NETICS ZYMOGENETICS

2001 Annual Report

Report

Improving Lives

Therapeutic Proteins

WE ARE ZYMOGENETICS

A biotechnology veteran with a track record of success: In business for over 20 years, we have been involved in the discovery or development of five therapeutic protein products that have reached the market with total annual sales of over $2 billion.

Focused on therapeutic proteins: We are discovering and developing therapeutic protein-based products, which we believe have a number of commercial advantages over small molecule drugs.

A promising pipeline of proprietary product candidates: We have an extensive pipeline, comprising over 70 proteins in various stages of research and development, targeting a broad range of diseases and conditions, with a balanced risk profile.

An early entrant in the race to decipher the human genome: We were early to see the opportunity in using genomic data to discover new products, we were prepared to exploit our discoveries, and we were focused, searching only for proteins that could themselves become drugs.

A broad intellectual property portfolio: We have more than 225 issued U.S. patents and more than 350 pending U.S. patent applications, which we believe represent a significant source of potential strategic and monetary value.

Jeff Ellsworth, Ph.D.
Senior Scientist / Discovering the biology of novel proteins

To Our Shareholders

EVOLUTION | PROGRESS

FROM DISCOVERY TO DEVELOPMENT

The past year has been one of tremendous evolution and progress for ZymoGenetics. We entered 2001 as a newly independent company after completing our separation from Novo Nordisk in late 2000, and ended the year positioned to complete an initial public offering. Along the way, we made significant advances in key product development and business areas:

➔ We identified three lead product candidates that we expect to move into human clinical trials late this year and next.

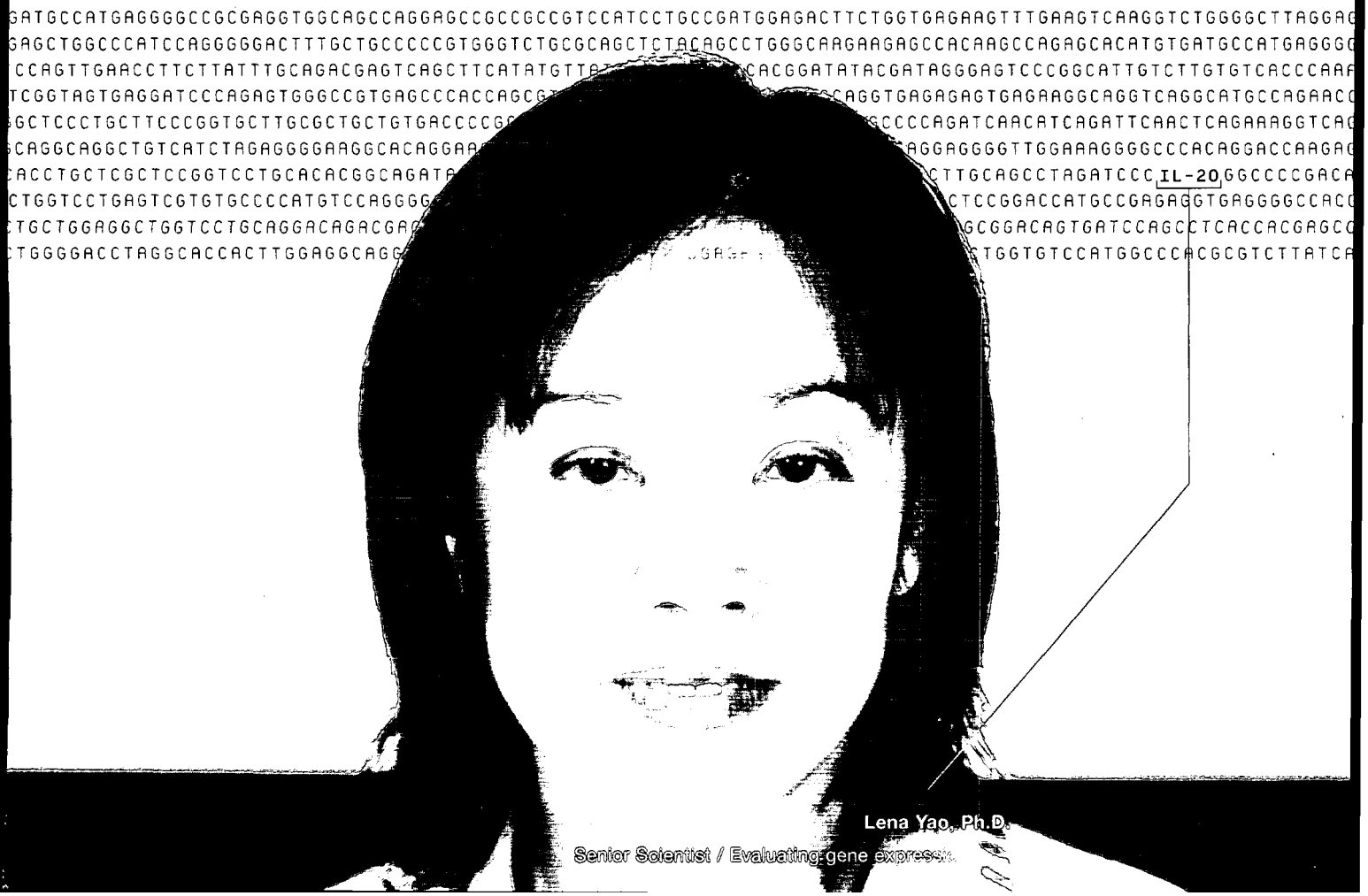
➔ We completed a co-development and commercialization agreement with Serono S.A. to advance TACI-Ig for the treatment of autoimmune disease.

➔ We completed the first initial public offering of 2002 by a biotechnology company, raising $120 million and increasing our cash and investment position to over $250 million.

These achievements mark our success as an independent company, positioning ZymoGenetics as an emerging leader in the biopharmaceutical industry, with the potential for many exciting new developments in the years to come.

Focus on Therapeutic Proteins

Throughout our 20-year history, we have focused on the discovery and development of proteins as potential therapeutics. This is at the center of our business strategy. Why are we focused on therapeutic proteins? First, we have a track record of success in this area. Today there are five marketed protein products that stem from discoveries made at ZymoGenetics. These products had sales in excess of $2 billion in 2001. Second, therapeutic proteins are generally positive acting, with the potential to stimulate repair processes or enhance normal cellular functions that are diminished due to disease and aging. This is in contrast with traditional medicinal chemistry drugs, which typically block or inhibit natural processes. Third, and most importantly, the development of protein therapeutics provides the best opportunity for market exclusivity. Unlike the development of traditional medicinal chemistry drugs, it is very difficult to design and develop a similar competing therapeutic protein without infringing the original protein patent.

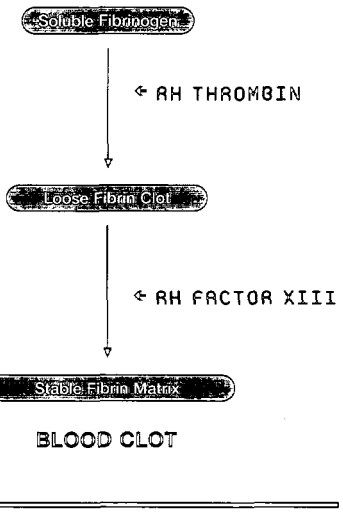


A POWERFUL

THROMBIN & FACTOR XIII
Role in Blood Clotting / Fig. 01 →

Thrombin, a key enzyme involved in the initial formation of a blood clot, converts soluble fibrinogen into an insoluble loose fibrin clot. Factor XIII induces cross-links between the fibrin molecules to form a stable clot that is more resistant to breakdown, reducing the chance for rebleeding.

FIG. 01 / BLOOD CLOT FORMATION



Lead Product Candidates

We have a robust pipeline of product candidates that are advancing towards clinical development. These products have the potential to treat a number of unmet clinical needs in areas such as cardiovascular disease, autoimmune disease, cancer, and tissue regeneration. Our two most advanced product candidates, recombinant human (rh) Factor XIII and rh Thrombin, are being developed as replacements for plasma-derived proteins already on the market.

rh Factor XIII is our most advanced product candidate, for which we expect to file an investigational new drug application (IND) with the FDA in late 2002. Factor XIII, the last enzyme in the blood-clotting cascade, cross-links fibrin strands in a blood clot to make it stronger and to reduce the chance of rebleeding. We are excited by the potential of rh Factor XIII to address a number of

Abdiazis Adan
Research Associate II / Developing DNA technologies

clinical indications that are poorly met with today's current therapies. These therapies include bleeding complications following cardiopulmonary bypass surgery and inflammatory bowel disease.

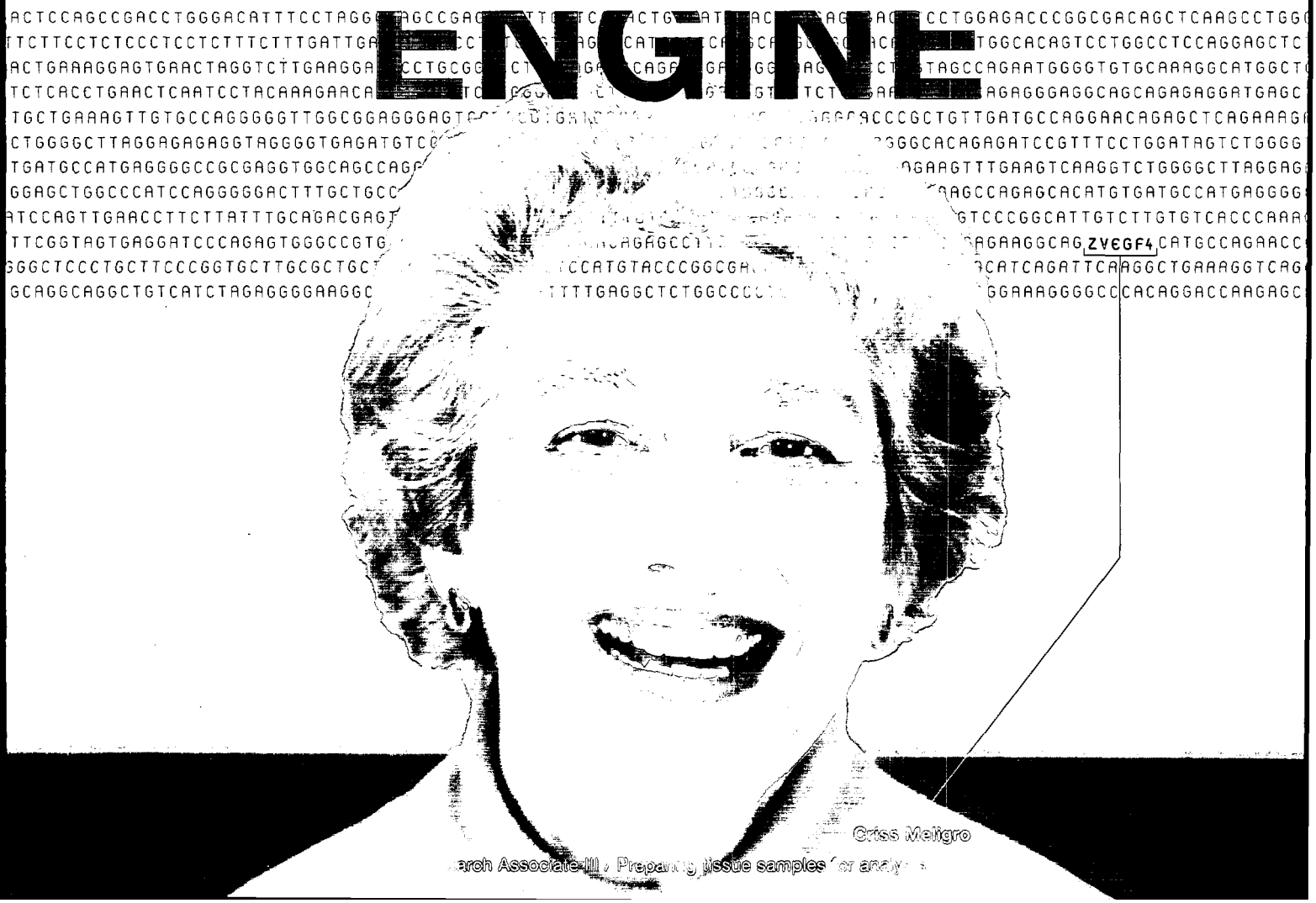
rh Thrombin is the second product candidate we intend to move into clinical trials, for which we expect to file an IND with the FDA in early 2003. Thrombin is a key enzyme involved in the formation of a blood clot, and is used clinically to control bleeding during surgery. The thrombin that is on the market today is derived from pooled bovine or human blood. We believe that a recombinant version of thrombin will be readily accepted in the marketplace as a safe replacement for the current plasma products due to the potential risks of viral contamination in blood products, and concerns regarding the transmission of the human form of "mad cow" disease with bovine products. Additionally, bleeding complications have been associated with contaminants present in the bovine plasma product that won't be present in the recombinant product.

Bioinformatics-Derived Product Candidates

Our bioinformatics-driven discovery strategy, which we initiated in the mid-1990s, has yielded a broad pipeline of product candidates with potential utility in a variety of therapeutic areas. The depth of this pipeline demonstrates the power of our discovery engine to decipher the raw DNA sequence information coming from the human genome sequencing efforts, and to turn this information into product candidates.

Our success within this area stems from several important factors. We were early to see the opportunities that lie in mining the human DNA databases. We began our gene discovery program in 1995. Additionally, from the very beginning we focused our discovery efforts on identifying those proteins that could themselves become therapeutic products, not just targets for drug intervention. Furthermore, as an established company, we had biology and bioinformatics expertise in place when the DNA sequence information became available, giving us a head start in determining the biological functions of these novel proteins. As a result, we have been first in the race to the patent office for many of these proteins. Our analysis of patent filings shows that ZymoGenetics is one of the top two companies in the world for being first to file patent applications for those proteins

DISCOVERY ENGINE



Criss Mellgro

arch Associate III, Preparing tissue samples for analy

TURNING SEQUENCE INFO

most likely to be the therapeutic proteins of the future. These patent applications include claims for both composition of matter and therapeutic utility.

