United States, and patent laws are evolving and undergoing revision in many countries. Changes in, or different interpretations of, patent laws in the United States and other countries may result in our inability to obtain patent protection for genes or proteins we discover or to enforce patents that have been issued to us, and may allow others to use our discoveries to develop and commercialize therapeutic protein-based products.

We expect to incur significant expenses in applying for patent protection and prosecuting our patent applications.

We may fail to secure meaningful patent protection relating to any of our existing or future product candidates, discoveries or technologies despite the expenditure of considerable resources. Our success depends significantly on the establishment of patent protection for the genes, proteins and related technologies we discover or invent. Consequently, we intend to continue our substantial efforts in applying for patent protection and prosecuting pending and future patent applications. These efforts have historically required the expenditure of considerable time and money, and we expect that they will continue to require significant expenditures. If future changes in United States or foreign patent laws complicate or hinder our efforts to obtain patent protection, the costs associated with patent prosecution may increase significantly.

We may be unable to protect our unpatented proprietary technology and information.

In addition to our patented intellectual property, we also rely on unpatented technology, trade secrets and confidential information. We may not be able to effectively protect our rights to this technology or information. Other parties may independently develop equivalent technologies or independently gain access to and disclose substantially equivalent information. Disputes may arise about inventorship and corresponding rights to know-how and inventions resulting from the joint creation or use of intellectual property by us and our corporate partners, licensees, scientific and academic collaborators and consultants. In addition, confidentiality agreements and material transfer agreements we have entered into with these parties and with employees and advisors may not provide effective protection of our technology or information or, in the event of unauthorized use or disclosure, may not provide adequate remedies.

Our plan to use collaborations to leverage our capabilities may not be successful.

As part of our business strategy, we have entered into collaboration arrangements with strategic partners to co-develop product candidates and will continue to evaluate similar opportunities. For our collaboration efforts to be successful, we must identify partners whose competencies complement ours. We must also successfully enter into collaboration agreements with them on terms attractive to us and integrate and coordinate their resources and capabilities with our own. We may be unsuccessful in entering into collaboration agreements with acceptable partners or negotiating favorable terms in these agreements. Also, we may be unsuccessful in integrating the resources or capabilities of these collaborators. In addition, our collaborators may prove difficult to work with or less skilled than we originally expected. If we are unsuccessful in our collaborative efforts, our ability to develop and market product candidates could be severely limited.

We may not be able to generate any revenue from product candidates developed by collaborators or licensees if they are unable to successfully develop those candidates.

We may be unable to derive any value from product candidates developed by collaborators or licensees. Our ability to generate revenues from existing or future collaborations and license arrangements is subject to numerous risks, including:

- the possibility that our collaborators or licensees lack sufficient financial, technical or other capabilities to develop these product candidates;
- the length of time that it takes for our collaborators or licensees to achieve various clinical development and regulatory approval milestones;

- the inability of collaborators or licensees to successfully address any regulatory or technical challenges they may encounter; and
- the possibility that these product candidates may not be effective or may prove to have undesirable side effects, unacceptable toxicities or other characteristics that preclude regulatory approval or prevent or limit commercial use.

Novo Nordisk has substantial rights to license proteins we discover, which may limit our ability to pursue other collaboration or licensing arrangements or benefit from our discoveries.

As part of our separation from Novo Nordisk, we granted Novo Nordisk options to license certain rights to several of our potential therapeutic proteins under an option agreement. Although we generally retain North American rights to the proteins licensed by Novo Nordisk pursuant to this agreement, Novo Nordisk has rights to these proteins in the rest of the world. In addition, under this agreement Novo Nordisk has worldwide rights, including rights in North America, to any licensed proteins that act to generate, expand or prevent the death of insulin-producing beta cells. Novo Nordisk has already licensed three proteins, and it may license other proteins in the future pursuant to this agreement. Our agreement with Novo Nordisk may:

- preclude or delay opportunities to seek other collaborators for our product candidates, due to the fact that we cannot explore other collaboration opportunities relating to proteins subject to the agreement until after Novo Nordisk has decided not to exercise an option with respect to the protein, which decision Novo Nordisk may withhold until well into the product development cycle;
- limit the financial benefits we may derive from product candidates by allowing Novo Nordisk to license proteins in exchange for predetermined payments and royalties and with predetermined cost-sharing arrangements, which payments and royalty rates may be less than, and which cost-sharing arrangements may be less favorable to us than, terms we might otherwise obtain in collaborative or licensing arrangements with other parties;
- result in Novo Nordisk licensing proteins with the most therapeutic and commercial potential, leaving us with fewer or less desirable product candidates to develop on our own or with other potential collaborators; and
- prevent us from collaborating with or licensing a product candidate to another company that, by virtue of its particular skills and capabilities, may be a more desirable collaborator or licensing partner for that particular product candidate than Novo Nordisk.

Environmental and health and safety laws may result in liabilities, expenses and restrictions on our operations.

State and federal laws regarding environmental protection, hazardous substances and human health and safety may adversely affect our business. The use of hazardous substances in our operations exposes us to the risk of accidental releases. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and fines. Future changes to environmental and health and safety laws could cause us to incur additional expenses or restrict our operations. In addition, the site where our principal headquarters and facilities are located has been listed as a contaminated property by the State of Washington due to its previous use by the City of Seattle as an electricity generating plant. The City of Seattle has agreed to defend us against and indemnify us for any claims that arise from this pre-existing contamination, except to the extent that we caused the claim through our negligence or intentional fault, or to the extent that we contributed to the contamination that is the subject of the claim, caused an increase in the clean-up costs or failed to comply with our obligations under our agreement with the City of Seattle. This indemnity may be insufficient and we may be subject to environmental liabilities or be prohibited from using or occupying some or all of the property as a result of environmental claims.

Financial and Market Risks

We anticipate incurring additional losses and may not achieve profitability.

As of December 31, 2003, we had an accumulated deficit of $201.0 million. We expect to continue to incur increasing losses over the next several years, and we may never become profitable. We are in the early stages of development as an independent company, and it will be a number of years, if ever, before we generate any revenues from our own product sales. Our revenues from existing collaborative and licensing arrangements are insufficient to cover our operating expenses, and we may never generate revenues from these or any future arrangements sufficient to cover these expenses. In addition, we will continue to incur substantial expenses relating to our research and development efforts. We anticipate that these expenses will increase as we focus on the laboratory tests and clinical trials required to obtain the regulatory approvals necessary for the sale of any products. The development of our product candidates will require significant further research, development, testing and regulatory approvals. We may not be able to complete such development or succeed in developing products that will generate revenues that will justify the costs of development.

If we do not obtain substantial additional funding on acceptable terms, we may not be able to continue to grow our business or generate enough revenue to recover our investment in research and development.

Our business does not currently generate the cash needed to finance our operations. We anticipate that we will continue to expend substantial funds on our research and development programs. We expect that these expenditures will increase significantly over the next several years as we continue to hire additional employees and expand our clinical development activities. We will need to seek additional funding through public or private financings, including equity financings, and through other arrangements, including collaborative and licensing arrangements. Poor financial results, unanticipated expenses or unanticipated opportunities that require financial commitments could give rise to additional financing requirements sooner than we expect. However, financing may be unavailable when we need it or may not be available on acceptable terms. If we raise additional funds by issuing equity or convertible debt securities, the percentage ownership of our existing shareholders will be diluted, and these securities may have rights superior to those of our common stock. If we are unable to raise additional funds when we need them, we may be required to delay, scale back or eliminate expenditures for some of our research or development programs. We may also be required to grant rights to third parties to develop and market product candidates that we would prefer to develop and market internally, and such rights may be granted on terms that are not favorable to us. If we were required to grant such rights, the ultimate value of these product candidates to us would be reduced.

Our operating results are subject to fluctuations that may cause our stock price to decline.

Our operating results have fluctuated in the past and are likely to continue to do so in the future. Our revenues are unpredictable and may fluctuate due to the timing of licensing fees or the achievement of milestones under new or existing licensing and collaborative arrangements, including our option agreement with Novo Nordisk. In addition, our expenses may fluctuate from quarter to quarter due to the timing of expenses, particularly with respect to contract manufacturing and clinical and nonclinical testing. We believe that period-to-period comparisons of our past operating results are not good indicators of our future performance and should not be relied on to predict our future operating results. For example, for periods prior to 2000, most of our revenues represented payments received from Novo Nordisk for research and development activities we conducted on its behalf. This arrangement terminated in 2000 in connection with our separation from Novo Nordisk. It is possible that in the future our operating results in a particular quarter or quarters will not meet the expectations of securities analysts or investors, causing the market price of our common stock to decline.

Risks Related to Our Industry

Many of our competitors have substantially greater capabilities and resources than we do and may be able to develop and commercialize products before we do.

We may be unable to compete successfully against our current or future competitors. We expect that competition in our field will continue to be intense. We face competition from other entities involved in the research and development of therapeutic proteins, including Genentech, Inc., Human Genome Sciences, Inc., Curagen, Inc. and Amgen Inc. We also face competition from entities developing other types of products related to particular diseases, including other biotechnology and pharmaceutical companies. Furthermore, our potential products, if approved and commercialized, may compete against well-established existing therapeutic protein-based products, many of which may be currently reimbursed by government health administration authorities, private health insurers and health maintenance organizations.

Many of our existing and potential competitors have substantially greater research and product development capabilities and financial, scientific, marketing and human resources than we do. As a result, these competitors may:

- succeed in identifying genes or proteins, or developing therapeutic protein-based products, earlier than we do;
- obtain approvals for products from the FDA or other regulatory agencies more rapidly than we do;
- obtain patents that block or otherwise inhibit our ability to develop and commercialize our product candidates;
- develop treatments or cures that are safer or more effective than those we propose to develop;
- devote greater resources to marketing or selling their products;
- introduce or adapt more quickly to new technologies or scientific advances, which could render our discovery technologies obsolete;
- introduce products that make the continued development of our potential products uneconomical;
- withstand price competition more successfully than we can;
- more effectively negotiate third-party collaborative or licensing arrangements; and
- take advantage of acquisition or other opportunities more readily than we can.

Our product candidates, even if approved by the FDA or foreign regulatory agencies, may not achieve market acceptance among hospitals, insurers or patients.

Our product candidates, even if approved by the FDA or foreign regulatory agencies, may fail to achieve market acceptance, which would impair our ability to become profitable. We believe that market acceptance of our potential products will depend on our ability to provide acceptable evidence of safety, efficacy and limited side effects, our ability to provide these potential products at reasonable prices and the availability of third-party reimbursement for these potential products. In addition, market acceptance depends on the effectiveness of our sales or marketing capabilities. To date, we have no direct sales or marketing capabilities.

If the health care system or reimbursement policies change, the prices of our potential products may fall or our potential sales may decline.

In recent years, officials have made numerous proposals to change the health care system in the United States. These proposals include measures that would limit or prohibit payments for certain medical procedures and treatments or subject the pricing of pharmaceuticals to government control. Government and other third-party payors increasingly have attempted to contain health care costs by limiting both coverage and the level of

reimbursement of newly approved health care products. They may also refuse to provide any coverage of uses of approved products for medical indications other than those for which the FDA has granted marketing approval. Governments may adopt future legislative proposals and federal, state or private payors for health care goods and services may take further action to limit payments for health care products and services. In addition, in certain foreign countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. Any of these factors could limit our ability to successfully commercialize our potential products.

Negative public opinion and increased regulatory scrutiny of genetic and clinical research may limit our ability to conduct our business.

Ethical, social and legal concerns about genetic and clinical research could result in additional regulations restricting or prohibiting some of our activities or the activities of our suppliers and collaborators. In recent years, federal and state agencies, congressional committees and foreign governments have expressed interest in further regulating the biotechnology industry. More restrictive regulations could delay nonclinical studies or future clinical trials, or prevent us from obtaining regulatory approvals or commercializing any products. In addition, animal rights activists may protest our use of animals in research and development and may attempt to disrupt our operations, which could cause us to incur significant expenses and distract our management's attention from other business concerns.

The failure to attract or retain key management or other personnel could decrease our ability to discover, develop and commercialize potential products.

We depend on our senior executive officers as well as key scientific and other personnel. Only a few of our key personnel are bound by employment agreements, and those with employment agreements are bound only for a limited period of time. Further, we have not purchased key-person life insurance policies for any of our executive officers or key personnel. Competition for scientists and other qualified employees is intense among pharmaceutical and biotechnology companies, and the loss of qualified employees, or an inability to attract, retain and motivate the additional highly skilled employees required for the expansion of our activities, could hinder our ability to discover, develop and commercialize potential products.

We may be required to defend lawsuits or pay damages in connection with alleged or actual harm caused by our product candidates.

We face an inherent business risk of exposure to product liability claims in the event that the use of our product candidates is alleged to have resulted in harm to others. This risk exists in clinical trials as well as in commercial distribution. We may incur significant expenses if product liability lawsuits against us are successful. Although we maintain product liability insurance, our coverage may not be adequate to cover such claims.

Risks Related to Ownership of Our Stock

Our stock price may be volatile.