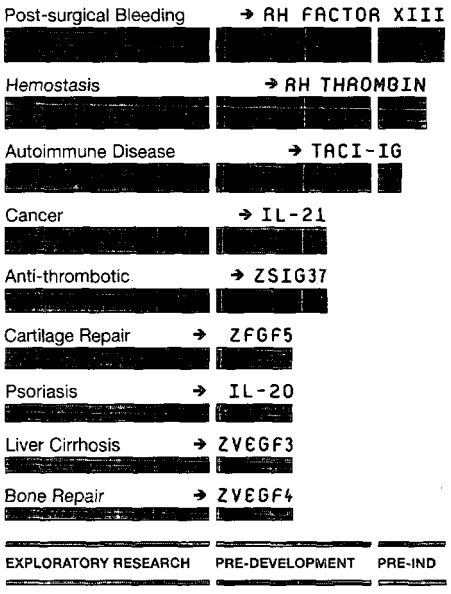
TACI-Ig is the first in a growing portfolio of product candidates stemming from our bioinformatics-driven discovery efforts. This protein is being developed for the treatment of autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, myasthenia gravis, and multiple sclerosis. TACI-Ig works by binding up a growth factor found in the blood that is a key mediator for the development of autoantibodies that result in autoimmune diseases. To enhance our development efforts for TACI-Ig, we established a co-development partnership with Serono S.A., a company with a proven track record in developing and marketing protein products for autoimmune disease. The agreement with Serono provides for license fee and milestone payments of up to $52.5 million. More importantly, we have retained the right to co-promote the product and share equally in the profits generated from the sale of TACI-Ig in North America. We anticipate entering clinical trials with this product candidate in the second half of 2003.

We are advancing a number of additional product candidates derived from our bioinformatics discovery efforts towards clinical development. These include interleukin-21 (IL-21) for the treatment of cancer. We have observed that this protein stimulates the proliferation and killing activity of cell types

Kristine Swiderek, Ph.D.
Research Director / Analyzing the structure of product candidates

called natural killer cells and cytotoxic T-cells, which play important roles in eliminating cancerous cells from the body. Studies in animals have shown that IL-21 is able to inhibit the growth of a number of different cancer types. Another candidate, Zsig37, is being developed for cardiovascular indications. Zsig37 has been shown in animal models to prevent clot formation at the site of blood vessel injury without any systemic impact on blood clotting.

Other proteins under investigation include Zfgf5 (also known as FGF18) which is being studied for potential use in cartilage repair, and interleukin 20 (IL-20), which is involved in the pathogenesis of psoriasis. We have more than 60 other proteins from our bioinformatics discovery effort that are at earlier stages of research. We believe this research pipeline will continue to provide us with



← PRODUCT PIPELINE / Fig. 02

ZymoGenetics has established a robust pipeline of product candidates. Our lead candidates, in the pre-IND stage, have been designated for development and are being advanced towards the filing of investigational new drug applications and the initiation of Phase I clinical trials.

INTO PRODUCTS

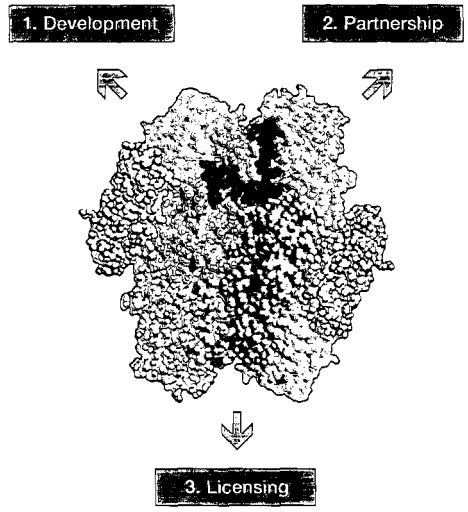
DEDICATED TEAM OF

high-quality product candidates for many years to come, giving us many "shots on goal" for the successful development of therapeutic protein products.

Commercialization Strategy

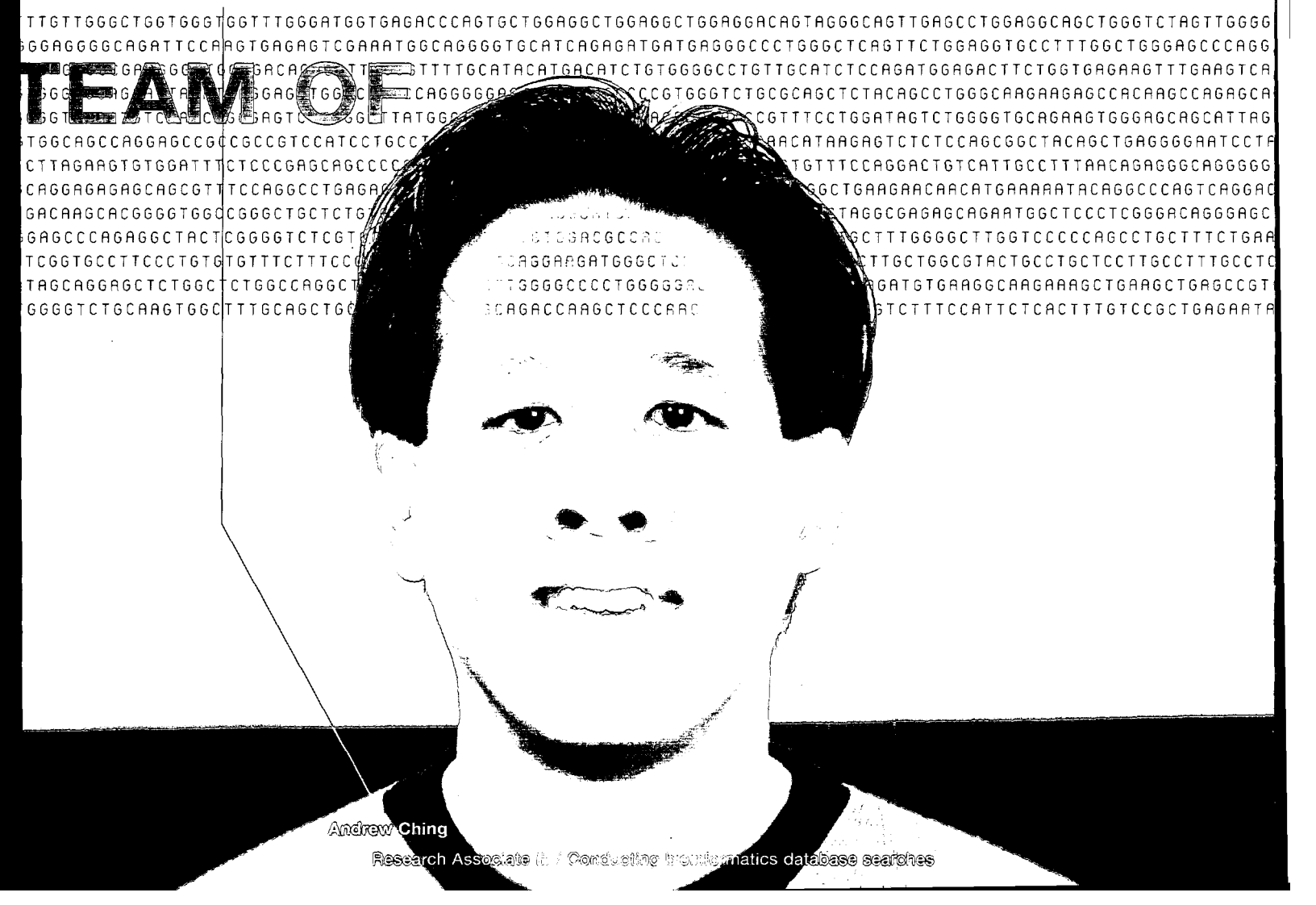
We believe our pipeline of therapeutic protein product candidates is of such depth that there will be more product candidates than we can handle ourselves. As a result, we are taking a three-pronged approach to commercialize these candidates. We intend to develop and market selected products on our own in North America. We believe that we must retain commercial rights to our products in order to build significant and sustainable value for our shareholders. There will be times, however, when it will be appropriate for us to establish co-development partnerships with other biotechnology or pharmaceutical companies, as we did with Serono. Additionally, we will actively seek out licensing opportunities for product candidates and intellectual property that exceed our internal capacity.

FIG. 03 / COMMERCIALIZATION STRATEGY



The discoveries made at ZymoGenetics have yielded a formidable portfolio of intellectual property, with more than 225 issued U.S. patents and more than 350 pending U.S. patent applications. Intellectual property that controls product candidates is a valuable asset, but one that declines in value over time. We therefore intend to out-license those product candidates and intellectual property that we are not able to develop ourselves, to generate revenue to support our internal development activities.

While our primary goal is to commercialize our intellectual property by internal develop-



Andrew Ching

Research Associate II / Conducting bioinformatics database searches

ment, in partnerships, and through license agreements, we will not hesitate to protect our patents from infringement by others. To that end, we recently filed a patent infringement lawsuit against Immunex Corporation related to our patents covering immunoglobulin fusion protein technology. The lawsuit alleges patent infringement by Immunex through its manufacture, importation and sale of Enbrel®, an etanercept dimeric fusion protein for the treatment of rheumatoid arthritis and other related conditions.

Financial Strength

We ended 2001 with cash equivalents and short-term investments totaling $147 million. Adjusted to reflect the proceeds from our initial public offering in February 2002, our cash and investments totaled $258 million as of December 31, 2001. In addition, we own outright our corporate headquarters buildings, which we believe are worth at least $50 million. We had revenues in 2001 of $17.8 million, which were derived from a combination of royalties on licensed products, and license and option fees. Collectively, our investments, cash, properties, and revenue streams will enable us to pursue our business strategy aggressively over the next several years.

→ COMMERCIALIZATION / Fig. 03

ZymoGenetics intends to commercialize its extensive portfolio of product candidates and intellectual property through internal development and direct marketing, development and marketing partnerships, and out-licensing of selected product candidates and intellectual property.

PEOPLE

Great People

ZymoGenetics is blessed with having a staff of people dedicated to the growth and success of the company. Our staff turnover is less than half of the industry average. We have a world-class group of researchers that have brought us to where

Jane Gross, Ph.D.

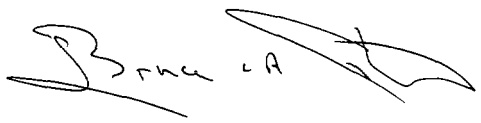
Scientific Fellow / Researching novel immunotherapeutics

IMPROVING LIVES

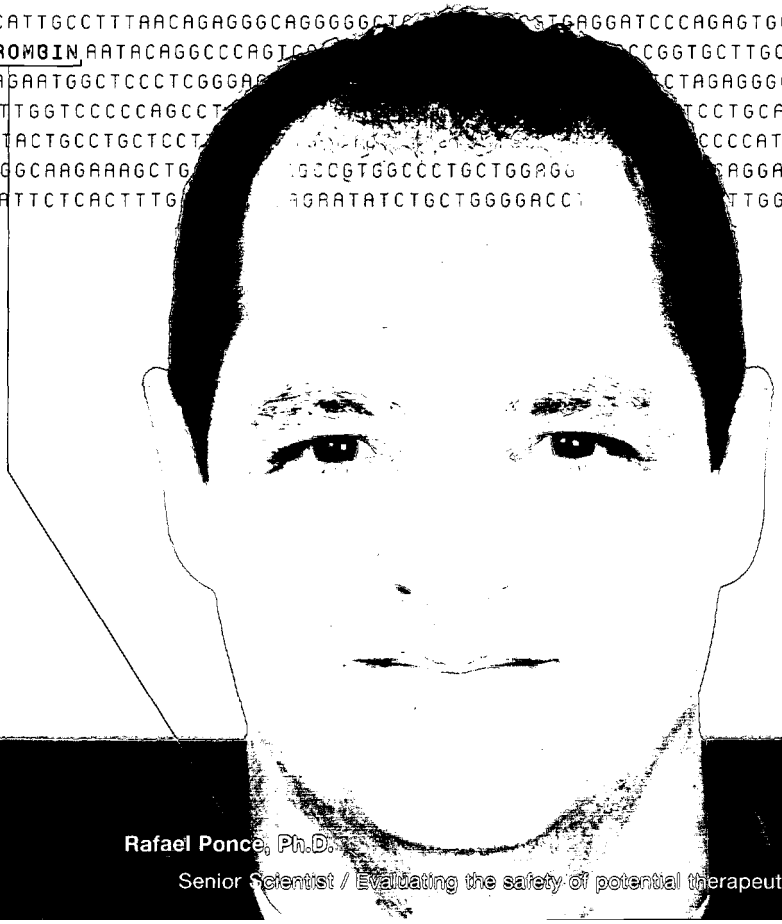
we are today, and that are leading us into the future. As we continue our evolution to a product development-focused company, we are expanding our staff to include people with experience in developing biopharmaceutical products. We have strengthened our management team with people who have experience with the successful development, manufacture and marketing of products for other companies, and are working to do the same at ZymoGenetics.

We also have the great fortune of having two of the founders of the biotechnology industry on our board of directors, Drs. George Rathmann and Ed Penhoet. Both of these individuals have led major biotechnology companies to success in the past. Their experience and guidance have been invaluable in leading the evolution of ZymoGenetics from a research subsidiary to the independent company we are today.

In closing, I want to thank you, our shareholders, for your support now and in the future. I am extremely proud to be at the helm of ZymoGenetics, and believe that there is no company better positioned for success in the coming years. We are excited about the future of ZymoGenetics and the wealth of opportunities that lie before us to improve the lives of people all over the world.



Bruce L. A. Carter, Ph.D.
President and Chief Executive Officer
May 20, 2002



Rafael Ponce, Ph.D.
Senior Scientist / Evaluating the safety of potential therapeutics

PRODUCT CANDIDATES:

RH FACTOR XIII:
Post-surgical Bleeding

Recombinant human (rh) Factor XIII, the last enzyme in the blood coagulation cascade, is being developed to treat bleeding complications associated with cardiopulmonary bypass surgery.

RH THROMBIN:
Hemostasis

Recombinant human (rh) Thrombin is being developed as a replacement product for plasma-derived thrombin, for the treatment of bleeding in surgical settings.

TACI-IG:
Autoimmune Disease

TACI-Ig is being developed for the treatment of autoimmune diseases, such as lupus, myasthenia gravis and rheumatoid arthritis.

IL-21:
Cancer

IL-21, being evaluated for the treatment of cancer, stimulates natural killer cells and cytotoxic T-cells, which play important roles in eliminating cancerous cells from the body.