The market price of our common stock may fluctuate significantly in response to many factors beyond our control, including:

- changes in the recommendations of securities analysts or changes in their financial estimates of our operating results;
- failures in meeting performance expectations of securities analysts or investors;
- fluctuations in the valuations of companies perceived by securities analysts or investors to be comparable to us; and
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares.

Furthermore, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies. In particular, there have been high levels of volatility in the market prices of securities of biotechnology companies. These fluctuations often have been unrelated or disproportionate to the operating performance of those companies. These market and industry fluctuations, as well as general economic, political and market conditions such as recessions, interest rate changes or international currency fluctuations, may negatively impact the market price of our common stock. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

Certain of our shareholders have significant control of our management and affairs, which they could exercise against other shareholders' best interests.

Novo Nordisk, together with Warburg, Pincus Equity Partners, L.P. and entities affiliated with Apax Partners, Inc., beneficially owned an aggregate of approximately 61% of our outstanding common stock as of December 31, 2003. Representatives of these shareholders hold five out of eight seats on our board of directors, and four of these positions are pursuant to contractual obligations. These shareholders, acting together, have the ability to control our management and affairs and matters requiring shareholder approval, including the election of directors and approval of significant corporate transactions, such as mergers, consolidations or the sale of substantially all of our assets. Consequently, these shareholders, acting together, have the ability to cause a change in control, as well as to delay or prevent a change in control. They may also discourage a potential acquirer from making a tender offer or otherwise attempting to effect a change in control, even if such a change in control would benefit our other shareholders.

Provisions in our charter documents could prevent or frustrate any attempts to replace our current board of directors or management by shareholders.

Our articles of incorporation and bylaws contain provisions, such as undesignated preferred stock and prohibitions on cumulative voting in the election of directors, which could make it more difficult for a third party to acquire us without the consent of our board of directors. Also, our articles of incorporation provide for a staggered board, removal of directors only for cause and certain requirements for calling special shareholder meetings. In addition, our bylaws require advance notice of shareholder proposals and nominations and impose restrictions on the persons who may call special shareholder meetings. These provisions may have the effect of preventing or hindering any attempts by our shareholders to replace our current board of directors or management.

Website Access to Our SEC Reports

Our Internet address is www.zymogenetics.com. We make our periodic SEC reports (Form 10-Q and Form 10-K), current reports (Form 8-K) and amendments to these reports available free of charge through our website as soon as reasonably practicable after they are filed electronically with the SEC. We may from time to time provide important disclosures to investors by posting them in the investor relations section of our website, as allowed by SEC rules.

Item 2. Properties

We are headquartered in Seattle, Washington, where we lease two buildings containing approximately 160,000 square feet. In 2003, construction began on an expansion of one of these buildings that will add approximately 45,000 square feet of additional laboratory, manufacturing and office space. We own land adjacent to one of the existing buildings, which we are holding for potential expansion in the future. In addition, we have leased approximately 30,000 square feet of space in a nearby office building. We believe that our

existing facilities, together with available, planned and potential expansion space, will be adequate to fulfill our needs for the foreseeable future.

Item 3. Legal Proceedings

None.

Item 4. Submission Of Matters To A Vote Of Security Holders

No matters were submitted to a vote of our shareholders during the fourth quarter of our fiscal year ended December 31, 2003.

PART II

Item 5. Market for Registrant's Common Equity and Related Shareholder Matters

Our common stock began trading on the Nasdaq Stock Market under the symbol ZGEN on February 1, 2002. As of March 1, 2004, we had approximately 67 shareholders of record. We have never paid cash dividends and do not anticipate paying them in the foreseeable future.

The following table sets forth, for the fiscal periods indicated, the range of high and low closing sales prices of our common stock as quoted on the Nasdaq Stock Market:

	High	Low
Year Ended December 31, 2003		
1st Quarter	$10.18	$ 8.03
2nd Quarter	16.98	9.00
3rd Quarter	16.20	11.36
4th Quarter	16.07	12.10
Year Ended December 31, 2002		
1st Quarter (from February 1, 2002)	$12.05	$ 8.70
2nd Quarter	12.94	7.05
3rd Quarter	8.78	5.37
4th Quarter	10.64	6.16

In January 2002, the U.S. Securities and Exchange Commission (the Commission) declared effective our Registration Statement on Form S-1 (Registration No. 333-69190) as filed with the Commission in connection with our initial public offering of common stock, without par value. Net proceeds of approximately $110 million have been invested in short-term, investment-grade, interest bearing instruments.

Item 6. Selected Financial Data

The following selected financial data should be read in conjunction with the financial statements and notes to the financial statements and "Management's Discussion and Analysis of Financial Condition and Results of Operations" contained elsewhere in this Form 10-K. The selected Statement of Operations Data for the years ended December 31, 2003, 2002 and 2001 and Balance Sheet Data as of December 31, 2003 and 2002 have been derived from our audited financial statements appearing elsewhere in this Form 10-K. The selected Statement of Operations Data for the years ended December 31, 2000 and 1999 and Balance Sheet Data as of December 31, 2001, 2000, and 1999 have been derived from our audited financial statements that are not included in this Form 10-K. Historical results are not necessarily indicative of future results. Amounts presented for the year ended December 31, 2002 have been restated. See the note entitled "Restatement of Financial Statements" in the notes to our financial statements for further information.

	Years Ended December 31,				
	2003	2002	2001	2000	1999
		(restated) (in thousands, except per share data)			
Statement of Operations Data:					
Revenues	$ 25,957	$ 52,775	$ 17,828	$ 32,464	$69,675
Operating expenses:					
Research and development(1)	67,860	65,508	48,052	49,337	48,415
General and administrative(2)	11,447	16,685	10,475	12,069	9,550
Noncash stock-based compensation expense	7,054	7,188	3,507	—	—
Total operating expenses	86,361	89,381	62,034	61,406	57,965
Income (loss) from operations	(60,404)	(36,606)	(44,206)	(28,942)	11,710
Other income (expense):					
Investment income	6,519	7,354	7,250	5,417	274
Interest expense	(5,610)	(896)	(13)	(848)	(56)
Other, net	(76)	(195)	—	(111)	(52)
Income (loss) before provision for income taxes	(59,571)	(30,343)	(36,969)	(24,484)	11,876
Benefit (provision) for income taxes	—	—	90	(5,893)	(2,454)
Net income (loss)	(59,571)	(30,343)	(36,879)	(30,377)	9,422
Preferred stock dividend and accretion	—	(1,718)	(20,610)	(2,903)	—
Net income (loss) attributable to common shareholders	$ (59,571)	$ (32,061)	$ (57,489)	$ (33,280)	$ 9,422
Basic net income (loss) per share	$ (1.26)	$ (0.75)	$ (4.85)	$ (3.38)	$ 1.11
Diluted net income (loss) per share	$ (1.26)	$ (0.75)	$ (4.85)	$ (3.38)	$ 0.80
Weighted-average shares used in computing basic net income (loss) per share	47,317	42,578	11,846	9,846	8,455
Weighted-average shares used in computing diluted net income (loss) per share	47,317	42,578	11,846	9,846	11,793
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$299,892	$285,438	$147,077	$172,976	$19,648
Working capital	287,413	272,236	138,493	166,245	19,504
Total assets	375,909	347,934	205,435	228,637	91,914
Mandatorily redeemable convertible preferred stock	—	—	260,540	239,930	—
Total shareholders' equity (deficit)	287,915	269,341	(79,402)	(27,269)	77,687

(1) The years ended December 31, 2003, 2002 and 2001 exclude noncash stock-based compensation expense of $4,543, $4,543 and $2,109, respectively.

(2) The years ended December 31, 2003, 2002 and 2001 exclude noncash stock-based compensation expense of $2,511, $2,645 and $1,398, respectively.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

Overview

We are a biopharmaceutical company focused on discovering, developing and commercializing therapeutic protein based products for the treatment of human diseases. The process for taking one of our discoveries to the marketplace is long, complex and very costly. It is difficult to predict the time it will take to commercialize any given product candidate, but it would not be unusual to span ten years or more and cost hundreds of millions of dollars. It is also a business of attrition; it is expected that less than 20% of the proteins entering human clinical trials will actually make it to the marketplace. For the products that do make it, particularly for those that address previously unmet medical needs, the markets can be significant, with a number of successful products selling in excess of $1 billion per year.

An important element of our strategy is that we intend to maintain all or a significant share of the commercial rights to our products in North American markets. As a result, we will be required to pay a significant portion of the development costs for our product candidates. A second important element of our strategy is that we are developing a broad portfolio of product candidates to give our company more opportunities to be successful. We currently have four product candidates in clinical development and expect to add additional proteins to this portfolio in the future. Thus, we are paying a significant portion of development costs for several potential products. Assuming these product candidates progress through clinical development successfully, the cost of clinical trials are expected to increase significantly.

Our most significant financial challenges are to obtain adequate funding to cover the cost of product development, and to control spending and direct it toward product candidates that will create the most value for the company's shareholders over the long term. It can be a complex and highly subjective process to establish the appropriate balance between cash conservation and value generation. There are a number of important factors that we consider in addressing these challenges, including the following:

- the nature, timing and magnitude of financing transactions, which would typically involve issuance of equity or equity-based securities;
- the nature and timing of product development collaborations, which would typically provide for funding of a portion of the respective product development costs, as well as bring in near-term potential revenues in the form of upfront fees and milestone payments;
- the breadth of product development programs, i.e. the number of potential disease indications for which a product candidate is tested in clinical trials;
- the number of products in our development portfolio and the decision to move new product candidates into clinical development; and
- periodic assessments of the relative capital requirements, risk and value of each of our product candidates.

We expect that it will be at least four to five years before we can generate enough product-related revenues to reach cash flow breakeven. In the interim, revenues from existing relationships will help to defray our expenses, but additional funding will be required, the amount of which could be significant. We may decide to enter into additional product development collaborations, which would reduce our funding requirements. We may also generate funding through licensing of patents that are not relevant to our product development programs.

It is likely that we will continue to look for opportunities to raise equity capital as a primary means of funding our company over the next several years. The equity markets for biotechnology stocks have tended to experience long cycles during which the sale of equity securities has been extremely difficult. It is not possible to predict the timing or length of these cycles. As a result, most biotechnology companies, including ours, have adopted an opportunistic strategy of raising equity capital when it is available. We believe this strategy is important to minimizing the financial risks to our company and our shareholders.

Our financial statements for the year ended December 31, 2002 have been restated to reflect a change in accounting for a sale-leaseback transaction. Subsequent to the issuance of these financial statements, we determined in consultation with our outside auditors, that the sale-leaseback transaction that occurred in October 2002 was improperly accounted for. We initially accounted for the transaction as a sale of the properties involved and as operating leases under the provisions of SFAS 13. Subsequently it was determined that the leases contain a technical provision that could, under certain remote circumstances, result in our continuing ownership involvement with respect to the properties. Due to the existence of this provision, the transaction is more properly accounted for as a financing rather than a sale and leaseback of the properties. See the note entitled "Restatement of Financial Statements" in the notes to our financial statements for further information. The following discussion and analysis gives effect to the restatement.

Results of Operations

Revenues

Royalties. We earn royalties on sales of certain products subject to license agreements with Novo Nordisk and several other companies. Royalty revenues declined by 12% from 2001 to 2002 reflecting a general flat to declining trend in the sales of products subject to the licenses. In 2003, despite the continuing lack of underlying sales growth, royalties increased by 18% due to the weakening of the U.S. dollar versus foreign currencies prominent in certain royalty calculations. We do not expect any change in the underlying sales trend in the future and, beginning in 2005, we expect substantial reductions in insulin royalties due to patent expirations in a number of major countries. In 2003, insulin royalties represented 59% of our total royalty revenues. We have opportunities to earn royalties in the future under other existing license agreements, but we cannot be certain when, or if, products will be sold subject to those licenses.

Option fee from related party. In all three years presented, we earned an annual option fee of $7.5 million from Novo Nordisk under an option and license agreement, pursuant to which we have given them an option to license certain rights to proteins that we discover. The initial term of this agreement expires in November 2004, but Novo Nordisk has the option of extending it and paying $7.5 million for two additional years. If they do not extend the agreement, option fee revenue will decline to approximately $6.5 million in 2004, all of which was included in deferred revenue at December 31, 2003, and none will be earned in future years.

Ig-fusion protein license fee. In 2002, as part of a lawsuit settlement, we earned a $30.0 million license fee related to the granting of a license to our Ig-fusion protein patents. This was a one-time payment for a fully paid-up license and, therefore, we will not earn any future revenues with respect to this agreement.

License fees, milestones and other. Revenues from license fees and other up-front payments are recognized over the period we are contractually required to provide other rights or services that represent continuing obligations. At December 31, 2003, $6.5 million of such revenues was included in deferred revenue, of which $1.6 million is expected to be recognized in 2004 and the remainder in future periods. For certain license agreements that require no continuing performance of us, we record license fees as revenue upon execution of the agreement. We recognize revenues from milestone payments that represent completion of separate and substantive earnings processes when the milestone is achieved and amounts are due and payable. From year to year, this revenue item can fluctuate substantially based on the completion of new licensing or collaborative agreements and the achievement of development related milestones. Although this revenue item increased both in 2002 and 2003 due to an increasing number of transactions and milestone payments, we cannot be certain this trend will continue in 2004 and beyond due to the uncertain nature of the events generating the revenue.

Operating Expenses

Research and development expense. Research and development expense has been our most significant expense to date, consisting primarily of salaries and benefit expenses, costs of consumables, facility costs and contracted services. Research and development expense increased in each of the past two years, by 4% in 2003 and by 36% in 2002. Our expense in 2003 reflects an offset of $4.9 million from costs reimbursed by Novo

Nordisk under an IL-21 preclinical collaboration agreement, which is expected to end in early 2004. Without the impact of this reimbursement, research and development expense would have increased by 11% in 2003. Increases over the periods reported largely resulted from significantly increased activities for the development of our four product candidates, rhThrombin, rFactor XIII, TACI-Ig and IL-21. Over the past three years, we have added approximately 50 employees who are focused on product development, and external costs for contract manufacturing, clinical trials and preclinical testing have increased substantially. These trends are shown in the following table (in thousands).

	2003	2002 (restated)	2001
Salaries and benefits	$34,477	$29,408	$24,301
Consumables	8,685	9,184	7,747
Facility costs	4,562	3,923	3,335
Contracted services	20,459	17,924	7,882
Depreciation and amortization	4,564	5,069	4,787
Subtotal	72,747	65,508	48,052
IL-21 cost reimbursement from Novo Nordisk	(4,887)	—	—
Net research and development expense	$67,860	$65,508	$48,052

We anticipate that research and development expense will continue to increase in the foreseeable future as we continue to advance, and potentially expand, our internal product development programs. In 2004 we expect that a number of factors, including the following, will contribute to a significant increase in research and development expense.

- costs related to scale-up and production of Phase 3 and commercial product for the rhThrombin and rFactor XIII programs;
- costs of significantly expanded clinical trial activity, particularly with respect to rhThrombin and TACI-Ig;
- increased staffing to support expanded product development efforts, particularly in the clinical, medical, regulatory and quality areas; and
- reduced cost reimbursements from Novo Nordisk with respect to development of IL-21.

Based on these factors, we estimate that research and development expense in 2004 will fall within the range of $100 million to $110 million, depending on the actual timing of these factors.

General and administrative expense. General and administrative expense consists primarily of salaries and benefit expenses, professional fees and other corporate costs. In 2002, this expense increased substantially due to:

- added administrative personnel;
- substantial legal costs associated with a patent infringement lawsuit settled in late 2002;
- write-off of design and engineering costs related to a terminated construction project; and
- increased expenses related to our operation as a public company.

In 2003, general and administrative expense declined substantially, resulting from normalization of legal costs; lack of a construction cost write-off; and cost control initiatives taken by the company in late 2002 and early 2003. We anticipate that general and administrative expense will increase in 2004 and subsequent years reflecting the additional administrative requirements of supporting our product development programs as they advance toward commercialization. In addition, we will incur additional professional fees in order to comply with the requirements of the Sarbanes-Oxley Act of 2002.

Noncash stock-based compensation expense. In 2001 and early 2002, prior to the completion of our initial public offering, stock options were granted to employees and directors at exercise prices below the estimated fair value of the common stock on the date of grant. As a result, we recorded total deferred stock-based compensation of $29.2 million. Deferred stock-based compensation is being amortized to expense over the vesting periods of the underlying options, generally four years, using the straight-line method. The expense recorded for 2001 represented a partial year of amortization. The expense declined from 2002 to 2003 due to cancellation of unvested options held by employees who terminated their employment with the company. We expect to amortize $6.3 million in 2004 and $3.1 million in 2005, although actual amounts may be lower if unvested options for which deferred stock-based compensation has been recorded are subsequently cancelled. Although we have no intention of doing so, the amount could increase if future options are granted with exercise prices below the estimated fair value of the common stock on the date of the grant.

Other Income (Expense)

Other income (expense) consists primarily of investment income and interest expense. Investment income is generated primarily from investment of our cash reserves in investment grade, fixed-income securities. There are three primary factors affecting the amount of investment income that we report: amount of cash reserves invested, the effective interest rate, and the amount of gains or losses recognized. The following table shows how each of these factors affected investment income for the three years reported (in thousands).

	2003	2002	2001
Weighted average amount of cash reserves	$256,471	$219,321	$154,967
Effective interest rate	2.16%	3.09%	4.62%
Investment income before gains and losses	5,535	6,772	7,155
Net gains on sales of investments	984	582	95
Investment income, as reported	$ 6,519	$ 7,354	$ 7,250

We have accounted for the sale-leaseback transaction completed in October 2002 as a financing transaction. Under this method of accounting, the net proceeds of the sale are considered to be a long-term interest bearing liability. Rent payments under the leases are considered to be payments toward the liability and are allocated to principal and interest. We recorded interest of $0.9 million for a partial year in 2002 and $5.6 million for the full year 2003.

Liquidity and Capital Resources

As of December 31, 2003, we had cash, cash equivalents and short-term investments of $299.9 million, which we intend to use to fund our operations and capital expenditures over the next several years. These cash reserves are held in a variety of investment-grade, fixed-income securities, including corporate bonds, commercial paper and money market instruments. We recently estimated that we expect to use approximately $85 million to $95 million of our cash reserves to fund our operations and capital expenditures in 2004. We believe that our existing cash resources should provide sufficient funding for approximately three years. If we complete additional collaborative development transactions, which would generate both revenues and cost reductions, we believe that these cash resources may fund our company for up to four years.

Cash flows from operating activities. The amount of cash used to fund our operating activities generally tracks our net losses, with the following exceptions:

- noncash expenses, such as depreciation and amortization, gain or loss on sale or disposal of assets, and noncash stock-based compensation, which do not result in uses of cash;
- net realized gains and amortization of premium on short-term investments, which are reflected as sources of cash from investing activities upon maturity or sale of the respective investments;

- changes in receivables, which generally represent temporary timing differences between the recognition of certain revenues and the subsequent receipt of cash payments;
- changes in deferred revenue, which reflect the difference in timing between the receipt of cash from option fees, license fees and other upfront payments and the subsequent recognition of these amounts as revenue over the period we are contractually required to provide other rights or services that represent continuing obligations; and
- changes in other assets and liabilities, which generally represent temporary timing differences between the recognition of certain expenses and their payment.

Generally, with the exception of changes in deferred revenue, we do not expect these items to generate material year-to-year fluctuations in the relationship between our net loss and the amount of net cash used in operating activities. Substantial license or upfront fees may be received upon the date we enter into new licensing or collaborative agreements and be recorded as deferred revenue. For example, in 2001 upon the execution of a collaborative agreement for TACI-Ig, we received an upfront fee of $7.5 million, which was recorded as deferred revenue and will be recognized as revenue over the collaboration period. The timing of these types of transactions are irregular and, thus, have the potential to create fluctuations in the relationship between our net loss and the amount of cash used in operating activities.

Cash flows from investing activities. Our most significant use of cash in investing activities is for capital expenditures. Our business requires us to expend a certain amount each year to adopt newly developed technologies and replace obsolete assets. In addition, we have used cash to purchase land and expand our facilities. The following table shows the amount of cash going toward each of these types of capital expenditures (in thousands):

	2003	2002	2001
Ongoing equipment/facility expenditures	$ 2,390	$5,923	$6,633
Purchases of land for future expansion	—	2,975	1,469
Expansion of R&D facility, including pilot scale manufacturing plant	10,172	1,045	79
Total	$12,562	$9,943	$8,181

The R&D facility expansion is an ongoing project, for which we have approved a total budget of approximately $26 million including all related equipment costs. The project will be partially funded by an allowance from our landlord expected to total approximately $15 million, which is reflected as cash flow from financing activities. The project began in April 2003 and is scheduled to be completed in mid-2004.

Cash flows from investing activities also reflect large amounts of cash used to purchase short-term investments and received from the sale and maturity of short-term investments. These amounts primarily relate to shifts between cash and cash equivalents and short-term investments. Because we manage our cash usage with respect to our total cash, cash equivalents and short-term investments, we do not consider these cash flows to be relevant to an understanding of our liquidity and capital resources.

Cash flows from financing activities. Net proceeds from common stock offerings constitute by far the largest element of financing cash flows. We received $110.7 million in net proceeds from our initial public offering in 2002 and $71.3 million from an underwritten follow-on offering completed in October 2003. In 2002, we received $50.5 million of net proceeds from the completion of a sale and leaseback of our headquarter buildings, which has been accounted for as a financing transaction. Our landlord has agreed to provide an allowance of approximately $15 million to be applied toward the cost of the R&D facility expansion project described above. We received $7.9 million of this amount in 2003 and expect to receive the remainder in 2004. Additionally, our landlord has committed to loan the company $3.0 million to cover costs of the project not otherwise funded by the allowance.

We expect to incur substantial additional costs as we continue to advance and expand our product development programs. We expect these expenditures to increase over the next several years, particularly if the outcomes of clinical trials are successful. Our plans include the internal development of selected product candidates and the co-development of product candidates with collaborators where we would assume a percentage of the overall product development costs. If, at any time, our prospects for financing these programs decline, we may decide to reduce our ongoing investment in our development programs. We could reduce our investment by discontinuing our funding under existing co-development arrangements, establishing new co-development arrangements for other product candidates to provide additional funding sources or out-licensing product candidates that we might otherwise develop internally. Additionally, we could consider delaying or discontinuing development of product candidates to reduce the level of our related expenditures.

Our long-term capital requirements and the adequacy of our available funds will depend on several factors, many of which may not be in our control, including:

- results of research and development programs;
- cash flows under existing and potential future arrangements with licensees, collaborators and other parties;
- costs involved in filing, prosecuting, enforcing and defending patent claims; and
- costs associated with the expansion of our facilities.

Over the next several years we will need to seek additional funding through public or private financings, including equity financings, and through other arrangements, including collaborative arrangements. Poor financial results, unanticipated expenses or unanticipated opportunities that require financial commitments could give rise to additional financing requirements sooner than we expect. However, financing may be unavailable when we need it or may not be available on acceptable terms. If we raise additional funds by issuing equity or equity-based securities, the percentage ownership of our existing shareholders would be reduced, and these securities could have rights superior to those of our common stock. If we are unable to raise additional funds when we need them, we could be required to delay, scale back or eliminate expenditures for some of our development programs or expansion plans, or grant rights to third parties to develop and market product candidates that we would prefer to develop and market internally, with license terms that are not favorable to us.

Contractual Obligations

At December 31, 2003 we are contractually obligated to make payments as follows (in thousands):

	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	4-5 Years	More than 5 Years
Building lease obligation	$136,639	$ 6,256	$14,497	$15,498	$100,388
Operating leases	9,860	1,078	2,328	2,482	3,972
Construction contract	12,568	12,568	—	—	—
Manufacturing contract	26,571	14,721	11,850	—	—
Total	$185,638	$34,623	$28,675	$17,980	$104,360

The building lease obligation, which resulted from the sale and leaseback financing transaction, includes lease payments that will commence upon completion of the ongoing expansion project and that will result from a reset of the lease terms to 15 years. Operating lease terms range from one to fifteen years with certain renewal provisions at our option. The construction contract relates to our ongoing facility expansion project, and the amount shown above represents the remaining balance on the contract as of December 31, 2003. The manufacturing contract is for Phase 3 and commercial production of rhThrombin. The amount shown above represents the base amount of the contract, assuming work proceeds as planned at the time the contract was signed. There are several points in the project at which we have the option to terminate further work, thereby reducing the amount of our commitment.

Critical Accounting Estimates

Royalty revenue. We earn royalties on two proteins marketed and sold by Novo Nordisk, insulin and glucagon. Royalties are received from Novo Nordisk annually within 60 days after the end of the calendar year. For insulin, the royalties are based on manufacturing costs for the quantity of insulin sold during the year. These costs are calculated in Danish Kroner, and then converted to U.S. Dollars based on the exchange rate at the end of the year. Royalties earned on sales of glucagon are calculated as a percentage of net sales. We accrue estimated royalties at the end of each quarter based on historical sales data, estimates provided to us by Novo Nordisk and changes in the Danish Kroner to U.S. Dollar exchange rate. Adjustments are made in the following year reflecting the difference between our estimates and actual reported royalties and, to date, have not been significant.

We also earn royalties on several products marketed by other companies. Royalties on these products are received within 30 to 60 days after the end of each calendar quarter. We accrue estimated royalties at the end of each quarter based on historical sales data. Adjustments are made in the following quarter reflecting the difference between our estimates and actual reported royalties.

License and upfront fees. We enter into various licensing and collaborative agreements that generate significant license or other upfront fees with subsequent milestone payments earned upon completion of development milestones. We use our best judgment to estimate the period over which we have continuing commitments to perform under these agreements. Revenue from upfront fees is recognized on a straight-line basis over this period, which has ranged in duration from six months to ten years. For certain license agreements that require no continuing performance on our part, license fee revenue is recognized immediately upon execution of the agreement.