ZSIG37:
Anti-thrombotic

Zsig37, a potent inhibitor of platelet activation, is being investigated for the treatment of clot formation at sites of vascular injury.

ZFGF5:
Cartilage Repair

Zfgf5, also known as FGF18, is being evaluated for use in the repair of cartilage damage.

IL-20:
Psoriasis

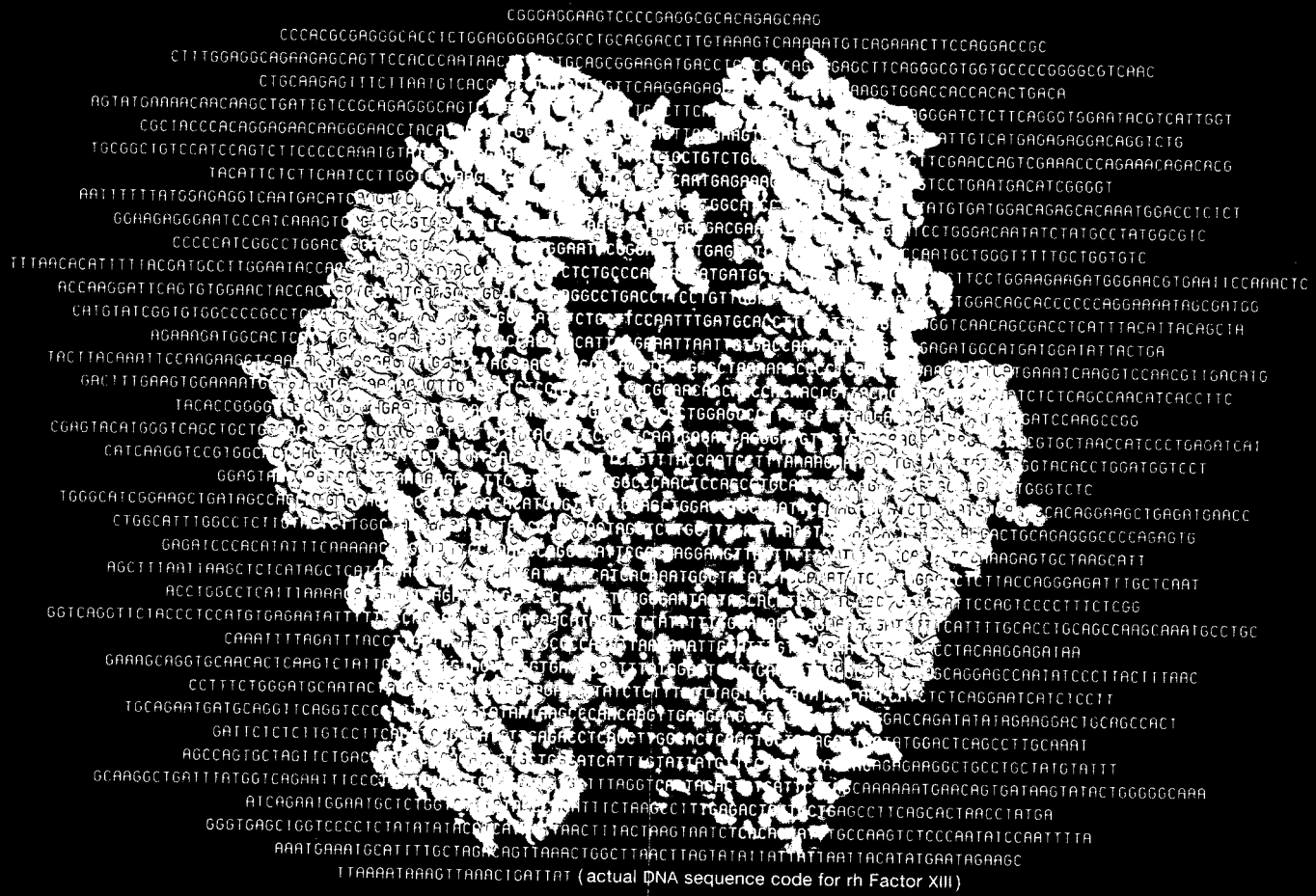
Antagonists to IL-20 and its receptor are being evaluated for the treatment of psoriasis.

ZVEGF3:
Liver Cirrhosis

Antagonists to Zvegf3, also known as PDGF-C, are being evaluated for the treatment of liver cirrhosis.

ZVEGF4:
Bone Repair

Zvegf4, also known as PDGF-D, is being evaluated for the treatment of bone fractures.



Three-dimensional model of recombinant human Factor XIII with each atom of the molecule shown as an individual sphere.

ZYMOGENETICS

FORM 10-K

2001

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, 2001

☐ 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. ☒

The approximate aggregate market value of the voting stock held by nonaffiliates of the registrant as of March 15, 2002 was: $152,901,963.

Common stock outstanding at March 15, 2002: 36,668,237 shares.

Non-voting common stock outstanding at March 15, 2002: 9,100,800 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 21, 2002 are incorporated by reference in Part III.

ANNUAL REPORT ON FORM 10-K

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For the Fiscal Year Ended December 31, 2001

PART I

ITEM 1. *BUSINESS*

This Annual Report on Form 10-K contains, in addition to historical information, forward-looking statements that involve risks and uncertainties. Our actual results could differ significantly from the results discussed in the forward-looking statements. 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.

OVERVIEW

We are 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, including 12 years as a wholly owned subsidiary of Novo Nordisk A/S, one of the world's largest producers of therapeutic proteins. We were incorporated in the state of Washington in 1981. In 1988, Novo Nordisk acquired our outstanding capital stock and we became a wholly owned subsidiary. From 1988 to 2000, we were the protein discovery operation for Novo Nordisk in North America. In November 2000, Novo Nordisk effected a significant restructuring. As part of this restructuring, we became an independent company in a transaction that included a $150 million private placement and the reduction of Novo Nordisk's ownership to approximately 62% of our outstanding capital stock and less than 50% of our outstanding voting stock.

We have contributed to the discovery or development of five marketed recombinant protein products with aggregate sales in 2000 of over $2 billion, which represented approximately 9% of the $23 billion market for therapeutic protein-based products. These products are Novolin® and NovoRapid® (insulin), NovoSeven® (Factor VIIa) and GlucaGen® (glucagon), marketed by Novo Nordisk, Regranex® (platelet-derived growth factor), marketed by Ortho-McNeil Pharmaceuticals, Inc., a Johnson & Johnson company, and Cleactor™ (tPA analog), marketed by Eisai Co., Ltd.

Early in our history, we built a core focus on protein chemistry and molecular and cellular biology. More recently, 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 known members with proven therapeutic value or potent biological activity. We believe this approach 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 currently have more than 200 issued or allowed United States patents and over 350 United States patent applications pending.

We have a growing pipeline of potential products that we expect to develop on our own or in collaboration with partners. Our two most advanced internal product candidates, rh Factor XIII and rh Thrombin, are being developed to replace currently marketed plasma-derived products. rh Factor XIII is a blood-clotting agent for the treatment of bleeding complications following cardiopulmonary bypass surgery, and rh Thrombin is a hemostatic agent for the control of bleeding during surgical procedures. We expect to file an investigational new drug application for rh Factor XIII by the end of 2002 and for rh Thrombin by the first quarter of 2003.

Our earlier-stage product candidates have resulted from our bioinformatics efforts. Using bioinformatics, we have been successful at identifying novel genes and, in combination with our biology expertise, demonstrating their potential medical relevance. Our most advanced bioinformatics-derived product candidates are TACI-Ig, IL-21 and Zsig37. TACI-Ig is a soluble receptor with potential applications for the treatment of autoimmune diseases, which we have agreed to develop jointly with Serono S.A., a leading global biotechnology company. IL-21 is a protein with potential applications for the treatment of cancer, and Zsig37 is a protein with potential applications for the treatment of cardiovascular diseases. We anticipate that an investigational new drug application will be filed for at least one of these product candidates in 2003.

BUSINESS STRATEGY

Our principal objective is to become a fully integrated biopharmaceutical company that commercializes 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 pursue a focused bioinformatics strategy 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 seek to develop a therapeutic protein directly, or, where appropriate, develop a monoclonal antibody or soluble receptor that targets the protein.
- *Pursue comprehensive intellectual property protection.* We seek to establish patent priority for our gene and protein discoveries at the earliest possible time. We use data generated from bioinformatics and exploratory biology to enhance 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 biology expertise.* We utilize a large number of biological assays and experimental systems to identify the biological functions of the genes and proteins we discover. Our comprehensive approach allows us to determine the medical relevance of proteins in a wider range of therapeutic areas. We believe companies that use a less thorough approach greatly limit their chances of discovering medically relevant biological activities associated with the genes and proteins they research.
- *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 higher likelihood of commercial success. Our two most advanced internal product development candidates are rh Factor XIII and rh Thrombin, 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 that do not fit within our future commercial focus.
- *Establish manufacturing capabilities.* We intend to develop our own manufacturing capabilities and to use third-party manufacturers when appropriate. We have initiated the design phase for a pilot

manufacturing plant, which we intend to use as a source of clinical product supply. We plan to subsequently develop larger-scale commercial manufacturing facilities as our product candidates progress through clinical development.

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. We also have out-licensed two product candidates, and we are developing a pipeline of internal product candidates. 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. Any clinical trials involving our product candidates may reveal that those candidates are ineffective or have unacceptable side effects. In addition, the results of preliminary studies are not necessarily indicative of clinical success, and larger and later-stage clinical trials may not produce the same results as earlier-stage trials or studies.

PRODUCT/PRODUCT CANDIDATE	INDICATION OR INTENDED USE	STATUS	STAGE OF DEVELOPMENT
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
Platelet-derived Growth Factor Receptor Antibody	Cancer	Out-licensed to Celltech Group plc	Phase I
Platelet-derived Growth Factor	Periodontal disease	Out-licensed to BioMimetic Pharmaceuticals, Inc.	Pre-IND
rh Factor XIII	Major cardiac surgery; Congenital Factor XIII deficiency	Internal development	Pre-IND
rh Thrombin	Critical care hemostat	Internal development	Pre-IND
TACI-Ig	Systemic lupus erythematosus; Other autoimmune diseases	Co-development with Serono S.A.	Pre-IND
IL-21	Cancer	Internal development in North America; to be out-licensed to Novo Nordisk outside North America	Pre-development
Zsig37	Cardiovascular diseases	Internal development	Pre-development

In the table above, Phase I refers to clinical trials designed primarily to determine safety and toxicology in humans; 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 application and the initiation of Phase I clinical trials; and pre-development refers to the stage in which confirmatory animal studies of the product candidate are being conducted in support of a medical hypothesis and protein manufacturing processes are being evaluated and developed.

Currently Marketed Products

We have participated in the discovery or development of five recombinant protein products marketed by other companies. These products had aggregate sales in 2000 in excess of $2 billion.

- 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 currently used by Novo Nordisk in the manufacture of these products.
- 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 potent 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 derive royalties on all of these products except for NovoSeven and NovoRapid, for which we received a one-time payment to satisfy future royalty obligations.

Out-licensed Product Candidates

We have contributed to the discovery and development of two product candidates that we have out-licensed to third parties in return for milestone payments and royalties.

- 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 has designated the product candidate CDP 860, and anticipates initiating Phase II clinical trials of CDP 860 in 2002 for the treatment of cancer.
- Platelet-derived growth factor, a potent growth factor that stimulates the growth of a variety of cell types. We have out-licensed this growth factor to BioMimetic Pharmaceuticals, Inc. for the treatment of periodontal disease and bone defects of the head and face.

Internal Product Candidates

We are developing several product candidates to treat a variety of serious diseases and medical conditions. These product candidates target several markets, including critical care, cardiovascular, autoimmune disease and cancer. We intend to develop and commercialize these product candidates on our own or in collaboration with other biotechnology or pharmaceutical companies.

rh Factor XIII. Factor XIII is the last enzyme to act in the blood clotting process. It functions by crosslinking 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 spontaneous bleeding and problems with wound healing. Acquired Factor XIII deficiency, a transient drop in Factor XIII levels, is much more common, having been reported in several diseases, such as chronic liver disease and inflammatory bowel disease. 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 and is marketed as Fibrogammin® P in Japan, South Africa and a few European countries. 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 for the treatment of congenital Factor XIII deficiency and several medical conditions associated with acquired Factor XIII deficiency. According to industry statistics and our own analysis, current annual worldwide sales of plasma-derived Factor XIII are estimated at $35 million. Japan is by far the largest single market for Factor XIII.

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 associated with these transfusions. Studies have indicated that levels of Factor XIII activity 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 35% 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.

We believe that there are several important advantages to a recombinant human form of Factor XIII. Such a product would alleviate concerns over viral contamination associated with plasma-derived products and decrease or eliminate the immune 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 rh Factor XIII represents not only an effective replacement product for the existing plasma-derived product, but also an opportunity for addressing a potentially significant untapped market. 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 major European countries, could facilitate significant expansion of the market and sales of Factor XIII. Recombinant protein replacement products have been successfully developed for Factor VIII and Factor IX, which are other blood-clotting factors.

Cardiopulmonary bypass surgery will be the first major indication pursued in our rh Factor XIII clinical development program. There are an estimated one million major cardiac surgical procedures performed annually involving cardiopulmonary bypass surgery. We have identified a number of other potential clinical indications for rh Factor XIII development, including replacement therapy for congenital Factor XIII deficiency and treatment of acquired Factor XIII deficiency such as in inflammatory bowel disease. We believe that we can benefit from the information currently available regarding the dosing and efficacy of plasma-derived Factor XIII in the design of our clinical development program. The use of this information may result in lower product development risks for rh Factor XIII than with other recombinant human protein products that are not being developed as replacement products.

We have developed a process for manufacturing rh Factor XIII in yeast. We have transferred the process to Avecia Limited, which has optimized and scaled up the process. Our initial investigational new drug application for rh Factor XIII was placed on hold in 1993 by the FDA, which cited insufficient information to assess the risks

of rh Factor XIII to subjects. Additional toxicology studies for rh Factor XIII began in early 2002 to support our planned submission of a new investigational new drug application. We anticipate that clinical grade product will be available by the middle of 2002, and we plan to complete toxicology studies, develop Phase I clinical trial protocols and file the investigational new drug application with the FDA by the end of 2002.

rh Thrombin. 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 crosslinks the fibrin molecules and strengthens the newly forming clot. In addition, thrombin stimulates platelet aggregation and acts as a potent cell activator.