Stock based compensation. As permitted by the provisions of Statement of Financial Accounting Standards No. 123, Accounting for Stock Based Compensation (SFAS 123), we have elected to follow Accounting Principles Board No. 25, Accounting for Stock Issued to Employees (APB 25), in accounting for employee stock option grants and apply the disclosure-only provisions of SFAS 123 to account for our stock option plans. Under APB 25, compensation expense is based on the excess, if any, of the estimated fair value of our stock at the date of grant over the exercise price of the option. Prior to the completion of our initial public offering, we granted options with exercise prices that were lower than the estimated fair value of the stock on the date of grant. We used our best judgment to estimate the fair value of our stock as of the various grant dates, which resulted in share prices ranging from $9.09 to $15.11. Based on these estimated values, we recorded $29.2 million of deferred compensation, which is being amortized over the vesting period of the individual options using the straight-line method.

Item 7A. Qualitative and Quantitative Disclosures About Market Risk

Our exposure to market risk is primarily limited to interest income sensitivity, which is affected by changes in the general level of United States interest rates, particularly because the majority of our investments are in short-term debt securities. The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive without significantly increasing risk. To minimize risk, we maintain our portfolio of cash, cash equivalents and short-term investments in a variety of interest-bearing instruments, including United States government and agency securities, high-grade United States corporate bonds, asset-backed securities, commercial paper and money market funds. Due to the nature of our short-term investments, we believe that we are not subject to any material market risk exposure. However, a change of 1% in the average annual interest rate could result in a change in interest income of $2.5 million. Certain of our royalty revenue agreements are denominated in foreign currency, estimated during the year and settled at year-end. We have no other material foreign currency exposure, nor do we hold derivative financial instruments.

Item 8. Financial Statements and Supplementary Data

REPORT OF INDEPENDENT AUDITORS

To the Board of Directors
and Shareholders of
ZymoGenetics, Inc.

In our opinion, the accompanying balance sheets and the related statements of operations, of changes in shareholders' equity and of cash flows present fairly, in all material respects, the financial position of ZymoGenetics, Inc. at December 31, 2003 and 2002, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2003 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management; our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with auditing standards generally accepted in the United States of America, which require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

ZymoGenetics, Inc. is related to a group of affiliated companies and, as disclosed in the financial statements, has extensive transactions and relationships with members of the group.

As described in Note 2, the Company has restated its financial statements at and for the year ended December 31, 2002.

/s/ PRICEWATERHOUSECOOPERS LLP
Seattle, Washington
March 23, 2004

ZYMOGENETICS, INC.

BALANCE SHEETS
(in thousands)

	December 31, 2003	December 31, 2002 (restated)
Assets		
Current assets		
Cash and cash equivalents	$ 97,576	$ 55,579
Short-term investments	202,316	229,859
Receivables		
Related party	3,458	388
Trade	1,189	1,110
Interest and other receivables	1,228	2,218
Prepaid expenses and other assets	2,777	2,253
Total current assets	308,544	291,407
Property and equipment, net	62,341	52,954
Other assets	5,024	3,573
Total assets	$ 375,909	$ 347,934
Liabilities and Shareholders' Equity		
Current liabilities		
Accounts payable	$ 4,808	$ 3,172
Accrued liabilities	8,301	5,689
Deferred revenue	8,022	10,310
Total current liabilities	21,131	19,171
Construction advance from landlord	7,918	—
Lease obligation	50,570	50,146
Deferred revenue	4,957	6,524
Deferred lease obligations	59	28
Other noncurrent liabilities	3,359	2,724
Commitments and contingencies		
Shareholders' equity		
Common stock, no par value, 150,000 shares authorized, 52,494 and 45,815 issued and outstanding at December 31, 2003 and 2002, respectively	498,602	427,010
Non-voting common stock, no par value, 30,000 shares authorized	—	—
Notes receivable from shareholders	(725)	(725)
Deferred stock compensation	(9,455)	(18,291)
Accumulated deficit	(201,033)	(141,462)
Accumulated other comprehensive income	526	2,809
Total shareholders' equity	287,915	269,341
Total liabilities and shareholders' equity	$ 375,909	$ 347,934

The accompanying notes are an integral part of these financial statements.

ZYMOGENETICS, INC.

STATEMENTS OF OPERATIONS
(in thousands, except per share data)

	Years ended December 31,		
	2003	2002 (restated)	2001
Revenues			
Royalties			
Related party	$ 6,409	$ 4,986	$ 5,151
Other	2,988	3,010	3,963
Option fee from related party	7,500	7,500	7,500
Ig-fusion protein license fee	—	30,000	—
License fees and milestone payments			
Related party	4,128	2,328	—
Other	4,932	4,951	1,214
Total revenues	25,957	52,775	17,828
Operating expenses			
Research and development (excludes noncash stock-based compensation expense of $4,543 in 2003, $4,543 in 2002 and $2,109 in 2001, respectively)	67,860	65,508	48,052
General and administrative (excludes noncash stock-based compensation expense of $2,511 in 2003, $2,645 in 2002 and $1,398 in 2001, respectively)	11,447	16,685	10,475
Noncash stock-based compensation expense	7,054	7,188	3,507
Total operating expenses	86,361	89,381	62,034
Loss from operations	(60,404)	(36,606)	(44,206)
Other income (expense)			
Investment income	6,519	7,354	7,250
Interest expense	(5,610)	(896)	(13)
Other, net	(76)	(195)	—
Loss before provision for income taxes	(59,571)	(30,343)	(36,969)
Benefit for income taxes	—	—	90
Net loss	(59,571)	(30,343)	(36,879)
Preferred stock dividend and accretion on mandatorily redeemable convertible preferred stock	—	(1,718)	(20,610)
Net loss attributable to common shareholders	$(59,571)	$(32,061)	$(57,489)
Net loss per share—basic and diluted	$ (1.26)	$ (0.75)	$ (4.85)
Weighted-average shares—basic and diluted	47,317	42,578	11,846

The accompanying notes are an integral part of these financial statements.

ZYMOGENETICS, INC.

STATEMENT OF CHANGES IN SHAREHOLDERS' EQUITY (DEFICIT)
(in thousands)

	Mandatorily redeemable convertible preferred stock		Shareholders' equity (deficit)						
			Common Stock		Notes receivable from shareholders	Deferred stock compensation	Accumulated deficit	Accumulated other comprehensive income	Total
	Shares	Amount	Shares	Amount					
Balance at January 1, 2001	6,540	$ 239,930	11,793	$ 46,971	$ —	$ —	$ (74,240)	$—	$ (27,269)
Comprehensive loss:									
Net loss	—	—	—	—	—	—	(36,879)	—	(36,879)
Unrealized gain on short-term investments	—	—	—	—	—	—	—	1,821	1,821
Total comprehensive loss									(35,058)
Common stock issued in connection with stock option exercises	—	—	10	28	—	—	—	—	28
Common stock issued in connection with stock option exercises for notes receivable	—	—	261	725	(725)	—	—	—	—
Deferred stock compensation related to stock options:									
Grants	—	—	—	28,742	—	(28,742)	—	—	—
Amortization	—	—	—	—	—	3,507	—	—	3,507
Accretion on mandatorily redeemable convertible preferred stock	—	1,048	—	(1,048)	—	—	—	—	(1,048)
Dividends accrued on mandatorily redeemable convertible preferred stock	—	19,562	—	(19,562)	—	—	—	—	(19,562)
Balance at December 31, 2001	6,540	260,540	12,064	55,856	(725)	(25,235)	(111,119)	1,821	(79,402)
Comprehensive loss:									
Net loss (restated)	—	—	—	—	—	—	(30,343)	—	(30,343)
Unrealized gain on short-term investments, net of reclassification adjustment	—	—	—	—	—	—	—	988	988
Total comprehensive loss (restated)									(29,355)
Common stock issued in connection with stock option exercises	—	—	208	596	—	—	—	—	596
Deferred stock compensation related to stock options:									
Grants	—	—	—	484	—	(484)	—	—	—
Forfeitures	—	—	—	(240)	—	240	—	—	—
Amortization	—	—	—	—	—	7,188	—	—	7,188
Accretion and dividends on mandatorily redeemable convertible preferred stock	—	1,718	—	(1,718)	—	—	—	—	(1,718)
Conversion of Series A and B mandatorily redeemable convertible preferred stock	(6,540)	(262,258)	23,543	262,258	—	—	—	—	262,258
Net proceeds from issuance of common stock	—	—	10,000	109,774	—	—	—	—	109,774
Balance at December 31, 2002 (restated)	—	—	45,815	427,010	(725)	(18,291)	(141,462)	2,809	269,341
Comprehensive loss:									
Net loss	—	—	—	—	—	—	(59,571)	—	(59,571)
Unrealized loss on short-term investments, net of reclassification adjustment	—	—	—	—	—	—	—	(2,283)	(2,283)
Total comprehensive loss									(61,854)
Common stock issued in connection with stock option exercises	—	—	579	2,060	—	—	—	—	2,060
Deferred stock compensation related to stock options:									
Forfeitures	—	—	—	(1,782)	—	1,782	—	—	—
Amortization	—	—	—	—	—	7,054	—	—	7,054
Net proceeds from issuance of common stock	—	—	6,100	71,314	—	—	—	—	71,314
Balance at December 31, 2003	—	$ —	52,494	$498,602	$(725)	$ (9,455)	$(201,033)	$526	$287,915

The accompanying notes are an integral part of these financial statements.

ZYMOGENETICS, INC.

STATEMENTS OF CASH FLOWS
(in thousands)

	Year ended December 31,		
	2003	2002 (restated)	2001
Cash flows from operating activities			
Net loss	$ (59,571)	$ (30,343)	$ (36,879)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation and amortization	5,447	5,898	5,405
Net loss on disposition of property and equipment	100	187	—
Noncash stock-based compensation	7,054	7,188	3,507
Net realized gain on sale of short-term investments	(984)	(582)	(95)
Amortization of premium on short-term investments	3,225	2,448	787
Changes in			
Receivables	(2,159)	339	381
Prepaid expenses and other assets	(1,945)	(705)	(366)
Accounts payable	(809)	(937)	2,149
Related party payables	—	—	(279)
Accrued liabilities	2,612	2,539	(996)
Deferred revenue	(3,855)	2,680	7,696
Deferred lease obligations	31	28	—
Other noncurrent liabilities	1,060	(117)	(250)
Net cash used in operating activities	(49,794)	(11,377)	(18,940)
Cash flows from investing activities			
Purchase of property and equipment	(12,562)	(9,943)	(8,181)
Purchase of short-term investments	(288,579)	(305,517)	(207,700)
Proceeds from sale of property and equipment	72	31	65
Proceeds from sale and maturity of short-term investments	311,568	184,614	98,146
Net cash provided by (used in) investing activities	10,499	(130,815)	(117,670)
Cash flows from financing activities			
Net proceeds from issuance of common stock	71,314	110,677	—
Construction advance from landlord	7,918	—	—
Proceeds from sale-leaseback financing	—	50,489	—
Principal payments on lease obligation	—	(385)	—
Proceeds from exercise of stock options	2,060	596	28
Net cash provided by financing activities	81,292	161,377	28
Net increase (decrease) in cash and cash equivalents	41,997	19,185	(136,582)
Cash and cash equivalents at beginning of period	55,579	36,394	172,976
Cash and cash equivalents at end of period	$ 97,576	$ 55,579	$ 36,394
Supplemental disclosure of cash flow information			
Cash paid during the period for interest	$ 5,197	$ 862	$ 13
Noncash financing activities			
Accretion on Series B mandatorily redeemable convertible preferred stock	$ —	$ 88	$ 1,048
Dividends accrued on Series A and Series B mandatorily redeemable convertible preferred stock	$ —	$ 1,630	$ 19,562
Other non-cash additions to property and equipment	$ 2,445	$ —	$ —
Recognition of prepaid offering costs	$ —	$ 902	$ —

The accompanying notes are an integral part of these financial statements.

ZYMOGENETICS, INC.

NOTES TO FINANCIAL STATEMENTS

1. Organization and summary of significant accounting policies

Nature of operations

ZymoGenetics, Inc. (the Company) was incorporated in the state of Washington in June 1981 and operated independently until it was acquired in 1988 by Novo Nordisk North America, a wholly owned subsidiary of Novo Nordisk A/S (Novo Nordisk). In November 2000, the Company became independent from Novo Nordisk upon completion of a private placement of Series B mandatorily redeemable convertible preferred stock with an investor consortium. In February 2002, the Company completed an initial public offering of common stock, at which time all Series A and B mandatorily redeemable convertible preferred stock was converted to common stock. In October 2003, the Company sold 6,100,000 shares of common stock in a follow-on public offering. At December 31, 2003, Novo Nordisk's ownership percentage was 41.5%.

As an independent biopharmaceutical company, the Company is focused on the discovery and development of protein therapeutics for the prevention or treatment of significant human diseases. The Company has generated a pipeline of proprietary product candidates and intends to commercialize them through internal development, collaborations with biopharmaceutical partners or out-licensing of patents.

Over the next several years the Company will need to seek additional funding through public or private financings, including equity financings, and through other arrangements, including collaborative arrangements. Poor financial results, unanticipated expenses or unanticipated opportunities that require financial commitments could give rise to additional financing requirements. However, financing may not be available when required, or may not be available on acceptable terms.