Excessive bleeding is a serious complication of major surgeries. Surgeons try to limit bleeding during surgery to control blood loss and maintain visibility in the operating field. Thrombin is widely used as a stand-alone hemostat to stop diffuse bleeding occurring during major surgical procedures or as a component of other hemostats, such as tissue sealants. All currently marketed thrombin products are derived from pooled human or bovine plasma. Plasma-derived thrombin products available today are provided in spray formulation for topical application directly on wounds, and as a freeze-dried powder, which is dissolved and absorbed onto a gel sponge for application to wounds. Plasma-derived thrombin is also being used as a hemostatic component in new vascular sealing devices, wound dressings and fibrin sealants.

We believe that there are several important advantages to a recombinant human form of thrombin. As with Factor XIII, a recombinant human form of thrombin would alleviate concerns of viral contamination. A recombinant human form of thrombin also would alleviate concerns associated with products of bovine origin, including the risk of contamination with the pathogen that causes the human form of "mad cow" disease. In addition, there is a risk of allergic reaction in patients sensitive to products of bovine origin. Some patients develop antibodies to bovine plasma-derived thrombin or to Factor V, a contaminant of the bovine plasma-derived product. Anti-Factor V antibodies are particularly difficult to manage and are 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 rh Thrombin as a replacement product for the currently marketed human and bovine plasma-derived thrombin products. Current worldwide sales of plasma-derived thrombin as a stand-alone product are estimated at $100 million annually. It is estimated that plasma-derived thrombin is used in more than one million surgical procedures annually worldwide, with the United States accounting for approximately 40% of these procedures. As with plasma-derived thrombin, rh Thrombin would be used in the clinical setting to control bleeding. Primary applications would include major surgeries, trauma and burn injuries. We believe the market for rh Thrombin could be further expanded by providing it to other companies for inclusion in topical hemostats, fibrin sealants and vascular sealing devices.

We have developed a patent-protected process that we believe will enable us to cost-effectively manufacture rh Thrombin in mammalian cells. We have made arrangements with third-party manufacturers for the optimization and scale up of the manufacturing process. We expect to have product available to begin toxicology studies by the third quarter of 2002. We anticipate that clinical grade product will be available by early 2003.
We expect to complete toxicology studies, develop Phase I clinical trial protocols and file an investigational new drug application by the first quarter of 2003 for the use of rh Thrombin as a general surgical hemostat.

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, rheumatoid arthritis, myasthenia gravis, multiple sclerosis and asthma. In an animal model of systemic lupus erythematosus, 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.

Systemic lupus erythematosus is a probable 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. There are over one million cases of systemic lupus erythematosus in the United States, a disease which primarily affects women. It is estimated that one in five patients has a severe form of the disease requiring treatment with immunosuppressive agents. No new FDA-approved treatments for systemic lupus erythematosus have been introduced in the last 40 years. Current therapies, including immunosuppressives and corticosteroids, are not very effective and may have severe side effects. We believe that patients with severe systemic lupus erythematosus would be candidates for treatment with TACI-Ig.

Rheumatoid arthritis appears to be a promising clinical indication for TACI-Ig. Rheumatoid arthritis is one of the most prevalent chronic inflammatory diseases, afflicting an estimated 1% of the world population, 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.

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. We expect that Serono will begin manufacturing clinical grade materials in the first half of 2002 and that toxicology and pharmacology studies in appropriate animal species will begin in the second half of 2002. We expect that an investigational new drug application will be filed in 2003.

IL-21. We discovered IL-21 and its receptor through our bioinformatics efforts. IL-21 is a protein belonging to a family of cytokines that modify the function of cells in the immune system. We have shown IL-21 to regulate the proliferation and functional activity of two populations of immune cells, B cells which produce antibodies and natural killer cells which are thought to be critical in defending the body against cancer cells. Specifically, we have shown IL-21 in cell culture experiments to inhibit the growth of some B-cell cancer lines, to stimulate the production of natural killer cells from bone marrow and to increase the ability of natural killer cells to destroy infected or cancerous cells. These activities suggest a possible therapeutic role for IL-21 in the treatment of diseases characterized by B-cell tumors.

We expect to pursue B-cell-derived Non-Hodgkin's lymphoma as an initial clinical indication for IL-21. Non-Hodgkin's lymphoma is a cancer of the lymphatic system resulting from overproduction of tumor cells derived from B-cell and T-cell lineages. Non-Hodgkin's lymphoma is the second fastest growing type of cancer in the United States, and an estimated 800,000 patients suffer from this disease in the United States, Europe and Japan. In animal models of Non-Hodgkin's lymphoma, IL-21 has been shown to prevent B-cell lymphoma tumor growth and significantly reduce animal death.

We are currently conducting studies to determine the breadth of IL-21's ability to treat B-cell lymphoma in cell lines and primary tumors thought to be most representative of human disease. We are also conducting studies to determine the possible role of natural killer cell activation in the anti-tumor effect of IL-21. In addition, we are testing the ability of IL-21 to reconstitute natural killer cells and lymphocytes in various conditions of compromised immunity. Novo Nordisk has exercised its option to license rights to IL-21 outside of North America pursuant to our option agreement with Novo Nordisk.

Zsig37. Zsig37 is a protein discovered through our bioinformatics efforts. The Zsig37 gene is expressed in many tissues, including heart, aorta, adrenal, thyroid, adipose and placenta. In laboratory experiments, Zsig37 has been shown to bind to many types of collagen and has been found to inhibit collagen-induced platelet activation. In a rabbit model that mimics the generation of blood clots in human arteries following acute injury to a blood vessel, Zsig37 was shown to prevent clot formation in a dose-dependent manner.

We believe Zsig37 may provide potential benefits in the treatment of cardiovascular diseases. There is a significant unmet need and a substantial market opportunity for new classes of anti-clotting drugs for use in connection with surgical procedures treating cardiovascular diseases. The use of anticoagulant and anti-platelet drugs in these procedures helps limit the extent of clot formation. In some cases, however, currently marketed drugs are ineffective in preventing the clotting process or have adverse side effects. As a result, there is a need for new anti-clotting agents that block platelet activation without inducing a systemic effect on the coagulation system. Zsig37 has been shown to bind to collagen exposed at sites of vascular injury, enabling it to inhibit clotting at the site of injury directly without generating a systemic impact on blood clotting. We believe that this quality may allow Zsig37 to be of clinical use in a variety of surgical procedures for the treatment of cardiovascular diseases.

We have generated a significant body of preclinical data in animal models demonstrating the potential of Zsig37 to provide therapeutic benefit. We are currently evaluating several therapeutic indications with the intent of choosing a lead indication for clinical development. We are also in the process of developing a manufacturing process capable of efficiently producing quantities of Zsig37 product for preclinical and clinical testing.

DISCOVERY AND DEVELOPMENT PROCESS

We have developed a fully integrated therapeutic protein discovery and development program that draws upon a broad range of skills and technologies, including high-throughput 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 genomics and early-stage 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 internal gene sequence database of approximately 13 million 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 proprietary EST sequences, where we have eliminated transcripts of highly expressed genes to concentrate on rare gene sequences; and
- genomic sequences published daily by the Human Genome Project.

Any use of bioinformatics to discover novel gene sequences in sequence databases must address the high degree of redundancy present in the genomic and EST sequence information currently available. We have developed a software program called ASIDE to address this problem. ASIDE reduces the amount of redundant sequence information present in the genomic sequence data we analyze and thereby enriches our database by emphasizing unique sequences that are used in our discovery efforts. During peak times of publication of sequence information by the Human Genome Project, we frequently downloaded highly redundant raw sequences containing approximately 10 billion nucleotides. ASIDE, which is much faster than current publicly available tools, allows us to computationally process such a download on a daily basis. We believe ASIDE improves our chances of being the first to discover novel therapeutic proteins and establish patent priority by rapidly analyzing the continuous flow of genomic data as it becomes available.

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.

Our bioinformatics tools allow us to mine both genomic sequence data and EST data to discover novel proteins. Using ESTs alone, it is difficult to identify the full-length gene from which an EST was derived. However, the use of EST data in combination with genomic sequence data is a powerful gene discovery tool. By using the EST data as a probe to look into genomic sequence databases, we can often extend the amount of sequence data associated with a particular EST, thus enhancing our ability to analyze the potential of the gene to code for a therapeutic protein. In addition, the use of EST data together with genomic sequence data affords us the opportunity to identify those rare genes that otherwise might go undetected using only EST databases. Genes that are expressed only at low levels are typically underrepresented in or absent from EST databases. It is these rarely expressed genes that often have potent biological activities with clinical utility. Analysis of genomic sequence data, either alone or in combination with EST sequence data, is critical for identifying these rarely expressed genes, as genomic sequence data is not biased toward highly expressed genes.

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 would receive 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 will be 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 II clinical trials. Upon completion of Phase II 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 exercised options to license IL-21, IL-20 and IL-20 receptor pursuant to this 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 will share research and development expenses worldwide with the exception of Japan, where Serono will cover all expenses. The research and development activities will be governed by a steering committee made up of representatives of both companies. Serono will be 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-funding and co-development obligations upon 90 days notice until the start of Phase II 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 so 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.

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 for preclinical use at up to 100-liter scale using various production systems, including yeast, E. coli and mammalian cells. Accordingly, we believe that we can manufacture adequate product for preclinical studies for our research and development programs. To supply product for toxicology studies and clinical trials over the next several years, we intend to utilize third-party contract manufacturers or to rely on co-development partners for the manufacture of clinical-grade product in accordance with current Good Manufacturing Practices regulations. In addition, we have begun the planning process for construction of our own pilot manufacturing plant, and we have acquired land adjacent to our existing facilities on which to build it. It will likely take a total of at least three years to plan, design, construct and validate this facility. When completed, this plant would be available for the manufacture of clinical-grade product, from both mammalian-cell and microbial processes.

For rh Factor XIII, which is made in yeast, large-scale manufacturing of preclinical and clinical grade product will be carried out by Avecia Limited. We have made arrangements with third parties for the manufacture of rh Thrombin, 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.

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 rh Factor XIII, rh Thrombin 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 worthwhile 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. We expect to out-license product candidates that do not fit within our future commercial focus, and to out-license rights to non-therapeutic applications of our discoveries, such as diagnostics.

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 200 issued or allowed United States patents, and over 350 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 historically 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 rh Factor XIII or rh Thrombin, 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 no 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. For example, we recently filed a patent infringement lawsuit against Immunex Corporation claiming infringement of certain of our patents related to dimeric fusion proteins. This lawsuit, and any others that may arise relating to our patents, may require significant expenditures, regardless of the outcome.

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. Our product candidate rh Factor XIII is currently the subject of an interference proceeding with Aventis Behring, and other product candidates may in the future be the subject of similar proceedings. Although we have entered into a cross-licensing agreement with Aventis Behring with respect to rh Factor XIII, the interference proceeding could result in the loss of or significant limitations on our patent protection for this product candidate. Furthermore, under the cross-licensing agreement, Aventis Behring retains the ability to market recombinant products that may compete with rh Factor XIII.

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 ASIDE software program, 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 confidentiality 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:

- preclinical laboratory and animal tests;
- compliance with product manufacturing requirements including, but not limited to, current Good Manufacturing Practices regulations;
- submission to the FDA of an investigational new drug 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.

Preclinical tests include laboratory evaluation of the product, as well as animal studies to assess the potential safety concerns and efficacy of the product. Preclinical tests must be conducted by laboratories that comply with current Good Laboratory Practices regulations. The results of preclinical 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 application, which must become effective before the initiation of clinical trials. The investigational new drug 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 proposed protocol raises concerns that must be resolved to the satisfaction of the FDA before the trials may proceed. If the FDA raises any concerns regarding a proposed protocol, it is possible that these concerns will not be resolved in a timely fashion, 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 part of the investigational new drug 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 I, 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 II 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 II evaluations, Phase III trials are undertaken to evaluate further clinical efficacy in comparison to standard therapies, generally within a broader patient population at geographically dispersed clinical sites. Phase III protocols are reviewed with the FDA to establish endpoints and data handling parameters. Phase I, Phase II or Phase III 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, preclinical trials 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 also must contain extensive manufacturing information, and each manufacturing facility must be inspected and approved by the FDA before the biologics license application will 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 are not satisfied. The FDA may also require additional testing or 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 to undertake development and marketing of products to treat relatively rare diseases or 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 drug that is considered by the FDA to be different from or clinically superior to a particular orphan drug, including any orphan drug of ours that has been so designated by the FDA, will not be precluded from sale in the United States during the seven-year exclusive marketing period. It is possible that none of our product candidates will be designated as an orphan drug by the FDA or, if so designated, will have a positive effect on our revenues.

To manufacture our potential products, a domestic or foreign drug manufacturing facility must be registered with the FDA as a manufacturing establishment, must submit to periodic inspection by the FDA and must comply with

current Good Manufacturing Practices regulations. 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.

Whether or not FDA approval has been obtained, approval of a product by comparable foreign regulatory authorities is necessary prior to the commencement of marketing of a product in 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 are in a race 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 high-speed gene sequencers and other sophisticated bioinformatics technologies to discover genes, including Celera Genomics Corporation, Curagen, Inc., Genentech, Inc., Human Genome Sciences, Inc., Incyte Genomics, Inc. and Millennium Pharmaceuticals, 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 human genome 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; all of our internal product candidates are still in various stages of preclinical development and 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, 2001, we had 309 full-time employees, 58 of whom hold degrees at the doctoral level. Currently, we have approximately 240 employees 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

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

We do not know whether we can successfully implement our bioinformatics-based therapeutic protein discovery strategy 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 not begun clinical trials of any 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 development or commercialization of any products.

We depend heavily on bioinformatics technology, which may prove to be ineffective in the discovery of therapeutic proteins.

Our bioinformatics capabilities may prove ineffective in discovering genes and proteins and may not be adequate to handle the daily flow of DNA sequence data. Other technologies for analyzing genomic data and discovering genes may enable other parties to discover novel genes or proteins that our technologies fail to identify or may enable other parties to discover them before we do. Any inadequacies of our bioinformatics technologies may prevent us from discovering genes or proteins with therapeutic potential or from obtaining patent priority relating to these genes or proteins.