Cash and cash equivalents

The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash and cash equivalents. The Company invests its cash and cash equivalents with major financial institutions, the amount of which exceeds federally insured limits. The Company has not experienced any losses on its cash and cash equivalents.

Short-term investments

Marketable securities are classified as available-for-sale. Available-for-sale securities are carried at fair value, with the unrealized gains and losses reported as a separate component of shareholders' equity. Interest on securities classified as available-for-sale is included in investment income. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in investment income. Realized gains and losses are included in investment income. The cost of securities sold is based on the specific identification method.

Fair value of financial instruments

The carrying values of cash and cash equivalents, accounts receivable, accounts payable and accrued liabilities approximate their respective fair values due to their relative short maturities. The carrying value of noncurrent liabilities approximate fair value as adjustments to market are recorded each period.

Property and equipment

Property and equipment are stated at cost. Additions, betterments and improvements are capitalized and depreciated. When assets are retired or otherwise disposed of, the cost of the assets and related depreciation is

eliminated from the accounts and any resulting gain or loss is reflected in the results of operations. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, which include five years for furniture and lab equipment, ten years for pilot plant equipment and 40 years for buildings. Expenditures for repairs and maintenance are charged to expense as incurred.

Leasehold improvements are amortized evenly over their estimated useful lives or the term of the lease, whichever is shorter. At December 31, 2003, the Company is amortizing its leasehold improvements over 10 years.

Impairment of long-lived assets

The Company assesses the impairment of long-lived assets whenever events or changes in business circumstances indicate that the carrying amounts of the assets may not be fully recoverable. Measurement of an impairment is required when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition is less than its carrying amount. The amount of a recognized impairment loss is the excess of an asset's carrying value over its fair value. The Company has not recognized any impairment losses through December 31, 2003.

Revenue recognition

The Company recognizes revenue in accordance with Staff Accounting Bulletin No. 101, *Revenue Recognition in Financial Statements* (SAB 101), as amended by Staff Accounting Bulletin No. 104, *Revenue Recognition* (SAB 104), and Emerging Issues Task Force Issue No. 00-21, *Revenue Agreements with Multiple Deliverables* (EITF 00-21). EITF 00-21 applies to arrangements entered into after June 30, 2003.

The Company earns royalties on two proteins marketed and sold by Novo Nordisk, insulin and glucagon. Royalities are received from Novo Nordisk annually within 60 days after the end of the calendar year. For insulin, the royalties are based on manufacturing costs for the quantity of insulin sold during the year. These costs are calculated in Danish Kroner, and then converted to U.S. Dollars based on the exchange rate at the end of the year. Royalties earned on sales of glucagon are calculated as a percentage of net sales. The Company accrues estimated royalties at the end of each quarter based on historical sales data, estimates provided to the Company by Novo Nordisk and changes in the Danish Kroner to U.S. Dollar exchange rate. Adjustments are made in the following year reflecting the difference between the Company's estimates and actual reported royalties and, to date, have not been significant.

The Company also earns royalties on several products marketed by other companies. Royalties on these products are received within 30 to 60 days after the end of each calendar quarter. The Company accrues estimated royalties at the end of each quarter based on historical sales data. Adjustments are made in the following quarter reflecting the difference between the Company's estimates and actual reported royalties and, to date, have not been significant.

The Company enters into various licensing and collaborative agreements that generate significant license or other upfront fees with subsequent milestone payments earned upon completion of development milestones. The Company uses its best judgment to estimate the period over which there are continuing commitments to perform under these agreements. Revenue from upfront fees is recognized on a straight-line basis over this period, which has ranged in duration from six months to ten years. For certain license agreements that require no continuing performance on the Company's part, license fee revenue is recognized immediately upon execution of the agreement. Revenues from milestone payments representing completion of separate and substantive earnings processes are recognized when the milestone is achieved and amounts are due and payable.

Deferred revenue arises from payments received in advance of the culmination of the earnings process. Deferred revenue expected to be recognized within the next twelve months is classified as a current liability. Deferred revenue will be recognized as revenue in future periods when the applicable revenue recognition criteria have been met.

In December 2002, the Company signed an agreement granting Amgen, Inc., Immunex Corporation and Wyeth a license to the Company's Ig-fusion protein patents. As a result of this agreement, the Company, Immunex and Amgen terminated a patent infringement lawsuit filed by the Company in March 2002 against Immunex Corporation (now owned by Amgen). The Company received a one-time lump sum payment, which was recorded as license fee revenue in 2002.

Research and development costs

Research and development costs consist of salaries and benefit expenses, costs of consumables, facility costs and contracted services and are expensed as incurred. Costs to acquire technologies that are utilized in research and development and that have no future use are expensed when incurred. Reimbursement for shared expenses received from collaboration partners are recorded as reductions to research and development expenses. Costs relating to filing and pursuing patent applications are expensed as incurred.

Income taxes

The Company records a provision for income taxes in accordance with Statement of Financial Accounting Standards No. 109, *Accounting for Income Taxes* (SFAS 109), which requires the liability method of accounting for income taxes. Deferred tax assets or liabilities are recorded for all temporary differences between financial and tax reporting. Deferred tax expense (benefit) results from the net change during the period of the deferred tax assets and liabilities. A valuation allowance is recorded when it is more likely than not that the deferred tax asset will not be realized.

Stock-based compensation

As permitted by the provisions of Statement of Financial Accounting Standards No. 123, *Accounting for Stock Based Compensation* (SFAS 123), the Company has accounted for employee stock option grants under Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees* (APB 25), and applied the disclosure-only provisions of SFAS 123 to account for its stock option plans. Under APB 25, compensation expense is based on the excess, if any, of the estimated fair value of the Company's stock at the date of grant over the exercise price of the option. Deferred compensation, relating to employee stock option grants awarded prior to the Company's initial public offering in February 2002, is amortized over the vesting period of the individual options using the straight-line method. All employee stock option grants awarded subsequent to the Company's initial public offering have been granted with exercise prices equal to the fair value of the Company's common stock on the date of grant.

The following table illustrates the effect on net loss attributable to common shareholders and net loss per share as if the fair value based method had been applied to all outstanding and unvested awards for each of the years ended December 31 (in thousands, except per share data):

	2003	2002 (restated)	2001
Net loss attributable to common shareholders, as reported	$(59,571)	$(32,061)	$(57,489)
Add: employee stock-based compensation under APB25 included in reported net loss attributable to common shareholders	7,054	7,188	3,507
Deduct: total employee stock-based compensation expense determined under the fair value method	(12,610)	(9,891)	(4,503)
Net loss attributable to common shareholders, pro forma	$(65,127)	$(34,764)	$(58,485)
Basic and diluted net loss per share, as reported	$ (1.26)	$ (0.75)	$ (4.85)
Basic and diluted net loss per share, pro forma	$ (1.38)	$ (0.82)	$ (4.94)

Comprehensive income or loss

The Company has adopted the provisions of Statement of Financial Accounting Standards No. 130, *Reporting Comprehensive Income* (SFAS 130). SFAS 130 requires the disclosure of comprehensive income or loss and its components in the financial statements. Comprehensive income or loss is the change in shareholder's equity resulting from net income or loss and unrealized gains and losses on short-term investments.

Use of estimates

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities; disclosure of contingent assets and liabilities at the date of the financial statements; and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Segments

Statement of Financial Accounting Standards No. 131, *Disclosures about Segments of an Enterprise and Related Information* (SFAS 131), establishes standards for the way public business enterprises report information about operating segments in annual financial statements and requires that those enterprises report selected information about operating segments in interim financial reports. The Company manages and evaluates its operations in one reportable segment.

Guarantees

In the normal course of business, the Company indemnifies other parties, including collaboration partners, lessors and parties to other transactions with the Company, with respect to certain matters. The Company has agreed to hold the parties harmless against losses arising from a breach of representations and covenants, or out of intellectual property infringement or other claims made against these parties. These agreements may limit the time within which an indemnification claim can be made and the amount of the claim. In addition, the Company's bylaws contain indemnification obligations to the Company's officers and directors. It is not possible to determine the maximum potential obligation under these indemnification agreements since any claim would be based on the facts and circumstances of the claim and the particular provisions of each agreement.

Reclassifications

Certain reclassifications have been made to prior year financial statements to conform to classifications used in the current year. These reclassifications had no impact on net loss, shareholders' equity or cash flows as previously reported.

Loss per share

Basic and diluted net loss per share has been computed based on net loss attributable to common shareholders and the weighted-average number of common shares outstanding during the applicable period. The Company has excluded all outstanding options to purchase common stock and shares subject to repurchase from the calculation of diluted net loss per share, as such shares are antidilutive for all periods presented.

The following table presents the calculation of basic and diluted net loss per share attributable to common shareholders for years ended December 31 (in thousands, except per share data):

	2003	2002 (restated)	2001
Net loss attributable to common shareholders	$(59,571)	$(32,061)	$(57,489)
Weighted-average shares used in computing basic and diluted net loss per share	47,317	42,578	11,846
Basic and diluted net loss per share	$ (1.26)	$ (0.75)	$ (4.85)
Securities not included in net loss per share attributable to common shareholders calculation:			
Mandatorily redeemable convertible preferred stock (as if converted)	—	—	23,543
Options to purchase common stock	9,378	8,267	7,307
Shares subject to repurchase	—	7	88
	9,378	8,274	30,938

Recent accounting pronouncements

In 2001, the Financial Accounting Standards Board (FASB) issued Statement of Financial Accounting Standards No. 143, *Accounting for Asset Retirement Obligations* (SFAS 143), which establishes requirements for the financial accounting and reporting for obligations associated with the retirement of tangible long-lived assets and the associated asset retirement costs. The standard is effective for fiscal years beginning after June 15, 2002, with earlier application encouraged. Adoption of this statement has not impacted the results of operations or the financial position of the Company.

In 2002, the FASB issued Statement of Financial Accounting Standards No. 145, *Rescission of FASB Statements No. 4, 44 and 64, Amendment to FASB Statement No. 13, and Technical Corrections* (SFAS 145). SFAS 145 eliminates the requirement in Statement of Financial Accounting Standards No. 4, (SFAS 4) that gains and losses from the extinguishments of debt be aggregated and classified as extraordinary items, net of the related income tax. The rescission of SFAS 4 is effective for fiscal years beginning after May 15, 2002. Adoption of this statement has not impacted the results of operations or the financial position of the Company.

In 2002, the FASB issued Statement of Financial Accounting Standards No. 146, *Accounting for Costs Associated with Exit or Disposal Activities* (SFAS 146). SFAS 146 requires the recognition of such costs when they are incurred rather than at the date of a commitment to an exit or disposal plan. The provisions of SFAS 146 are to be applied prospectively to exit or disposal activities initiated after December 31, 2002. Adoption of this statement has not impacted the results of operations or the financial position of the Company.

In 2002, the Emerging Issues Task Force (EITF) finalized its tentative consensus on EITF Issue No. 00-21, *Revenue Arrangements With Multiple Deliverables* (EITF 00-21), which provides guidance on the timing and method of revenue recognition for sales agreements that include delivery of more than one product or service. EITF 00-21 is effective prospectively for arrangements entered into in fiscal periods beginning after June 15, 2003. Adoption of this statement has not impacted the results of operations or the financial position of the Company.

In January 2003, the FASB issued Interpretation No. 46, *Consolidation of Variable Interest Entities* (FIN 46), which addresses consolidation by business enterprises of variable interest entities that either: (1) do not have sufficient equity investment at risk to permit the entity to finance its activities without additional subordinated financial support, or (2) the company will hold a significant variable interest in, or have significant involvement with, an existing variable interest entity. FIN 46 is effective as of the first interim period beginning after June 15, 2003. However, an October 2003 FASB Staff Position deferred the effective date for applying the provisions of FIN 46 for interests held by public entities in variable interest entities or potential variable interest entities created before February 1, 2003 and nonregistered investment companies. Adoption of this interpretation has not impacted the results of operations or the financial position of the Company.

In May 2003, the FASB issued Statement of Financial Accounting Standards No. 149, *Amendment of Statement 133 on Derivative Instruments and Hedging Activities* (SFAS 149), effective for contracts entered into or modified after June 30, 2003 and for hedging relationships designated after June 30, 2003. This rule amends SFAS 133, *Accounting for Derivative Instruments and Hedging Activities*, as amended, to provide more consistent reporting of contracts as either derivatives or hybrid instruments. Adoption of this statement has not impacted the results of operations or the financial position of the Company.

In May 2003, the FASB issued Statement of Financial Accounting Standards No. 150, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity* (SFAS 150), effective for financial instruments entered into or modified after May 31, 2003, and otherwise is effective at the beginning of the first interim period beginning after June 15, 2003. In October 2003, the FASB deferred certain provisions of SFAS 150 relating to mandatorily redeemable non controlling interests. Adoption of this statement has not impacted the results of operations or the financial position of the Company.