The availability of novel genomic data may decrease in the future, which may adversely affect our ability to discover novel therapeutic proteins.

We rely on the continuing availability of existing genomic data and the continuous generation of new genomic data for the discovery of genes and proteins. Because many companies and government or public agencies are analyzing the genomic data that is currently publicly available, it has become increasingly difficult for us to be the first to discover novel genes through the analysis of this data. Companies and government or public agencies

have already mapped and made available significant portions of the human genome, and the flow of novel genetic sequence data will likely decrease significantly in the future. This expected decrease in the rate of generation of novel sequence data could impair our ability to discover novel therapeutic proteins.

We may not be able to develop commercially viable products from the key protein categories on which we focus.

We may not be able to discover any new therapeutic proteins of commercial value in the key therapeutic protein categories we target in our discovery and development efforts. Prior successes of other companies in commercializing protein-based products derived from these categories provide no indication that we will be able to discover any therapeutic proteins within these categories beyond those that we have already discovered. Also, we may not be able to successfully commercialize any novel therapeutic proteins we have discovered or may discover in the future. In addition, some of the protein categories we concentrate on have not yielded any successful therapeutic protein products or late-stage clinical trial candidates. Discovery 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. In addition, other classes of drugs may prove to have superior therapeutic benefits or be easier and more cost-effective to produce than therapeutic 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 historically 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.

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

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 our intellectual property. Also, as a result of such determinations, we may be enjoined from commercializing potential products or may be required to obtain licenses, if available, to third-party patents or develop or obtain alternative technology. In addition, enforcing our patents against third parties may require significant expenditures regardless of the outcome of such efforts. For example, we recently filed a patent infringement lawsuit against Immunex Corporation claiming infringement of certain of our patents related to dimeric fusion proteins. This lawsuit, and any others that may arise relating to our patents, may require significant expenditures, regardless of the outcome.

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 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 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 rh Factor XIII or rh Thrombin, 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 no 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.

If other parties publish information about the genes or proteins we discover before we apply for patent protection, we may be unable to obtain patent protection.

Public disclosures of genetic sequence information may limit the scope of our patent claims or result in the denial of subsequent patent applications that we file on genes and their corresponding proteins. Washington University has identified genes through partial sequencing funded by Merck & Co., Inc. and has deposited these partial sequences in a public database. Also, in January 1997, The Institute for Genomic Research disclosed more than 35,000 full-length DNA sequences that were assembled from partial gene sequences available in publicly accessible databases or sequenced at the Institute. In addition, the Human Genome Project and Celera Genomics Corporation completed an initial sequencing of the human genome and published papers on this sequencing in February 2001. We may be unable to obtain patent protection for sequences published in these disclosures if they represent prior art.

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 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 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. 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 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 proprietary technology and information.

In addition to our patented intellectual property, we also rely on unpatented technology, trade secrets and confidential information, including our ASIDE software program, our genetic sequence database and our bioinformatics algorithms. 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.

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 did not include clinical trials, manufacturing, 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 we, our collaborators or our licensees intend to market the product candidates. Each of our product candidates must undergo extensive preclinical studies and clinical trials as a condition to regulatory approval. Preclinical studies and clinical trials are time-consuming and expensive and together take several years to complete, and to date we have not completed any clinical trials 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 preclinical 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;
- poor effectiveness 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 enter or complete clinical trials in any of the markets in which we, our collaborators or licensees intend to sell those product candidates. Accordingly, we, our collaborators or licensees 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, are unacceptably toxic 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. For example, in 1998, Amgen Inc. halted Phase III clinical trials in the United States relating to our product candidate Thrombopoietin in the treatment of

chemotherapy-induced thrombocytopenia after reports of the development of neutralizing antibodies in both cancer patients and volunteer donors in platelet donation 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 2001, Celltech Group plc discontinued development of platelet-derived growth factor receptor antibody, a product candidate that Celltech licensed from us and designated as CDP 860, for the treatment of restenosis. Celltech concluded that the Phase II clinical trial results did not justify further development of CDP 860 as a restenosis therapy.

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 United States Food and Drug Administration, or 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 preclinical studies and clinical trials of each product candidate, is lengthy, expensive and uncertain. Securing FDA approval requires the submission of extensive preclinical 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. Any FDA or other regulatory approval of our product candidates, once obtained, may be withdrawn. In addition, 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.

We may encounter difficulties developing or commercializing our product candidate rh Factor XIII.

We may encounter difficulties developing or commercializing our product candidate rh Factor XIII due to regulatory impediments and intellectual property challenges. The FDA placed our initial investigational new drug application for rh Factor XIII on hold in 1993, citing insufficient information to assess its risks to subjects. Although we intend to submit a new investigational new drug application for rh Factor XIII to the FDA, the FDA may raise additional questions or require additional data, which could delay or prevent the initiation of clinical trials. In addition, rh Factor XIII is currently the subject of a patent interference proceeding with Aventis Behring L.L.C. Although we have entered into a cross-licensing agreement with Aventis Behring with respect to rh Factor XIII, the interference proceeding could result in the loss of or significant limitations on our patent protection for this product candidate. Furthermore, under the cross-licensing agreement, Aventis Behring retains the ability to market recombinant products that may compete with rh Factor XIII.

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 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 exercised options to license 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.

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 preclinical studies. We intend to rely on collaborators and third-party contract manufacturers to produce the quantities of drug materials needed for preclinical studies, clinical trials and commercialization of our potential products. We will have to rely on these manufacturers to deliver materials on a timely basis and to comply with regulatory requirements, including current Good Manufacturing Practices regulations enforced by the FDA through its facilities inspection program. These manufacturers 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. 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 preclinical studies and clinical trials may be delayed. Delays in preclinical studies could postpone the filing of investigational new drug 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 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 Good Manufacturing Practices regulations in the manufacture of therapeutic proteins. Although we intend to develop limited manufacturing facilities internally, construction of an initial pilot manufacturing plant will take at least three years and require substantial expenditures. In addition, we will need to hire and train employees to staff this facility if we are able to complete construction. We do not anticipate that this initial pilot manufacturing plant will provide us with the capability to produce drug materials for commercial sale. To develop this capability we would need to further expand our manufacturing facilities. If any of our future facilities cannot pass a pre-approval plant inspection, the FDA pre-market 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 control 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, 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. 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.

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. We purchased this property from the City of Seattle. 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.

We anticipate incurring additional losses and may not achieve profitability.

As of December 31, 2001, we had an accumulated deficit of $111.1 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 discovery 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 in excess of the costs of development.

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, including payments owed by us under collaborative or licensing arrangements. 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 their 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.

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 discovery and development programs. We expect that these expenditures will increase significantly over the next several years as we hire additional employees, expand our preclinical development activities and begin internal clinical trials. 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 discovery 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 are required to grant such rights, the ultimate value of these product candidates to us would be reduced.

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 preclinical 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.

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 using high-speed gene sequencers and other sophisticated bioinformatics technologies to discover genes, including Celera Genomics Corporation, Curagen, Inc., Genentech, Inc., Human Genome Sciences, Inc., Incyte Genomics, Inc. and Millennium Pharmaceuticals, 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. In addition, we face competition from other parties that conduct research to identify genes and conduct human genome research similar to or competing with our focus on gene discovery, including biotechnology and pharmaceutical companies; privately or publicly financed research institutes or programs, such as those sponsored by the United States government and the governments of France, Germany, Japan and the United Kingdom; and laboratories associated with universities or other not-for-profit organizations. 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.

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 bioinformatics 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.

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.

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.

We may be required to defend lawsuits or pay damages in connection with the 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. In addition, the pharmaceutical and biotechnology industries in general have been subject to significant medical malpractice litigation. We may incur significant expenses if product liability or malpractice lawsuits against us are successful. Although we may obtain product liability insurance, any coverage we obtain may not be adequate to cover such claims.

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.

Our existing shareholders have significant control of our management and affairs, which they could exercise against your best interests.

Novo Nordisk, together with Warburg, Pincus Equity Partners, L.P. and entities affiliated with Patricof & Co. Ventures, Inc., beneficially own an aggregate of approximately 62% of our outstanding voting common stock. Novo Nordisk beneficially owns 100% of our outstanding non-voting common stock. In addition, Novo Nordisk and Warburg, Pincus Equity Partners have rights to designate director nominees to our board of directors. 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 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 management.

ITEM 2. *PROPERTIES*

We are headquartered in Seattle, Washington, where we own two buildings containing approximately 160,000 square feet. We also own a parcel of land contiguous to one of the buildings on which we believe we could expand by adding 20,000 to 40,000 additional square feet of laboratory and office space. Recently we purchased land adjacent to our existing facilities on which we intend to construct a pilot manufacturing plant. In addition, we have leased approximately 15,000 square feet of space in a nearby office building. We believe that our existing facilities, together with available or planned expansion space, will be adequate to fulfill our needs for the next several years. However, within that time frame, we may be required to locate alternative or additional facilities depending on the extent of our growth.

ITEM 3. *LEGAL PROCEEDINGS*

From time to time, we may become involved in litigation relating to claims arising from the ordinary course of our business, including actions relating to intellectual property rights.

On March 7, 2002, we filed a patent infringement lawsuit against Immunex Corporation in the United States District Court for the Western District of Washington in Seattle. The lawsuit charges Immunex with directly and willfully infringing United States Patent Numbers 5,843,725, 6,018,026, 6,291,212 B1, 6,291,646 B1, 6,300,099 B1 and 6,323,323 B1 through the manufacture, importation and sale of Enbrel®, a dimeric fusion protein. While it is impossible to predict accurately or to determine the eventual outcome of this matter, we believe that the outcome will not have a material adverse effect on our financial position or results of operations.

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, 2001.

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. At March 15, 2002, we had 67 shareholders of record. We have never paid cash dividends and do not anticipate paying them in the foreseeable future.

In fiscal year 2001, we granted stock options to purchase 3,629,066 shares of common stock, with exercise prices ranging from $2.78 to $4.72 per share, under our Amended and Restated 2000 Stock Incentive Plan. To date, options for 361,894 shares have been canceled without being exercised and options for 271,080 shares have been exercised. There were 7,307,092 total options outstanding as of December 31, 2001. The sales and issuances of these securities were exempt from registration under the Securities Act pursuant to Rule 701 promulgated thereunder on the basis that these options were offered and sold either pursuant to a written compensatory benefit plan or pursuant to written contracts relating to consideration, as provided by Rule 701, or pursuant to Section 4(2) thereof, on the basis that the transactions did not involve a public offering.

On January 31, 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. The offering was managed by Lehman Brothers Inc., Merrill Lynch & Co., Bear, Stearns & Co. Inc. and Pacific Growth Equities, Inc. The date of commencement of the initial public offering was February 1, 2002. Pursuant to the registration statement, we registered and sold an aggregate of 10,000,000 shares of common stock for a gross aggregate offering price of $120.0 million. In connection with the offering, we incurred total expenses of approximately $10.0 million, including underwriting discounts and commissions of approximately $8.4 million and other expenses of approximately $1.6 million. All of these expenses were direct or indirect payments to others and not payments to our directors or officers (or their associates) or to our affiliates or 10% shareholders. Net proceeds of approximately $110.0 million have been invested in short-term, investment-grade, interest bearing instruments.

ITEM 6. *SELECTED FINANCIAL DATA*

The following table shows selected financial data for the five years ended December 31:

(in thousands, except per share data)	2001	2000	1999	1998	1997
STATEMENT OF OPERATIONS DATA:					
Revenues	**$ 17,828**	$ 32,464	$69,675	$66,744	$67,679
Operating expenses:					
Research and development(1)	**48,052**	49,337	48,415	49,886	50,428
General and administrative(2)	**10,475**	12,069	9,550	9,339	12,308
Noncash stock-based compensation expense	**3,507**	—	—	—	—
Total operating expenses	**62,034**	61,406	57,965	59,225	62,736
Income (loss) from operations	**(44,206)**	(28,942)	11,710	7,519	4,943
Other income (expense):					
Interest income	**7,152**	5,417	274	29	285
Interest expense	**(13)**	(848)	(56)	(485)	(207)
Other, net	**98**	(111)	(52)	(72)	134
Income (loss) before provision for income taxes	**(36,969)**	(24,484)	11,876	6,991	5,155
Benefit (provision) for income taxes	**90**	(5,893)	(2,454)	(1,273)	(895)
Net income (loss)	**(36,879)**	(30,377)	9,422	5,718	4,260
Preferred stock dividend and accretion	**(20,610)**	(2,903)	—	—	—
Net income (loss) attributable to common shareholders	**$ (57,489)**	$ (33,280)	$ 9,422	$ 5,718	$ 4,260
Basic net income (loss) per share	**$ (4.85)**	$ (3.38)	$ 1.11	$ 0.68	$ 0.50
Diluted net income (loss) per share	**$ (4.85)**	$ (3.38)	$ 0.80	$ 0.48	$ 0.36
Weighted-average shares used in computing basic net income (loss) per share	**11,846**	9,846	8,455	8,455	8,455
Weighted-average shares used in computing diluted net income (loss) per share	**11,846**	9,846	11,793	11,793	11,793
BALANCE SHEET DATA:					
Cash, cash equivalents and short-term investments	**$147,077**	$172,976	$19,648	$ 5,738	$ 4,194
Working capital	**138,493**	166,245	19,504	12,566	13,509
Total assets	**205,435**	228,637	91,914	83,473	88,929
Mandatorily redeemable convertible preferred stock	**260,540**	239,930	—	—	—
Total shareholders' equity (deficit)	**(79,402)**	(27,269)	77,687	68,265	62,547

(1) The year ended December 31, 2001 excludes noncash stock-based compensation expense of $2,109.

(2) The year ended December 31, 2001 excludes noncash stock-based compensation expense of $1,398.

ITEM 7. *MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS*

OVERVIEW

We are a biopharmaceutical company focused on the discovery, development and commercialization of therapeutic protein-based products for the treatment of human disease. We have been involved in the discovery and development of therapeutic protein-based products for over 20 years, including 12 years as a wholly owned subsidiary of Novo Nordisk, a Danish pharmaceutical company. During this time, we contributed to the discovery or development of five products currently marketed by other companies. In August 1988, we were acquired by and became a wholly owned subsidiary of Novo Nordisk. From the date of our acquisition through December 31, 1999, we earned the majority of our revenues by conducting research and development activities for Novo Nordisk. We were paid at a rate of 110% of our research and development costs incurred in connection with all

projects performed on behalf of Novo Nordisk pursuant to a funding agreement. We had net income of $4.3 million in 1997, $5.7 million in 1998 and $9.4 million in 1999.