2. Restatement of Financial Statements

The Company's financial statements for the year ended December 31, 2002 have been restated to reflect a change in accounting for a sale-leaseback transaction. Subsequent to the issuance of the 2002 financial statements, the Company determined in consultation with its outside auditors, that the sale-leaseback transaction that occurred in October 2002 was improperly accounted for. The Company initially accounted for the transaction as a sale of the properties involved and as operating leases under the provisions of SFAS 13. Subsequently it was determined that the leases contain a technical provision that could, under certain remote circumstances, result in the Company's continuing ownership involvement with respect to the properties. Due to the existence of this provision, the transaction is more properly accounted for as a financing rather than a sale and leaseback of the properties. The following table summarizes the impact of this restatement on the Company's December 31, 2002 financial statements (in thousands, except per share data):

	As Reported	As Restated
At December 31, 2002:		
Property and equipment, net	$ 17,253	$ 52,954
Deferred gain on sale of asset, current	960	—
Deferred gain on sale of asset, noncurrent	13,206	—
Deferred lease obligations	380	28
Lease obligation	—	50,146
Accumulated deficit	(141,535)	(141,462)
For the year ended December 31, 2002:		
Research and development expense	66,469	65,508
General and administrative expense	16,925	16,685
Loss from operations	(37,807)	(36,606)
Interest expense	—	(896)
Other income (expense), net	37	(195)
Net loss	(30,416)	(30,343)
Net loss attributable to common shareholders	(32,134)	(32,061)
Net loss per share—basic and diluted	(0.75)	(0.75)
Net cash used in operating activities	(11,762)	(11,377)
Net cash used in investing activities	(80,326)	(130,815)
Net cash provided by financing activities	111,273	161,377

3. Short-term investments

Short-term investments consisted of the following (in thousands):

	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Estimated Fair Value
December 31, 2003				
Type of security:				
Corporate debt securities	$ 47,253	$ 272	$ (26)	$ 47,499
Asset-backed securities	71,985	184	(122)	72,047
U.S. government and agency securities	78,432	232	(37)	78,627
Foreign government securities	4,120	23	—	4,143
	$201,790	$ 711	$(185)	$202,316
Maturity date:				
Less than one year	$137,170			$137,538
Due in 1-3 years	64,620			64,778
	$201,790			$202,316

	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Estimated Fair Value
December 31, 2002				
Type of security:				
Commercial paper and money market	$ 4,660	$ —	$ —	$ 4,660
Corporate debt securities	55,626	908	(1)	56,533
Asset-backed securities	48,332	371	(4)	48,699
U.S. government and agency securities	113,546	1,450	—	114,996
Foreign government securities	4,886	85	—	4,971
	$227,050	$2,814	$ (5)	$229,859
Maturity date:				
Less than one year	$ 99,924			$100,822
Due in 1-3 years	127,126			129,037
	$227,050			$229,859

The Company has concluded that unrealized losses are temporary due to the ability of the Company to realize the full value of its investments at maturity. Such unrealized losses have existed for less than 12 months.

At December 31, 2003, the aggregate estimated fair value of the investments with realized losses was as follows (in thousands):

Corporate debt securities	$10,947
Asset-backed securities	20,627
U.S. government and agency securities	10,038
	$41,612

Realized gains were $1.3 million and $863,000 for the years ended December 31, 2003 and 2002, respectively. Realized losses were $313,000 and $281,000 for the years ended December 31, 2003 and 2002, respectively. Reclassification adjustments reflected in other comprehensive income for net realized gains and losses were $1.0 million and $595,000 for the years ended December 31, 2003 and 2002, respectively.

4. Property and equipment

Property and equipment consisted of the following at December 31 (in thousands):

	2003	2002 (restated)
Land and buildings	$ 52,998	$ 52,934
Leasehold improvements	518	6,232
Furniture and equipment	34,506	40,314
Construction in progress	14,022	1,463
	102,044	100,943
Less: Accumulated depreciation and amortization	(39,703)	(47,989)
	$ 62,341	$ 52,954

Land and buildings include assets deemed owned in connection with the sale and leaseback financing transaction described in Note 6.

5. Accrued liabilities

Accrued liabilities consisted of the following at December 31 (in thousands):

	2003	2002
Vacation pay	$2,219	$2,022
Incentive compensation	2,418	172
Contract services	3,195	2,756
City and state taxes	37	255
Severance payments	165	73
Other	267	411
	$8,301	$5,689

6. Lease obligation

In October 2002, the Company completed a sale and leaseback transaction involving its headquarter buildings located in Seattle, Washington. The three buildings were sold for a total sale price of $52.3 million. Net proceeds from the transaction amounted to $50.5 million. Simultaneously, the Company agreed to lease the buildings from the purchaser for a period of 15 years, subject to four five-year renewal options. The initial rental payment of $5.1 million per year increases by 3.5% each year during the term. Rent for the renewal terms under these lease agreements will be the greater of fair market value or 90% of the rent for the last year prior to renewal. The Company has provided the lessor a security deposit in the form of pledged securities equal to two months base rent.

The Company has accounted for the transaction as a financing due to a technical provision within the leases related to condemnation, which could, under remote circumstances, result in continuing ownership involvement by the Company in the three buildings. Under this method of accounting, the net proceeds of the sale are considered to be a long-term interest bearing liability. Rent payments under the leases are considered to be payments toward the liability and are allocated to principal and interest. The Company has recorded a liability of $50.5 million with an effective annual interest rate of approximately 11%. At the end of the lease term, the remaining balance of the liability will approximate the net book value of the buildings leased.

The Company has exercised an option to expand one of the leased buildings. The project began in April 2003 and is scheduled to be completed in mid-2004. The expansion project is expected to cost $26 million, including all related equipment costs, of which approximately $15 million will be funded by the landlord. Over the course of the construction period, the landlord is advancing a proportionate share of construction costs incurred by the Company. At December 31, 2003, the Company had incurred total project costs of $13.5 million and recorded an advance from the landlord of $7.9 million. The initial rental payment for the expansion space of $1.5 million per year will increase by 3.5% each year during the term. Upon completion of the expansion project, the lease terms for all of the buildings will be reset to 15 years from the date of occupancy of the new space.

The following table presents the Company's scheduled payments under the lease obligation, including the additional payments related to the expansion and the reset of the lease term to 15 years:

Year ending December 31,	
2004	$ 6,256
2005	7,124
2006	7,373
2007	7,622
2008	7,876
Thereafter	100,388
	$136,639

7. Transactions and accounts with related parties

Novo Nordisk has been granted an option to obtain an exclusive license to an unlimited number of proteins discovered after August 1995 that modulate insulin producing beta cells and for up to the greater of eight or 25% of the Company's protein candidates other than those related to beta cells over a period of four years beginning November 10, 2000. In return, the Company is entitled to receive four annual payments of $7.5 million, the last of which was received in November 2003. The option payments are being recognized ratably over the term of the agreement. Novo Nordisk may elect to extend the agreement for a period of two additional years, with the right to license up to four more protein candidates in return for continuing the $7.5 million annual payments to the Company. For each protein licensed by Novo Nordisk, the Company will receive an up-front license fee, the amount of which is dependent on the stage of the product candidate licensed. Additionally, Novo Nordisk will be obligated to make payments upon the achievement of predefined development milestones and to pay royalties on sales of resulting products.

The Company earns royalties on several products marketed and sold by Novo Nordisk, including recombinant insulin and recombinant glucagon. Royalties are based on contracts predating the Company's acquisition by Novo Nordisk. The Company earned total royalties from Novo Nordisk of approximately $6.4 million, $5.0 million and $5.2 million for the years ended December 31, 2003, 2002 and 2001, respectively.

On February 1, 2002, the Company completed its initial public offering. Upon the completion of the initial public offering, each share of Series A and Series B mandatorily redeemable convertible preferred stock held by

Novo Nordisk converted to 3.6 shares of non-voting and voting common stock, respectively. Effective June 24, 2002, all shares of non-voting common stock were converted into the same number of shares of voting common stock.

In December 2002, the Company completed a collaborative agreement with Novo Nordisk for the preclinical development of IL-21. Under the terms of the agreement, the Company and Novo Nordisk are collaborating on all research and development activities leading up to the filing of an Investigational New Drug application (IND) in the United States. Upon signing, Novo Nordisk paid $4.0 million to the Company as reimbursement of a portion of the Company's costs incurred prior to the agreement. This amount was deferred and is being recognized as revenue ratably over the estimated period leading to the IND filing. Novo Nordisk also agreed to pay the Company up to $7.0 million for its 50% share of IL-21 development costs incurred from the date of the agreement through the filing of the IND. In 2003, such payments totaled $4.9 million, which were recorded as an offset to the Company's research and development costs.

Amounts receivable from Novo Nordisk were approximately $3.5 million and $389,000 at December 31, 2003 and 2002, respectively.

8. Retirement plans

Defined contribution

The Company has established a 401(k) retirement plan covering substantially all of its employees. The plan provides for matching and discretionary contributions by the Company. Such contributions were approximately $1.5 million, $2.1 million and $1.7 million for the years ended December 31, 2003, 2002 and 2001, respectively.

Deferred compensation plan

The Company has a Deferred Compensation Plan (DCP) for key employees. Eligible plan participants are designated by the Company's board of directors. The DCP allows participants to defer up to 15% of their annual compensation and up to 100% of any bonus. At December 31, 2003 and 2002, approximately $3.4 million and $2.7 million, respectively, was deferred under the DCP and was recorded both as a noncurrent asset and a noncurrent liability.

9. Income taxes

At December 31, 2003, the Company had net operating loss carryforwards of approximately $112.0 million, research and development tax credit carryforwards of approximately $18.7 million, a rehabilitation tax credit carryforward of $1.5 million and alternative minimum tax credit carryforwards of $1.2 million. The carryforwards are available to offset future tax liabilities. The net operating loss, research and development tax credit and rehabilitation tax credit carryforwards will expire in the years 2008 to 2023. The alternative minimum tax credit will carry forward indefinitely. The Company completed an initial public offering on February 1, 2002 and pursuant to the provisions of Internal Revenue Code Section 382 the offering may qualify as a change in ownership. Accordingly, a portion of the net operating loss carryforwards may be limited.

Components of income tax benefit were as follows for the years ended December 31 (in thousands):

	2003	2002	2001
Current	$—	$—	$ (90)
Deferred	—	—	—
	$—	$—	$ (90)

Deferred tax assets and liabilities arise from temporary differences between financial and tax reporting. The Company has provided a valuation allowance at December 31, 2003 and 2002 to offset the excess of deferred tax assets over the deferred tax liabilities, due to the Company's status as a stand-alone taxpayer and the uncertainty of realizing the benefits of the net deferred tax asset. Deferred tax assets and liabilities were as follows as of December 31 (in thousands):

	2003	2002 (restated)
Deferred tax assets:		
Net operating loss carryforwards	$ 39,212	$ 18,382
Research and development tax credit carryforwards	18,707	14,953
Alternative minimum tax credit carryforwards	1,242	1,242
Rehabilitation tax credit carryforward	1,507	1,507
Intellectual property purchased from Novo Nordisk	7,497	8,747
Deferred gain on sale of assets	4,958	4,958
Other	8,456	6,227
	81,579	56,016
Deferred tax liabilities:		
Deferred revenue	(6,282)	(3,938)
	75,297	52,078
Less: Valuation allowance	(75,297)	(52,078)
Net deferred tax asset	$ —	$ —

The valuation allowance increased by $23.2 million, $5.4 million and $14.6 million in 2003, 2002 and 2001, respectively, to fully reserve the net deferred tax assets.

In October 2000, the Company entered into a tax sharing agreement with Novo Nordisk. The agreement states that all research and development tax credit carryforwards generated by the Company prior to November 9, 2000 used by the Company to generate a tax benefit in future periods shall be reimbursed to Novo Nordisk. The total amount paid shall not exceed $12.0 million.

Realization of the deferred tax asset associated with intellectual property purchased from Novo Nordisk will be reflected as increases in shareholders' equity and will not be reflected as tax benefits in the statement of operations.

The reconciliation between the Company's effective tax rate and the income tax rate is as follows for the years ended December 31:

	2003	2002	2001
Federal income tax rate	(35)%	(35)%	(35)%
Research and development tax credits	(6)	(7)	(6)
Valuation allowance	39	34	39
Other	2	8	2
Effective tax rate	0%	0%	0%

10. Commitments

Operating leases

The Company leases certain office space, near its corporate headquarters in Seattle, Washington, under noncancellable operating lease agreements.

In November 2001, the Company entered into a lease agreement for office space. The lease term began on February 1, 2002. In October 2003, the Company began construction on additional office space within the same building. The lease on the additional office space will begin in February 2004. The terms of both leases run through January 2012, with options to renew both leases for up to two additional terms of five years each. Total annual lease payments under these leases average approximately $900,000 per year over their terms.

Gross rental expense for the years ended December 31, 2003, 2002, and 2001 was approximately $700,000, $2.6 million and $1.9 million, respectively. Cash received under sublease agreements was approximately $100,000, $2.0 million and $2.0 million for the years ended December 31, 2003, 2002 and 2001, respectively.

The following table presents the Company's commitments for future minimum rental payments under noncancelable operating leases with initial or remaining terms in excess of one year (in thousands):

Year ending December 31,	
2004	$1,078
2005	1,159
2006	1,169
2007	1,234
2008	1,248
Thereafter	3,972
	$9,860

Other

Certain key employees have employment agreements with the Company which provide for salary, health insurance and certain additional severance benefits.

11. Serono S.A. agreement

In August 2001, the Company entered into a collaborative development and marketing agreement with Ares Trading S.A. (Serono), a wholly owned subsidiary of Serono S.A. Under the agreement, the Company is collaborating with Serono to develop biopharmaceutical products based on two receptors, TACI and BCMA. The Company could receive license fee and milestone payments of up to an aggregate of $52.5 million in connection with the development and approval of products, of which $10.5 million has been received to date. The Company will share research and development expenses worldwide, with the exception of Japan, where Serono will cover all expenses. The Company retains an option to co-promote products with Serono in North America while Serono will have exclusive rights to market products in the remainder of the world, for which the Company will receive royalties. The Company has the option of discontinuing funding of research and development and commercialization costs, and forgoing its right to co-promote products in North America. If the Company chooses to discontinue funding, Serono would have exclusive marketing rights in North America, and the Company would receive a royalty on any sales in North America in lieu of sharing in the net sales,

commercialization expenses and profits from the products. Serono is responsible for manufacturing all products for both clinical trials and commercial sale. The Company received a $7.5 million payment from Serono in 2001, which is being amortized over the estimated term of the development program, approximately nine years.

12. Mandatorily redeemable convertible preferred stock

In November 2000, the Company issued 4,011,768 shares of Series B mandatorily redeemable convertible preferred stock to a group of investors at a price per share of $37.39, which provided proceeds to the Company of approximately $142.5 million, net of offering costs of approximately $7.5 million. In the same period, the Company declared a dividend on the outstanding common stock owned by Novo Nordisk, issuing 2,528,000 shares of Series A mandatorily redeemable convertible preferred stock. The holders of both Series A and B shares were entitled to receive a cumulative dividend of 8% per annum on the then current liquidation value. Each share of preferred stock was convertible into 3.6 shares of common stock.

On February 1, 2002, the Company completed its initial public offering, which resulted in the conversion of each share of Series A and Series B mandatorily redeemable convertible preferred stock to 3.6 shares of non-voting and voting common stock, respectively. Effective June 24, 2002, all outstanding shares of non-voting common stock were converted into the same number of shares of voting common stock.

13. Shareholders' equity

The Company's authorized capital stock consists of 150,000,000 shares of no par value voting common stock, 30,000,000 shares of no par value non-voting common stock and 30,000,000 shares of no par value preferred stock. On January 9, 2002, the Company effected a 3.6-for-1 stock split of its common stock in the form of a stock dividend. All common stock share and per share amounts in the financial statements have been adjusted retroactively to reflect the stock split.

Common stock

On February 1, 2002, the Company sold 10,000,000 shares of common stock in an initial public offering, raising net proceeds of $110.7 million. Upon the completion of the initial public offering the 4,011,768 shares of Series B mandatorily redeemable convertible preferred stock converted to 14,442,359 shares of voting common stock, and the 2,528,000 shares of Series A mandatorily redeemable convertible preferred stock converted to 9,100,800 shares of non-voting common stock. Effective June 24, 2002, all shares of non-voting common stock were converted into the same number of shares of voting common stock. In October 2003, the Company sold 6,100,000 shares of common stock in a public offering, raising net proceeds of $71.3 million.

Stock options

In March 2000, the Company adopted the 2000 Stock Incentive Plan (the 2000 Plan). Upon completion of the Company's initial public offering in February 2002, the 2000 Plan was suspended and the 2001 Stock Incentive Plan (the 2001 Plan) became effective. Both Plans provide for the issuance of incentive stock options and nonqualified stock options to employees, directors, consultants and other independent contractors who provide services to the Company. The Company's board of directors is responsible for administration of the Plans and determines the term of each option, exercise price and the vesting terms. Options generally vest over a four-year period and expire ten years from the date of grant. The 2001 Plan provides for an annual increase in authorized shares effective the first day of each year equal to the least of (i) 2,700,000 shares; (ii) 5% of the outstanding common stock as of the end of the Company's preceding fiscal year; and (iii) a lesser amount as

determined by the Board of Directors. The first annual increase under the 2001 Plan occurred upon completion of the Company's initial public offering. Any shares from the 2000 Plan that are not actually issued shall continue to be available for issuance under the 2001 Plan. The Company has reserved a total of 11,713,932 shares of common stock for issuance under the Plans, of which 1,277,572 are available for future grant at December 31, 2003. Certain board members were granted options to purchase 144,000 shares that are immediately exercisable. Options to purchase 141,085 shares were granted in 2003 and 2002 to certain board members. These options vest and become exercisable as of the one-year anniversary of the grant date.

A summary of stock option activity under the Plans is presented below:

	Shares available for grant	Shares subject to options granted	Weighted-average exercise price per share	Weighted-average fair value at grant date
Balance, January 1, 2001	4,509,000	4,311,000	$ 2.78	
Granted	(3,629,066)	3,629,066	$ 3.94	$ .79
Exercised	—	(271,080)	$ 2.78	
Canceled	361,894	(361,894)	$ 3.03	
Balance, December 31, 2001	1,241,828	7,307,092	$ 3.35	
Additional shares reserved	603,180			
Granted	(1,241,410)	1,241,410	$ 8.34	$5.05
Exercised	—	(208,272)	$ 2.86	
Canceled	72,833	(72,833)	$ 3.73	
Balance, December 31, 2002	676,431	8,267,397	$ 4.10	
Additional shares reserved	2,290,752			
Granted	(2,188,272)	2,188,272	$11.02	$6.65
Exercised	—	(579,344)	$ 3.60	
Canceled	498,661	(498,661)	$ 6.09	
Balance, December 31, 2003	1,277,572	9,377,664	$ 5.64	

The exercise prices of options granted during 2001 and through January 9, 2002 were less than the estimated fair value of the Company's shares at the date of grant. Estimated fair values during this time period ranged from $9.09 to $15.11 per share and, accordingly, the Company recorded total deferred compensation of $29.2 million. The exercise prices of options granted for the remainder of 2002 and through December 31, 2003, were equal to the fair value of the Company's shares at the date of grant.

The following table summarizes information about options outstanding at December 31, 2003:

	Options outstanding			Options exercisable	
Exercise price	Weighted-average exercise prices	Number of shares	Weighted-average remaining contractual life (in years)	Number of shares	Weighted-average exercise prices
$ 2.77 – $ 3.88	$ 2.78	4,223,536	6.8	3,537,429	$2.78
$ 3.89 – $11.80	$ 7.19	4,606,707	8.4	1,499,424	$5.60
$11.81 – $15.64	$14.70	547,421	9.7	—	—
$ 2.77 – $15.64	$ 5.64	9,377,664	7.8	5,036,853	$3.62

Stock Options exercisable at:

December 31, 2002	3,848,876	$3.10
December 31, 2001	2,494,545	$2.79

Estimated fair values of stock options granted have been determined using the Black-Scholes option pricing model with the following assumptions:

	2003	2002	2001
Expected dividend yield	0%	0%	0%
Expected stock price volatility	70%	70%	0%
Risk-free interest rate	3.17%	3.85%	4.48%
Expected life of options	5 years	5 years	5 years

For options granted prior to September 10, 2001, the fair value of each option is estimated on the date of grant using the minimum value method allowable for nonpublic companies with the weighted-average assumptions shown in the table above. For options granted subsequent to September 10, 2001, volatility was assumed to be 70%.

On September 14, 2001, the Company made loans to certain executives totaling $725,000, pursuant to promissory notes in connection with the purchase of shares of common stock upon the exercise of non-qualified stock options by the executives. The loans bear interest at a rate equal to the applicable federal rate. This interest is nonrefundable and nonprepayable. All outstanding principal on the notes is payable on the three-year anniversary of the notes, with accrued interest payable annually on each anniversary of the notes. Each of these notes is collateralized by a pledge of the shares of common stock issued in connection with the extension of the loan. Each of the executives' personal liability is limited to 50% of the original principal amount of the note and 100% of the accrued interest and costs, including attorney's fees, due under the note.

14. Quarterly financial results (unaudited)

The following table contains selected statements of operations information, which is unaudited and should be read in conjunction with the accompanying financial statements and related notes. The Company believes that the following unaudited information reflects all normal recurring adjustments necessary for a fair presentation of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period. Operating results for each quarter of 2003 and 2002 are summarized as follows (in thousands, except per share data):

	March 31 (restated)	June 30 (restated)	September 30 (restated)	December 31
Year ended December 31, 2003:				
Revenue	$ 6,233	$ 5,721	$ 8,212	$ 5,791
Net loss	$(13,471)	$(13,828)	$(14,995)	$(17,277)
Basic and diluted net loss per common share	$ (0.29)	$ (0.30)	$ (0.32)	$ (0.34)

	March 31	June 30	September 30	December 31 (restated)
Year ended December 31, 2002:				
Revenue	$ 5,799	$ 6,960	$ 5,925	$34,091
Net income (loss)	$(11,803)	$(15,132)	$(14,466)	$11,058
Net income (loss) attributable to common shareholders	$(13,521)	$(15,132)	$(14,466)	$11,058
Net income (loss) per common share:				
Basic	$ (0.41)	$ (0.33)	$ (0.32)	$ 0.24
Diluted	$ (0.41)	$ (0.33)	$ (0.32)	$ 0.23

The Company's quarterly financial results for the first three quarters of 2003 have been restated as described in Note 2. The following table summarizes the impact of the restatement on the Company's financial statements as reported in the Company's reports on Form 10-Q for such quarters (in thousands, except per share data):

	March 31, 2003		June 30, 2003		September 30, 2003	
	As Reported	As Restated	As Reported	As Restated	As Reported	As Restated
Property and equipment, net	$ 17,088	$ 52,395	$ 18,890	$ 53,803	$ 21,965	$ 56,563
Deferred gain on sale of asset, current	960	—	960	—	960	—
Deferred gain on sale of asset, noncurrent	12,966	—	12,726	—	12,486	—
Deferred lease obligations	752	35	1,124	42	1,497	49
Lease obligation	—	50,211	—	50,342	—	50,476
Accumulated deficit	(154,672)	(154,933)	(168,100)	(168,761)	(182,771)	(183,756)
Research and development expense	16,676	15,675	15,893	14,893	19,767	18,703
General and administrative expense	3,344	3,094	3,329	3,079	2,888	2,622
Loss from operations	(15,553)	(14,302)	(15,399)	(14,149)	(16,150)	(14,820)
Interest expense	(3)	(1,348)	(1)	(1,412)	(4)	(1,418)
Other income (expense), net	751	510	532	292	322	82
Net loss	(13,137)	(13,471)	(13,428)	(13,828)	(14,671)	(14,995)
Net loss per share—basic and diluted	(0.29)	(0.29)	(0.29)	(0.30)	(0.32)	(0.32)

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None

Item 9A. Controls and Procedures

Our principal executive officer and principal financial officer, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) as of the end of the period covered by this report, have concluded that as of such date our disclosure controls and procedures were effective. No change was made to our internal control over financial reporting in connection with this evaluation that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART III

Item 10. Directors and Executive Officers of the Registrant

(a) The information required by this item with respect to our directors is incorporated by reference to the sections captioned "Election of Directors" and "Report by the Audit Committee" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2004. We will file the proxy statement within 120 days of December 31, 2003, our fiscal year end.

(b) The information required by this item with respect to our executive officers is incorporated by reference to the section captioned "Executive Officers" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2004.

(c) The information required by this item with respect to our code of ethics is incorporated by reference to the section captioned "Other Matters" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2004.

Item 11. Executive Compensation

The information required by this item with respect to executive compensation is incorporated by reference to the section captioned "Executive Compensation" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2004.

Item 12. Security Ownership of Beneficial Owners and Management

The information required by this item with respect to beneficial ownership is incorporated by reference to the section captioned "Security Ownership of Certain Beneficial Owners and Management" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2004.

The following table provides information regarding our equity compensation plans at December 31, 2003.

Plan category	Number of securities to be issued upon exercise of outstanding options, warrants and rights	Weighted-average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plans(1)
Equity compensation plans approved by security holders	9,377,664	$5.64	1,277,572
Equity compensation plans not approved by security holders	—	—	—
Total	9,377,664	$5.64	1,277,572

(1) Does not include an increase of 2,624,718 shares, effective January 1, 2004, pursuant to a provision of the 2001 Plan that provides for an annual increase effective the first day of each year equal to the least of (i) 2,700,000 shares; (ii) 5% of the outstanding common stock as of the end of the Company's preceding fiscal year; and (iii) a lesser amount as determined by the Board of Directors.

Item 13. Relationships and Related Transactions

The information required by this item is incorporated by reference to the section captioned "Certain Transactions" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2004.

Item 14. Principal Accountant Fees and Services

The information required by this item is incorporated by reference to the section captioned "Independent Public Accountants" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2004.