In anticipation of our separation from Novo Nordisk pursuant to a planned restructuring by Novo Nordisk, the funding agreement was terminated effective January 1, 2000. Also effective January 1, 2000, Novo Nordisk contributed to us the rights inside the United States to certain intellectual property, including patents on products on which we currently generate royalty revenues. Concurrently, we purchased the rights outside the United States to this intellectual property from Novo Nordisk, paying them $35.7 million in October 2000. In addition, in September 2000, we assigned to Novo Nordisk patents and other rights relating to Factor VII, including NovoSeven, and insulin analogues, including NovoRapid, for a one-time payment of $90.1 million, which was recorded as a capital contribution. As a result of this transaction, effective September 2000 we no longer receive royalties on sales of Factor VII and insulin analogues.

In November 2000, Novo Nordisk effected the restructuring. As part of the restructuring, we became an independent company in a transaction that included a $150.0 million private placement of our Series B preferred stock and the reduction of Novo Nordisk's ownership to approximately 62% of our outstanding capital stock and less than 50% of our outstanding voting stock. At the same time, we granted Novo Nordisk an option to license certain rights to potential therapeutic proteins pursuant to an option agreement, including rights to a defined number of proteins outside of North America over a period of four years in return for option fees of $7.5 million per year. Novo Nordisk may elect to extend the option agreement for an additional two years in return for continuing option fees of $7.5 million per year. For each exercise of an option by Novo Nordisk, we would receive a license fee, the amount of which depends on the development stage of the protein licensed. We are entitled to additional amounts upon the achievement of predefined milestones. In addition, we would earn royalties on sales of any resulting products. To date, Novo Nordisk has exercised options to license three proteins pursuant to this agreement.

We incurred net losses of $36.9 million and $30.4 million for the years ended December 31, 2001 and December 31, 2000. As of December 31, 2001, we had an accumulated deficit of $111.1 million. The accumulated deficit resulted from net losses and certain capital transactions with Novo Nordisk. The net losses resulted from the termination of the funding agreement and are expected to increase in the future as we continue to expand our research, development and clinical trial activities and to build additional infrastructure.

Our current revenue sources are limited, and we do not generate any direct revenues from product sales. We earn royalties on sales of products by several licensees, including Novo Nordisk. For the year ended December 31, 2001, revenues from royalties were $9.1 million. In the near term, we expect our revenues to consist primarily of product royalties, the option fees from Novo Nordisk and revenues generated under existing collaborative agreements. Additionally, we may generate revenues from the establishment of new collaborative research and development arrangements and license agreements. Ultimately, we intend to derive revenues from commercial product sales. Because a substantial portion of our revenues for the foreseeable future will depend on achieving research, development and clinical milestones, our results of operations may vary substantially from year to year.

We recognized revenues from our funding agreement with Novo Nordisk when costs were incurred on Novo Nordisk-related projects. We recognize revenues from royalties when amounts are due and considered collectible. We recognize revenues from license fees, option fees and up-front payments in connection with other rights or services that represent continuing obligations systematically over the period that the fees or payments are earned. We will recognize revenues from milestone payments representing completion of separate and substantive earnings processes when the milestone is achieved and amounts are due and payable. These amounts are dependent on the completion of research, development or clinical milestones, which may not be achieved.

Operating expenses consist of research and development expenses, general and administrative expenses and noncash stock-based compensation expense. Research and development expenses have been our most

significant expenses to date and consist primarily of salaries and benefit expenses, consumable expenses, facility costs, professional fees and external collaboration costs. General and administrative expenses consist primarily of salaries and benefit expenses, professional fees and other corporate costs. We expect our research and development and general and administrative expenses to increase in the foreseeable future as we continue to grow. We expect that a large percentage of our research and development expenses will be incurred in support of our internal product development programs for rh Factor XIII, rh Thrombin, TACI-Ig, IL-2I and Zsig37. None of these product candidates are expected to enter clinical trials before late 2002. It is not unusual for the clinical development of these types of products to take five years or more, and to cost well over $100 million. The time and cost of completing the clinical development of these product candidates will depend on a number of factors, including the disease or medical condition to be treated, clinical trial design and endpoints, availability of patients to participate in trials and the relative efficacy of the product versus treatments already approved. Due to these many uncertainties, we are unable to estimate the length of time or the costs that will be required to complete the development of these product candidates.

Under our Amended and Restated 2000 Stock Incentive Plan, stock options granted for the year ended December 31, 2000 were granted with exercise prices equal to the estimated fair value of the common stock at the date of grant. Noncash stock-based compensation expense for the year ended December 31, 2001 resulted from stock options granted to employees and directors within the year at exercise prices below the estimated fair value of the common stock on the date of grant. We recorded total deferred stock-based compensation of $28.7 million as of December 31, 2001. 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. For the deferred stock-based compensation recorded as of December 31, 2001, we amortized noncash stock-based compensation expense of $3.5 million in 2001, and expect to amortize $7.2 million in 2002, $7.2 million in 2003, $7.2 million in 2004 and $3.6 million in 2005. The amount of noncash stock-based compensation expense expected to be recorded in future periods may decrease if unvested options for which deferred stock-based compensation has been recorded are subsequently cancelled or may increase if future option grants are made with exercise prices below the estimated fair value of the common stock on the date of the grant.

Other income (expense) consists primarily of interest income and interest expense. Interest income is generated primarily from investment of our cash reserves. In addition, we earned $2.3 million in interest from Novo Nordisk on a royalty payment received in March 2000. Interest expense relates generally to periodic short-term borrowings from Novo Nordisk, all of which occurred and were repaid in full prior to our separation from Novo Nordisk in November 2000.

Benefit (provision) for income taxes consists of income taxes computed at federal statutory rates less applicable credits. Subsequent to November 10, 2000, we have provided full valuation allowances for net deferred tax assets. As of December 31, 2001, we had net operating loss carryforwards of approximately $43.7 million, research and development tax credit carryforwards of $12.9 million, a rehabilitation tax credit carryforward of $1.5 million, and alternative minimum tax credit carryforwards of $1.2 million. These credits will expire during the period from 2008 through 2021. Due to the uncertainty regarding the ultimate utilization of these tax benefits, a valuation allowance has been recorded for the entire amount of the related net deferred tax assets. On October 20, 2000, we entered into a tax sharing agreement related to our separation from Novo Nordisk. This agreement requires that all research and development credit carryforwards generated prior to November 10, 2000 that we use to generate a tax benefit in future periods be reimbursed to Novo Nordisk, provided that the total reimbursement will not exceed $12.0 million.

Due to the evolving nature of our business, and as a result of our separation from Novo Nordisk in November 2000, we believe that period-to-period comparisons of our operating results are not necessarily meaningful and should not be relied on as an indication of future performance.

RESULTS OF OPERATIONS

Years Ended December 31, 2001 and 2000

Revenues. Revenues decreased by $14.7 million, from $32.5 million in 2000 to $17.8 million in 2001. This difference was due primarily to a one-time royalty payment of $15.2 million from Novo Nordisk received in March 2000, which was recorded as revenue in the first quarter of 2000 when the amount was determined and collectability was probable. Additionally, $5.0 million of NovoSeven royalties were earned in 2000 prior to the assignment of our related rights to Novo Nordisk. These decreases were partially offset by an increase in the amount of option fee revenues earned under our agreement with Novo Nordisk.

Research and development expenses. Research and development expenses, exclusive of noncash stock-based compensation expense of $2.1 million in 2001, decreased by $1.2 million, from $49.3 million in 2000 to $48.1 million in 2001. This decrease was due primarily to reduced expenses related to discovery research collaborations and database subscriptions. We also introduced cost awareness programs related to consumables, resulting in decreases in spending. The decrease was partially offset by an increase in costs associated with patenting activities and the addition of employees in research and development. We anticipate that research and development expenses will increase in the forseeable future as we continue to support our internal product development programs.

General and administrative expenses. General and administrative expenses, exclusive of noncash stock-based compensation expense of $1.4 million in 2001, decreased by $1.6 million from $12.1 million in 2000 to $10.5 million in 2001. This decrease was due primarily to changes in the value of outstanding Novo Nordisk stock appreciation rights previously granted to administrative personnel, which resulted in a decrease in compensation expense of $1.1 million. As of December 31, 2000, all of these rights had been exercised and none remained outstanding. The decrease was also due to the termination of fees associated with administrative services provided by Novo Nordisk and a reduction in state and city taxes. We anticipate that general and administrative expenses will increase in the foreseeable future as we incur additional costs relating to our operation as a public company.

Noncash stock-based compensation expense. Noncash stock-based compensation expense was $3.5 million in 2001 and $0 in 2000. The 2001 expense resulted from the granting of stock options in 2001 with estimated fair values exceeding the exercise prices of the options.

Other income (expense). Other income (expense) increased by $2.8 million from $4.4 million in 2000 to $7.2 million in 2001. This increase was due primarily to an increase in interest income from $5.4 million in 2000 to $7.2 million in 2001. The increase in interest income resulted from higher average balances of cash and cash equivalents and short-term investments in 2001, reflecting the net proceeds of $142.5 million from a private equity financing completed in November 2000. The increase in other income was also due to a decrease in interest expense of $0.8 million. During 2000, we entered into various loans with Novo Nordisk, which were fully repaid by the end of the year.

Benefit (provision) for income taxes. The income tax provision in 2000 was $5.9 million, which reflects a valuation allowance for our cumulative net deferred tax assets partially offset by the benefit from our net operating loss for the period from January 1, 2000 through November 9, 2000, the date of separation from Novo Nordisk. The income tax benefit in 2001 of $0.1 million represents the final payment according to the tax sharing agreement we entered into with Novo Nordisk prior to our separation. No additional income tax benefit was recognized in 2001 because the benefit from our net losses was uncertain.

Years Ended December 31, 2000 and 1999

Revenues. Revenues decreased by $37.2 million from $69.7 million in 1999 to $32.5 million in 2000. Revenues in 1999 consisted primarily of research and development funding of $63.7 million from Novo Nordisk pursuant to our funding agreement with Novo Nordisk. This agreement terminated effective January 1, 2000. Revenues in

2000 consisted of a one-time royalty payment of $15.2 million from Novo Nordisk in March 2000, royalties of $5.0 million earned through September 2000 from sales of NovoSeven, royalties of $11.3 million from sales of other products and recognition of $1.0 million of the option fee received from Novo Nordisk. Effective September 2000, we no longer receive royalties on sales of NovoSeven.

Research and development expenses. Research and development expenses increased by $0.9 million from $48.4 million in 1999 to $49.3 million in 2000. This increase was due primarily to increases in salary and benefit costs as a result of an increase in research and development personnel in 2000. The increase was also due to increased spending for patent filings in 2000. The increase was partially offset by decreases in our external research collaboration costs and decreases in spending for consumables.

General and administrative expenses. General and administrative expenses increased by $2.5 million from $9.6 million in 1999 to $12.1 million in 2000. This increase was primarily due to changes in the value of outstanding Novo Nordisk stock appreciation rights previously granted to administrative personnel, which resulted in an increase in compensation expense of $1.3 million. As of December 31, 2000, all of these rights had been exercised and none remained outstanding. The increase was also due to a $0.9 million increase in state and local business and occupation taxes. For the year ended December 31, 1999, we were entitled to certain state business and occupation tax benefits as a result of our funding agreement with Novo Nordisk. The termination of the funding agreement effective January 2000 resulted in diminished tax benefits available to us for the year ended December 31, 2000. In addition, we incurred real estate transfer tax expense of $0.6 million in 2000 related to our separation from Novo Nordisk.

Other income (expense). Other income (expense) increased by $4.3 million from $0.2 million in 1999 to $4.5 million in 2000. This increase was due primarily to an increase in interest income from $0.3 million in 1999 to $5.4 million in 2000. The increase in interest income was due to higher average balances of cash, cash equivalents and short-term investments in 2000, due primarily to the net proceeds from the private equity financing completed in November 2000, and to the receipt of $2.3 million in interest from Novo Nordisk on a one-time royalty payment of $15.2 million from Novo Nordisk in March 2000. Interest expense increased from $0.1 million in 1999 to $0.8 million in 2000. This increase was due to loans from Novo Nordisk, which were fully repaid in 2000.

Benefit (provision) for income taxes. The income tax provision in 1999 was $2.5 million or an effective rate of 21%. The low effective rate resulted from the utilization of research and development tax credits. The income tax provision in 2000 was $5.9 million. The provision reflects a valuation allowance for our cumulative net deferred tax assets partially offset by the benefit from our net operating loss for the period from January 1, 2000 through November 9, 2000.

LIQUIDITY AND CAPITAL RESOURCES

From August 1988, when we were acquired by Novo Nordisk, through December 31, 1999, our operations were funded primarily by research and development revenues earned under our funding agreement with Novo Nordisk. The total amount of research and development revenue from Novo Nordisk during this period was $425.0 million. The funding agreement was terminated effective January 1, 2000. From January 1, 2000 through December 31, 2001, our operations were funded by proceeds of $90.1 million from the assignment to Novo Nordisk of patents and other rights relating to NovoSeven and NovoRapid, net proceeds of $142.5 million from our November 2000 private equity financing, the option fees received from Novo Nordisk, revenues under other royalty-bearing agreements and investment income. As of December 31, 2000, we had cash, cash equivalents and short-term investments of $173.0 million, which decreased to $147.1 million as of December 31, 2001. In February 2002, we completed our initial public offering, raising net proceeds of approximately $110 million. Our cash reserves are held in a variety of investment-grade, fixed-income securities, including corporate bonds, commercial paper and money market instruments.

Net cash used in operating activities was $38 million in 2000 and $18.9 million in 2001. In 2001, cash used in operating activities was less than our net loss of $36.9 million due to non-cash items, such as depreciation and amortization and stock-based compensation expense, and revenues received but deferred to future periods. Net cash used in operating activities in 2000 was higher than our net loss of $30.4 million due to an income tax payment of $31.5 million to Novo Nordisk partially offset by non-cash reconciling items related to a deferred tax valuation allowance, depreciation and amortization expense, and changes in operating assets and liabilities. In 1999, $21.0 million of cash was provided by our operating activities due to payments received from Novo Nordisk pursuant to a funding agreement. We expect to continue the trend of using cash to fund our operating activities in the future. This use of cash is expected to increase over time as we expand our research and development activities and move product candidates into clinical trials.