PART IV

Item 15. Exhibits, Financial Statement Schedule and Reports on Form 8-K

(a) The following documents are filed as part of this Form 10-K:

1. *Financial Statements*. The following financial statements are contained in Item 8 of this report:

2. *Financial Statement Schedules*

All financial statement schedules have been omitted because the required information is either included in the financial statements or the notes thereto or is not applicable.

3. *Exhibits*

Exhibit No.	Description	
3.1	Amended and Restated Articles of Incorporation of ZymoGenetics, Inc.	(A)
3.2	Amended and Restated Articles of Incorporation of ZymoGenetics, Inc.	(D)
3.3	Amended and Restated Bylaws.	(A)
9.1	Voting Agreement, dated October 20, 2000, by and between Warburg, Pincus Equity Partners, L.P. and Ernesto Bertarelli.	(A)
9.2	Agreement and Waiver of Co-Sale Rights, dated July 16, 2001, by and among ZymoGenetics, Inc., the holders of Series B Preferred Stock listed on the signature pages thereto and Serono B.V.	(A)
9.3	Share Transfer and Voting Agreement, dated January 2, 2001, by and between Warburg, Pincus Equity Partners, L.P. and Mount Everest Advisors, L.L.C. and acknowledged by ZymoGenetics, Inc.	(A)
10.2†	Employment Agreement, dated March 21, 2001, between ZymoGenetics, Inc. and Jan K. Öhrström.	(A)

Exhibit No.		Description	
10.3†		Employment Agreement, dated March 23, 2001, between ZymoGenetics, Inc. and Patrick J. O'Hara.	(A)
10.4†		Employment Agreement, dated April 23, 2001, between ZymoGenetics, Inc. and Frank D. Collins.	(A)
10.5†		Employment Agreement, dated April 30, 2001, between ZymoGenetics, Inc. and James A. Johnson.	(E)
10.6†		Employment Agreement, dated January 2, 2002, between ZymoGenetics, Inc. and Mark D. Young.	(A)
10.7†		Employment Agreement, dated February 12, 2002, between ZymoGenetics, Inc. and Suzanne Shema.	(B)
10.8†		Employment Agreement, dated September 17, 2003, between ZymoGenetics, Inc. and Fredrik Henell.	(F)
10.9†		Amended and Restated 2000 Stock Incentive Plan.	(A)
10.10†		2001 Stock Incentive Plan.	(A)
10.11†		Stock Option Grant Program for Nonemployee Directors under the ZymoGenetics 2001 Stock Incentive Plan.	(E)
10.12†		Deferred Compensation Plan for Key Employees.	(A)
10.13		Form of Promissory Note, dated September 14, 2001, between ZymoGenetics, Inc. and the executive officers listed on Schedule A thereto.	(A)
10.14		Form of Pledge and Security Agreement, dated September 14, 2001, between ZymoGenetics, Inc. and the executive officers listed on Schedule A thereto.	(A)
10.15		Pledge and Security Agreement, dated September 14, 2001, between ZymoGenetics, Inc. and Bruce L.A Carter.	(A)
10.16	*	Insulin Agreement, dated August 6, 1982, between ZymoGenetics, Inc. and Novo Industri A/S.	(A)
10.17	*	Letter Agreement, dated March 13, 1987, between ZymoGenetics, Inc. and Novo Industri A/S.	(A)
10.18	*	Amended and Restated Human Glucagon, Analogues of Human Glucagon, Analogues of Human Insulin Letter Agreement, dated September 28, 2000, between ZymoGenetics, Inc. and Novo Nordisk A/S.	(A)
10.19	*	License Agreement for Analogues of Human Insulin, dated September 28, 2000, between the registrant and Novo Nordisk Health Care AG.	(A)
10.20		License Agreement, dated February 23, 1989, between ZymoGenetics, Inc. and the University of Washington.	(A)
10.21	*	License Agreement, dated January 18, 1994, including Amendment No. 1, dated January 1, 1997, and Amendment No. 2, dated June 5, 2000, between and among ZymoGenetics, Inc., Novo Nordisk A/S, Johnson & Johnson and Chiron Corporation.	(A)
10.22	*	Royalty Agreement pertaining to the January 18, 1994 Agreement Relating to Platelet Derived Growth Factor, dated January 1, 2000, between ZymoGenetics, Inc. and Novo Nordisk.	(A)
10.23	*	License Agreement, dated December 31, 1998, as amended on February 4, 1999 and October 23, 2000, between ZymoGenetics, Inc. and St. Jude Children's Research Hospital.	(A)
10.24	*	Option and License Agreement, effective November 10, 2000, as amended effective as of June 16, 2000 and October 20, 2000, between ZymoGenetics, Inc. and Novo Nordisk A/S.	(A)
10.25	*	Cross-License Agreement, effective November 10, 2000, between ZymoGenetics, Inc. and Novo Nordisk A/S, Enzyme Business.	(A)

Exhibit No.	Description	
10.26*	Cross-License Agreement, effective November 10, 2000, between ZymoGenetics, Inc. and Novo Nordisk A/S.	(A)
10.27	Kunitz Protein Agreement, effective November 10, 2000, between ZymoGenetics, Inc. and Novo Nordisk A/S.	(A)
10.28	Collaborative Development and Marketing Agreement, effective August 30, 2001 by and between ZymoGenetics, Inc. and Ares Trading S.A.	(A)
10.29*	Collaborative Agreement for IL-21, dated December 14, 2002, between ZymoGenetics, Inc. and Novo Nordisk A/S.	(E)
10.30*	Exclusive Patent License Agreement, effective December 18, 2002, between ZymoGenetics, Inc. and Aventis Behring GmbH.	(E)
10.31	Series B Preferred Stock Purchase Agreement, dated October 20, 2000, by and among ZymoGenetics, Inc., Novo Nordisk A/S and the other investors listed on Exhibit A thereto.	(A)
10.32	Shareholders' Agreement by and among ZymoGenetics, Inc., Novo Nordisk A/S, Novo Nordisk Pharmaceuticals, Inc. and the investors listed on Schedule A thereto, effective as of November 10, 2000.	(A)
10.33	First Amendment to Shareholders' Agreement by and among ZymoGenetics, Inc., Novo Nordisk A/S, Novo Nordisk Pharmaceuticals, Inc. and the investors listed on Schedule A thereto, dated as of February 4, 2002.	(C)
10.34	Investors' Rights Agreement by and among ZymoGenetics, Inc., Novo Nordisk Pharmaceuticals, Inc. and the persons listed on Schedule A thereto, effective as of November 10, 2000.	(A)
10.35	Tax Sharing Agreement, effective October 20, 2000, between ZymoGenetics, Inc. and Novo Nordisk of North America, Inc.	(A)
10.36	Office Lease Agreement, dated November 9, 2001, between ZymoGenetics, Inc. and 1144 Eastlake LLC.	(A)
10.37	Lease Agreement, dated October 4, 2002, between ZymoGenetics, Inc. and ARE-1201/1208 Eastlake Avenue, LLC.	(E)
10.38	Lease Agreement, dated October 4, 2002, between ZymoGenetics, Inc. and ARE-1208 Eastlake Avenue, LLC.	(E)
10.39*	Development and Supply Agreement, dated October 1, 2003, between ZymoGenetics, Inc. and Abbott Laboratories.	
23.1	Consent of PricewaterhouseCoopers LLP, independent auditors.	
31.1	Certifications of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	
31.2	Certifications of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	
32.1	Certification of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	

† Management contract or compensatory plan or arrangement.

* Portions of these exhibits have been omitted based on a grant of confidential treatment from the Securities and Exchange Commission. The omitted portions of these exhibits have been filed separately with the SEC.

(A) Incorporated by reference to ZymoGenetics Registration Statement on Form S-1 (No. 333-69190) filed on September 10, 2001, as amended.

(B) Incorporated by reference to ZymoGenetics Annual Report on Form 10-K for the year ended December 31, 2001.

(C) Incorporated by reference to ZymoGenetics Quarterly Report on Form 10-Q for the quarter ended March 31, 2002.
(D) Incorporated by reference to ZymoGenetics Quarterly Report on Form 10-Q for the quarter ended June 30, 2002.
(E) Incorporated by reference to ZymoGenetics Annual Report on Form 10-K for the year ended December 31, 2002.
(F) Incorporated by reference to ZymoGenetics Quarterly Report on Form 10-Q for the quarter ended September 30, 2003.

(b) Reports on Form 8-K

On October 15, 2003, the Company filed a Current Report on Form 8-K to file with the SEC certain information and agreements to be incorporated by reference into its Registration Statement on Form S-3 (File No. 333-107355) originally filed on July 25, 2003.

On November 6, 2003, the Company furnished a Current Report on Form 8-K to the SEC to report the issuance of a press release announcing the Company's results of operations and financial condition for the three and nine months ended September 30, 2003.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Company has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

ZYMOGENETICS, INC.

Date: March 25, 2004

By: /s/ BRUCE L.A. CARTER, PH.D.
Bruce L.A. Carter, Ph.D.
President and Chief Executive Officer

Each person whose individual signature appears below hereby authorizes and appoints Bruce L.A. Carter and James A. Johnson, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file, any and all amendments to this Report, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his or her substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report has been signed below by the following persons on behalf of the Company and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ BRUCE L.A. CARTER, PH.D. **Bruce L.A. Carter, Ph.D.**	President, Chief Executive Officer and Director (Principal Executive Officer)	March 25, 2004
/s/ JAMES A. JOHNSON **James A. Johnson**	Senior Vice President, Chief Financial Officer and Treasurer (Principal Accounting and Financial Officer)	March 25, 2004
/s/ GEORGE B. RATHMANN, PH.D. **George B. Rathmann, Ph.D.**	Chairman of the Board of Directors	March 25, 2004
/s/ DAVID I. HIRSH, PH.D. **David I. Hirsh, Ph.D.**	Director	March 25, 2004
/s/ JONATHAN S. LEFF **Jonathan S. Leff**	Director	March 25, 2004
/s/ KURT ANKER NIELSEN **Kurt Anker Nielsen**	Director	March 25, 2004
/s/ EDWARD E. PENHOET, PH.D. **Edward E. Penhoet, Ph.D.**	Director	March 25, 2004
/s/ LORI F. RAFIELD, PH.D. **Lori F. Rafield, Ph.D.**	Director	March 25, 2004
/s/ LARS REBIEN SØRENSEN **Lars Rebien Sørensen**	Director	March 25, 2004

BOARD OF DIRECTORS

George B. Rathmann, Ph.D.
Chairman of the Board
Former Chief Executive Officer
ICOS Corporation and Amgen, Inc.

Bruce L.A. Carter, Ph.D.
President and Chief Executive Officer
ZymoGenetics, Inc.

David I. Hirsh, Ph.D
Executive Vice President for Research
Columbia University

Jonathan S. Leff
Managing Director
Warburg Pincus LLC

Kurt Anker Nielsen
Former Co-Chief Executive Officer
Novo A/S

Edward E. Penhoet, Ph.D.
Chief Program Officer
The Gordon and Betty Moore Foundation

Lori F. Rafield, Ph.D.
Partner
Apax Partners, Inc.

Lars Rebien Sørensen
President, Chief Executive Officer
Novo Nordisk A/S

EXECUTIVE OFFICERS

Bruce L.A. Carter, Ph.D.
President and Chief Executive Officer

Frank D. Collins, Ph.D.
Senior Vice President, Research
Chief Scientific Officer

Fredrik Henell, M.D., Ph.D.
Senior Vice President, Business Development

James A. Johnson
Senior Vice President
Chief Financial Officer, Treasurer

Jan K. Öhrström, M.D.
Senior Vice President, Development
Chief Medical Officer

Suzanne M. Shema, J.D.
Senior Vice President, Intellectual Property and Legal Affairs

Mark D. Young, Ph.D.
Senior Vice President, Technical Operations

COMPANY HEADQUARTERS

ZymoGenetics, Inc.
1201 Eastlake Avenue E.
Seattle, Washington 98102
Telephone 206 442-6600
www.zymogenetics.com

TRANSFER AGENT AND REGISTRAR

Mellon Investor Services LLC
85 Challenger Road
Ridgefield Park, New Jersey 07660
Telephone 800 522-6645

GENERAL COUNSEL

Perkins Coie LLP
Seattle, Washington

INDEPENDENT ACCOUNTANTS

PricewaterhouseCoopers LLP
Seattle, Washington

STOCK LISTING

ZymoGenetics' common stock is traded on The Nasdaq Stock Market under the symbol ZGEN.

ANNUAL MEETING

The annual meeting of shareholders will be held at 8:00 a.m. on Thursday, June 10, 2004 at the Company headquarters.

SHAREHOLDER INQUIRIES

Information about the Company can be found on the Internet at www.zymogenetics.com. Inquiries regarding the Company and its activities may be directed to the Communications Department at the Company headquarters. Communications concerning stock and transfer requirements, lost certificates and changes of address should be directed to the Transfer Agent.

DESIGN: PHINNEY / BISCHOFF DESIGN HOUSE

ZYMOGENETICS

1201 EASTLAKE AVENUE EAST, SEATTLE, WA 98102-3702

T 206 442-6600 F 206 442-6608 E INFO@ZGI.COM WWW.ZYMOGENETICS.COM