Net cash used in investing activities was $5.6 million in 2000 and $117.7 million in 2001. Net cash used in investing activities in 2000 consisted primarily of capital expenditures. Net cash used in investing activities in 2001 included $109.6 million for purchases of short-term investments, net of proceeds from sales and maturities, and $8.1 million for capital expenditures, including $1.5 million for the purchase of land to be used for the construction of a pilot manufacturing plant. We anticipate that our capital expenditures will increase in the future, particularly with respect to construction of the pilot manufacturing plant and a possible expansion of our existing research and development facilities.

Cash provided by financing activities was $196.9 million in 2000 and $28,000 in 2001. Financing activities in 2000 included the receipt of net proceeds of $142.5 million from the private equity financing completed in November 2000 and the receipt of $90.1 million for the assignment to Novo Nordisk of patents and other rights relating to Factor VII and insulin analogues, offset by a payment of $35.7 million to Novo Nordisk to purchase rights to certain intellectual property.

We expect to incur substantial costs as we continue to expand our research and development activities, particularly as we move product candidates into clinical trials, and expect that these expenditures will increase significantly over the next several years. 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. We believe that our existing cash resources, together with the net proceeds of our recent initial public offering, will provide sufficient funding for these development programs for at least the next three years. If, at any time, our prospects for internally 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.

We may need to expand our current facilities to meet the demands for our anticipated growth. If an expansion project is pursued, we expect the project to be completed by the end of 2004 and cost approximately $20 million. To date, we have made no material financial commitments related to the facility expansion. We are in the process of purchasing land for and designing a pilot manufacturing plant to be completed by the end of 2004. The cost of the pilot manufacturing plant is currently expected to be approximately $50 million. We intend to explore alternatives for financing these projects, including the mortgage or leasing of new or existing properties. To the extent we are unable to obtain such financing, we intend to use our working capital to pay for the projects.

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:

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

- the 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 convertible debt securities, the percentage ownership of our existing shareholders will be reduced, 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 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.

CRITICAL ACCOUNTING POLICIES

Our critical accounting policies are as follows:

Revenue Recognition

We derive our revenue primarily from three different sources: option fees, product royalties and license fees.

Option fees—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 our protein candidates other than those related to beta cells over a period of four years beginning November 10, 2000. In return, we are entitled to receive four annual payments of $7.5 million, the first of which was received in November 2000. 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 us. Upon exercise of an option by Novo Nordisk, we 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. Each of the $7.5 million option payments is being recognized ratably over the twelve months following receipt.

Product royalties—We earn royalties on several products marketed and sold by Novo Nordisk and other companies. Royalty reports are received within 30 to 60 days after the end of each quarter. We record estimates at the end of each quarter based on historical sales information. Adjustments are made in the following quarter reflecting the difference between our estimate and actual reported royalties.

License and milestone fees—We enter into various licensing agreements that generate up-front payments with subsequent milestone payments earned based on the completion of development milestones. We exercise our best judgment in determining the period over which we have continuing commitments to perform under the agreements. Revenue is recognized on a straight-line basis over this period, which has ranged in duration from one to ten years. Revenue from milestone payments is recognized when the milestone is achieved and amounts are due and payable.

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. Management has exercised its judgment in determining the fair value of our stock with share prices varying from $9.09 to $15.11 in 2001. Deferred compensation is amortized over the vesting period of the individual options, using the straight-line method.

RECENT ACCOUNTING PRONOUNCEMENTS

In 1998, the Financial Accounting Standards Board (FASB) issued Statement of Financial Accounting Standards No. 133, *Accounting for Derivative Financial Instruments and for Hedging Activities* (SFAS 133), which provides a comprehensive and consistent standard for the recognition and measurement of derivatives and hedging activities. SFAS 133 is effective for fiscal years beginning after June 15, 2000 and did not have an impact on our results of operations or financial condition when adopted as we hold no derivative financial instruments and do not currently engage in hedging activities.

In 1999, the Securities and Exchange Commission (SEC) issued Staff Accounting Bulletin No. 101, *Revenue Recognition* (SAB 101), which provides guidance on the recognition, presentation and disclosure of revenue in financial statements filed with the SEC. SAB 101 outlines the basic criteria that must be met to recognize revenue and provides guidance for disclosures related to revenue recognition policies. SAB 101 became effective and was implemented for the year ended December 31, 2000. The adoption of SAB 101 had no material effect on our financial position or results of operations.

In 2001, the FASB issued Statement of Financial Accounting Standards No. 141, *Business Combinations* (SFAS 141), which provides a comprehensive standard of accounting for business combinations. SFAS 141 is effective for all business combinations after June 30, 2001.

In 2001, the FASB issued Statement of Financial Accounting Standards No. 142, *Goodwill and Other Intangible Assets* (SFAS 142), which requires a change in accounting for goodwill and certain other intangible assets. SFAS 142 is effective for fiscal years beginning after December 15, 2001 and is not anticipated to have an impact on our results of operations or financial condition when adopted, as we have no goodwill or other intangible assets.

In 2001, the FASB issued Statement 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. We are currently assessing the impact of SFAS 143 on our financial statements.

In 2001, the FASB issued Statement No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets to be Disposed of* (SFAS 144). The provisions of this Statement shall be effective for financial statements issued for fiscal years beginning after December 31, 2001, and interim periods within those fiscal years. SFAS 144 is not anticipated to have an impact on our results of operations or financial condition when adopted.

ITEM 7A. *QUALITATIVE AND QUANTITATIVE DISCLOSURES ABOUT MARKET RISK*

Our exposure to market risk is 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 and restricted 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. We do not have any foreign currency exposure, nor do we hold derivative financial instruments.

ITEM 8. *FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA*

REPORT OF INDEPENDENT ACCOUNTANTS

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 mandatorily redeemable convertible preferred stock and shareholders' equity (deficit) and of cash flows present fairly, in all material respects, the financial position of ZymoGenetics, Inc. at December 31, 2001 and 2000, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2001 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.

PRICEWATERHOUSECOOPERS LLP

Seattle, Washington
February 6, 2002, except for the third paragraph
of Note 15, as to which the date is
March 7, 2002

ZYMOGENETICS, INC.
BALANCE SHEETS

DECEMBER 31,	2001	2000
ASSETS		
CURRENT ASSETS		
Cash and cash equivalents	$ 36,393,551	$172,976,483
Short-term investments	110,683,392	—
Receivables		
Related party	449,314	3,406,503
Other	3,606,421	1,029,820
Prepaid expenses and other assets	2,291,270	1,675,673
Total current assets	153,423,948	179,088,479
Property and equipment, net	49,128,094	46,416,094
Other assets	2,882,522	3,132,368
Total assets	$ 205,434,564	$228,636,941
LIABILITIES, MANDATORILY REDEEMABLE CONVERTIBLE PREFERRED STOCK AND SHAREHOLDERS' EQUITY (DEFICIT)		
CURRENT LIABILITIES		
Accounts payable	$ 4,109,382	$ 1,960,556
Related party payable	—	278,975
Accrued liabilities	3,150,220	4,145,766
Deferred revenue	7,671,521	6,458,333
Total current liabilities	14,931,123	12,843,630
Other noncurrent liabilities	2,882,522	3,132,368
Deferred revenue	6,482,416	—
Total liabilities	24,296,061	15,975,998
Commitments		
Mandatorily redeemable convertible preferred stock, no par value, 30,000,000 shares authorized		
Series A, 2,528,000 shares authorized, issued and outstanding; aggregate liquidation preference of $103,148,879 and $95,587,126 at December 31, 2001 and 2000, respectively	103,148,879	95,587,126
Series B, 4,011,768 shares authorized, issued and outstanding; aggregate liquidation preference of $163,690,417 and $151,690,417 at December 31, 2001 and 2000, respectively	157,391,508	144,343,045
Shareholders' deficit		
Common stock, no par value, 130,000,000 shares authorized, 12,063,600 and 11,792,520 issued and outstanding at December 31, 2001 and 2000, respectively	55,855,870	46,971,022
Non-voting common stock, no par value, 30,000,000 shares authorized and no shares issued and outstanding	—	—
Notes receivable from shareholders	(725,000)	—
Deferred stock compensation	(25,234,712)	—
Accumulated deficit	(111,119,557)	(74,240,250)
Accumulated other comprehensive income	1,821,515	—
Total shareholders' deficit	(79,401,884)	(27,269,228)
Total liabilities, mandatorily redeemable convertible preferred stock and shareholders' deficit	$ 205,434,564	$228,636,941

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

ZYMOGENETICS, INC.

STATEMENTS OF OPERATIONS

YEAR ENDED DECEMBER 31,	2001	2000	1999
Revenues			
Royalties			
Related parties	$ 5,151,347	$ 29,310,940	$ 5,733,561
Other	3,962,881	2,111,640	271,358
Option fee from related party	7,500,000	1,041,667	—
License fees	1,213,870	—	—
Research and development agreements with related parties	—	—	63,670,390
Total revenues	17,828,098	32,464,247	69,675,309
Operating expenses			
Research and development (excludes noncash stock-based compensation expense of $2,109,246 in 2001)	48,051,455	49,336,648	48,415,034
General and administrative (excludes noncash stock-based compensation expense of $1,398,106 in 2001)	10,474,904	12,069,226	9,550,001
Noncash stock-based compensation expense	3,507,352	—	—
Total operating expenses	62,033,711	61,405,874	57,965,035
Income (loss) from operations	(44,205,613)	(28,941,627)	11,710,274
Other income (expense)			
Interest income	7,152,351	5,417,089	273,990
Interest expense	(13,489)	(848,040)	(56,302)
Other, net	97,838	(111,080)	(52,085)
Income (loss) before provision for income taxes	(36,968,913)	(24,483,658)	11,875,877
Benefit (provision) for income taxes	89,606	(5,893,402)	(2,453,514)
Net income (loss)	(36,879,307)	(30,377,060)	9,422,363
Preferred stock dividend and accretion	(20,610,216)	(2,903,535)	—
Net income (loss) attributable to common shareholders	$(57,489,523)	$(33,280,595)	$ 9,422,363
Net income (loss) per share—basic	$ (4.85)	$ (3.38)	$ 1.11
Net income (loss) per share—diluted	$ (4.85)	$ (3.38)	$ 0.80
Weighted-average number of shares used in computing basic net income (loss) per share	11,846,093	9,845,870	8,455,406
Weighted-average number of shares used in computing diluted net income (loss) per share	11,846,093	9,845,870	11,792,520

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

STATEMENT OF CHANGES IN MANDATORILY REDEEMABLE CONVERTIBLE PREFERRED STOCK AND SHAREHOLDERS' EQUITY (DEFICIT)

	MANDATORILY REDEEMABLE CONVERTIBLE PREFERRED STOCK		SHAREHOLDERS' EQUITY (DEFICIT)									
			CONVERTIBLE PREFERRED STOCK		COMMON STOCK		ADDITIONAL PAID-IN CAPITAL	NOTES RECEIVABLE FROM SHAREHOLDERS	DEFERRED STOCK COMPENSATION	ACCUMULATED EARNINGS (DEFICIT)	ACCUMULATED OTHER COMPREHENSIVE INCOME	
	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT						TOTAL
Balance at January 1, 1999	—	$ —	926,976	$ 9,270	8,455,406	$ 84,554	$49,780,733	$ —	$ —	$ 18,390,512	$ —	$ 68,265,069
Net income and comprehensive income	—	—	—	—	—	—	—	—	—	9,422,363	—	9,422,363
Balance at December 31, 1999	—	—	926,976	9,270	8,455,406	84,554	49,780,733	—	—	27,812,875	—	77,687,432
Conversion from $.01 par value to no par value common stock	—	—	—	—	—	49,780,733	(49,780,733)	—	—	—	—	—
Conversion of Class A and Class B convertible preferred stock to common stock	—	—	(926,976)	(9,270)	3,337,114	9,270	—	—	—	—	—	—
Issuance of dividend in form of Series A mandatorily redeemable convertible preferred stock	2,528,000	94,521,920	—	—	—	—	—	—	—	(94,521,920)	—	(94,521,920)
Issuance of Series B mandatorily redeemable convertible preferred stock (net of offering costs of $7,495,290)	4,011,768	142,504,716	—	—	—	—	—	—	—	—	—	—
Intellectual property purchased from related party (net of deferred taxes of $11,245,499)	—	—	—	—	—	—	—	—	—	(24,454,501)	—	(24,454,501)
Payments received for future royalties from related party (net of income taxes of $31,524,691)	—	—	—	—	—	—	—	—	—	58,545,855	—	58,545,855
Accretion on mandatorily redeemable convertible preferred stock	—	147,918	—	—	—	(147,918)	—	—	—	—	—	(147,918)
Dividends accrued on mandatorily redeemable convertible preferred stock	—	2,755,617	—	—	—	(2,755,617)	—	—	—	—	—	(2,755,617)
Valuation allowance to reflect realizability of tax benefits related to purchase of intellectual property from related party	—	—	—	—	—	—	—	—	—	(11,245,499)	—	(11,245,499)
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	(30,377,060)	—	(30,377,060)
Balance at December 31, 2000	6,539,768	239,930,171	—	—	11,792,520	46,971,022	—	—	—	(74,240,250)	—	(27,269,228)
Common stock issued in connection with stock option exercises	—	—	—	—	10,080	28,000	—	—	—	—	—	28,000
Common stock issued in connection with stock option exercises for notes receivable	—	—	—	—	261,000	725,000	—	(725,000)	—	—	—	—
Deferred stock compensation related to grants of stock options	—	—	—	—	—	28,742,064	—	—	(28,742,064)	—	—	—
Amortization of deferred stock compensation	—	—	—	—	—	—	—	—	3,507,352	—	—	3,507,352
Accretion on mandatorily redeemable convertible preferred stock	—	1,048,462	—	—	—	(1,048,462)	—	—	—	—	—	(1,048,462)
Dividends accrued on mandatorily redeemable convertible preferred stock	—	19,561,754	—	—	—	(19,561,754)	—	—	—	—	—	(19,561,754)
	6,539,768	260,540,387	—	—	12,063,600	55,855,870	—	(725,000)	(25,234,712)	(74,240,250)	—	(44,344,092)
Net loss	—	—	—	—	—	—	—	—	—	(36,879,307)	—	(36,879,307)
Other comprehensive income												
Unrealized gain on short-term investments	—	—	—	—	—	—	—	—	—	—	1,821,515	1,821,515
Comprehensive loss	—	—	—	—	—	—	—	—	—	(36,879,307)	1,821,515	(35,057,792)
Balance at December 31, 2001	6,539,768	$260,540,387	—	$ —	12,063,600	$55,855,870	$ —	$(725,000)	$(25,234,712)	$(111,119,557)	$1,821,515	$(79,401,884)

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

ZYMOGENETICS, INC.

STATEMENTS OF CASH FLOWS

YEAR ENDED DECEMBER 31,	2001	2000	1999
CASH FLOWS FROM OPERATING ACTIVITIES			
Net income (loss)	**$ (36,879,307)**	$ (30,377,060)	$ 9,422,363
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities			
Depreciation and amortization	**5,404,635**	5,689,451	6,090,347
Net loss on disposition of property and equipment	**77**	111,080	52,085
Provision for deferred income taxes	**—**	13,731,405	(1,742,762)
Income taxes on future royalty payments from related party	**—**	(31,524,691)	—
Noncash stock-based compensation	**3,507,352**	—	—
Net realized gain on sale of short-term investments	**(94,748)**	—	—
Amortization of premium on short-term investments	**786,834**	—	—
Changes in			
Receivables	**380,588**	2,850,238	10,023,529
Prepaid expenses and other assets	**(365,751)**	(220,556)	(1,816,364)
Accounts payable	**2,148,826**	521,860	(835,748)
Related party payables	**(278,975)**	(4,281,414)	672,677
Accrued liabilities	**(995,546)**	1,731,110	(1,333,053)
Stock appreciation plan liability, net of cash distributions	**—**	(3,712,369)	(424,702)
Deferred revenue	**7,695,604**	6,458,333	—
Other noncurrent liabilities	**(249,846)**	1,032,166	939,600
Net cash provided by (used in) operating activities	**(18,940,257)**	(37,990,447)	21,047,972
CASH FLOWS FROM INVESTING ACTIVITIES			
Purchase of property and equipment	**(8,181,492)**	(5,617,038)	(7,353,698)
Purchase of short-term investments	**(207,700,172)**	—	—
Proceeds from sale of property and equipment	**64,780**	60,789	216,051
Proceeds from sale and maturity of short-term investments	**98,146,209**	—	—
Net cash used in investing activities	**(117,670,675)**	(5,556,249)	(7,137,647)
CASH FLOWS FROM FINANCING ACTIVITIES			
Net proceeds from sale of Series B mandatorily redeemable convertible preferred stock (net of offering costs of $7,495,290)	**—**	142,504,716	—
Proceeds from issuance of common stock	**28,000**	—	—
Purchase of intellectual property from related party	**—**	(35,700,000)	—
Proceeds from assignment of patents and other rights to related party	**—**	90,070,546	—
Net cash provided by financing activities	**28,000**	196,875,262	—
Net increase (decrease) in cash and cash equivalents	**(136,582,932)**	153,328,566	13,910,325
Cash and cash equivalents at beginning of period	**172,976,483**	19,647,917	5,737,592
Cash and cash equivalents at end of period	**$ 36,393,551**	$172,976,483	$19,647,917
SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION			
Cash paid to related party during the period for interest	**$ —**	$ 844,629	$ —
Cash paid during the period for interest	**$ 13,489**	$ 3,411	$ 56,302
Cash paid during the period for income taxes	**$ —**	$ 29,196,276	$ 2,307,363
Noncash financing activities			
Accretion on Series B mandatorily redeemable convertible preferred stock	**$ 1,048,462**	$ 147,918	$ —
Conversion of Class A and Class B convertible preferred stock to common stock	**$ —**	$ 9,270	$ —
Issuance of dividend in form of Series A mandatorily redeemable convertible preferred stock	**$ —**	$ 94,521,920	$ —
Dividends accrued on Series A and Series B mandatorily redeemable convertible preferred stock	**$ 19,561,754**	$ 2,755,617	$ —

The accompanying notes are an integral part of these 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 August 1988 by Novo Nordisk North America, a wholly owned subsidiary of Novo Nordisk A/S (Novo Nordisk). Effective November 9, 2000, the Company became an independent corporate entity with the completion of a private placement of Series B mandatorily redeemable convertible preferred stock with an investor consortium. As of December 31, 2001, Novo Nordisk's ownership percentage is 61.11% and its voting percentage is 47.76%. As described in Note 15, in February 2002, the Company completed its initial public offering, which further reduced Novo Nordisk's ownership stake in the Company.

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 broad 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 be unavailable when required or may not be available on acceptable terms.

CASH AND CASH EQUIVALENTS

The Company considers all highly liquid investments purchased with an original maturity of three months or less to be 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 (deficit). The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest income. Realized gains and losses are included in other income. The cost of securities sold is based on the specific identification method. Interest on securities classified as available-for-sale are included in interest income.

FAIR VALUE OF FINANCIAL INSTRUMENTS

The carrying values of cash, accounts receivable and payable, and accrued liabilities in the financial statements approximate fair value because of the short-term nature of these instruments.

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 includes five years for furniture and lab equipment, ten years for pilot plant equipment and leasehold improvements and 40 years for the buildings. Expenditures for repairs and maintenance are charged to expense as incurred.

Leasehold improvements are amortized evenly over either their estimated useful lives or the term of the lease, whichever is shorter.

IMPAIRMENT OF LONG-LIVED ASSETS

In accordance with the provisions of Statement of Financial Accounting Standards No. 121, *Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of* (SFAS 121), the Company reviews long-lived assets, including intangible assets and property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amounts of the assets may not be fully recoverable. An impairment loss will be recognized when estimated undiscounted future cash flows expected to result from the use of an asset and its eventual disposition are less than its carrying amount. In that event, a loss is recognized based on the amount by which the carrying value exceeds the fair value of the long-lived asset. While the Company's current operating and cash flow losses are indicators of impairment, the Company believes the future cash flows to be received from the long-lived assets will exceed the assets' carrying value, and accordingly, the Company has not recognized any impairment losses through December 31, 2001.

PATENTS AND LICENSING AGREEMENTS

It is the Company's practice to seek patent protection on processes and products in various countries. Patent application costs are expensed as incurred, as recoverability of such expenditures is uncertain.

REVENUE RECOGNITION

During the year ended December 31, 1999, the Company earned revenues by conducting contract research for Novo Nordisk and related entities. The Company's revenues were based on an agreement with Novo Nordisk whereby the Company was paid 110% of its research and development costs incurred in connection with approved projects. The Company recognized revenues related to this agreement as expenses were incurred. This agreement was terminated effective January 1, 2000.

Revenues from royalties are received from related and third parties for sales of products that include technology developed by the Company. Revenues are recognized when due and amounts are considered collectible.

Revenues from license fees, option fees and up-front payments, which are received in connection with other rights or services that represent continuing obligations of the Company, are recognized systematically over the period that the fees or payments are earned. Revenues from milestone payments representing completion of separate and substantive earnings processes will be recognized when the milestone is achieved and amounts are due and payable.

RESEARCH AND DEVELOPMENT COSTS

Research and development costs, including personnel costs, supplies, depreciation, amortization and other indirect costs, are charged to expenses 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 utilizes 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 recovered.

Through November 9, 2000, the Company was included in the consolidated federal income tax return of Novo Nordisk. A provision for income taxes was made in accordance with a tax sharing agreement between the Company and Novo Nordisk that requires a "separate company" basis, allocating taxes to each party as if it were a separate taxpayer. Subsequent to November 9, 2000, the Company files its income tax return as a stand-alone taxpayer.

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 elected to follow Accounting Principles Board No. 25, *Accounting for Stock Issued to Employees* (APB 25), in accounting for its employee stock option grants and apply the disclosure-only provisions of SFAS 123 to account for its stock option plan. 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 is being amortized over the vesting period of the individual options, using the straight-line method.

OTHER COMPREHENSIVE INCOME (LOSS)

Comprehensive income (loss) is comprised of net income (loss) and unrealized gains and losses on short-term investments. For all periods through December 31, 2000, net income (loss) equaled the comprehensive income (loss). For the year ended December 31, 2001, comprehensive loss was $35.1 million.

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.

EARNINGS (LOSS) PER SHARE

Basic net income (loss) per share has been computed based on net income (loss) available to common shareholders and the weighted-average number of common shares outstanding during the applicable period. For periods in which the Company has experienced net losses available to common shareholders, common stock equivalents are excluded from the computation of diluted net loss per share because they are antidilutive. For periods for which the Company experienced net income available to common shareholders, common stock equivalents are included in the denominator on a weighted-average basis for computing diluted net income per share. The Company first issued stock options in 2000. Common stock equivalents in 1999 consisted solely of shares of convertible preferred stock. Shares subject to repurchase have been excluded from the denominator for both the basic and diluted computations.

The following table presents the calculation of basic and diluted net income (loss) per share for years ended December 31:

	2001	2000	1999
Net income (loss) attributable to common shareholders	**$(57,489,523)**	$(33,280,595)	$ 9,422,363
Weighted-average shares used in computing basic net income (loss) per share	**11,846,093**	9,845,870	8,455,406
Convertible preferred stock	**–**	–	3,337,114
Weighted-average shares used in computing diluted net income (loss) per share	**11,846,093**	9,845,870	11,792,520
Net income (loss) per share–basic	**$ (4.85)**	$ (3.38)	$ 1.11
Net income (loss) per share–diluted	**$ (4.85)**	$ (3.38)	$ 0.80
Antidilutive securities not included in net loss per share calculation			
Mandatorily redeemable convertible preferred stock (as if converted)	**23,543,159**	23,543,159	–
Options to purchase common stock	**7,307,092**	4,311,000	–
Shares subject to repurchase	**87,750**	–	–
	30,938,001	27,854,159	–

RECENT ACCOUNTING PRONOUNCEMENTS

In 1998, the Financial Accounting Standards Board (FASB) issued Statement of Financial Accounting Standards No. 133, *Accounting for Derivative Financial Instruments and for Hedging Activities* (SFAS 133), which provides a comprehensive and consistent standard for the recognition and measurement of derivatives and hedging activities. SFAS 133 is effective for fiscal years beginning after June 15, 2000 and did not have an impact on the Company's results of operations or financial condition when adopted as the Company holds no derivative financial instruments and does not currently engage in hedging activities.

In 1999, the Securities and Exchange Commission (SEC) issued Staff Accounting Bulletin No. 101, *Revenue Recognition* (SAB 101), which provides guidance on the recognition, presentation and disclosure of revenue in financial statements filed with the SEC. SAB 101 outlines the basic criteria that must be met to recognize revenue and provides guidance for disclosures related to revenue recognition policies. SAB 101 became effective and was implemented for the year ended December 31, 2000. The adoption of SAB 101 had no material effect on the financial position or results of operations of the Company.

In 2001, the FASB issued Statement of Financial Accounting Standards No. 141, *Business Combinations* (SFAS 141), which provides a comprehensive standard of accounting for business combinations. SFAS 141 is effective for all business combinations after June 30, 2001.

In 2001, the FASB issued Statement of Financial Accounting Standards No. 142, *Goodwill and Other Intangible Assets* (SFAS 142), which requires a change in accounting for goodwill and certain other intangible assets. SFAS 142 is effective for fiscal years beginning after December 15, 2001 and is not anticipated to have an impact on the Company's results of operations or financial condition when adopted, as the Company has no goodwill or other intangible assets.

In 2001, the FASB issued Statement 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. The Company is currently assessing the impact of SFAS 143 on its financial statements.

In 2001, the FASB issued Statement No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets to be Disposed of* (SFAS 144). The provisions of this Statement shall be effective for financial statements issued for fiscal years beginning after December 31, 2001, and interim periods within those fiscal years. SFAS 144 is not anticipated to have an impact on the Company's results of operations or financial condition when adopted.

2. SHORT-TERM INVESTMENTS

Short-term investments consisted of the following at December 31, 2001:

	AMORTIZED COST	GROSS UNREALIZED GAIN	GROSS UNREALIZED LOSS	ESTIMATED FAIR VALUE
Type of security:				
Commercial paper and money market	$ 1,473,989	$ –	$ –	$ 1,473,989
Corporate debt securities	48,647,341	953,566	(11,597)	49,589,310
Asset-backed securities	24,810,834	288,079	(5,772)	25,093,141
U.S. government and agency securities	33,929,713	625,743	(28,504)	34,526,952
	$108,861,877	$1,867,388	$(45,873)	$110,683,392

The following table summarizes contractual maturity information for the securities at December 31, 2001:

	ESTIMATED FAIR VALUE	AMORTIZED COST
Maturity date:		
Less than one year	$ 22,040,421	$ 21,808,678
Due in 1-5 years	88,642,971	87,053,199
	$110,683,392	$108,861,877

Realized gains and losses for the year ended December 31, 2001 were approximately $132,000 and $37,000, respectively.

3. PROPERTY AND EQUIPMENT

Property and equipment consisted of the following at December 31:

	2001	2000
Land and building	$ 49,344,651	$ 44,690,770
Leasehold improvements	5,737,412	5,737,412
Furniture and equipment	36,830,103	34,344,331
Construction in progress	710,248	286,160
	92,622,414	85,058,673
Less: Accumulated depreciation and amortization	(43,494,320)	(38,642,579)
	$ 49,128,094	$ 46,416,094

4. ACCRUED LIABILITIES

Accrued liabilities consisted of the following at December 31:

	2001	2000
Accrued vacation pay	$ 1,737,960	$ 1,419,946
Accrued incentive compensation	134,668	1,272,073
Accrued contract research	744,573	576,387
Accrued city and state taxes	25,280	434,070
Accrued severance payments	179,167	193,246
Other	328,572	250,044
	$ 3,150,220	$ 4,145,766

5. 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 first of which was received in November 2000. 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. Upon exercise of an option 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.

During 1999, the Company performed significant portions of its research and development for its former parent, Novo Nordisk, and affiliated companies. The Company had an agreement with Novo Nordisk effective as of January 1, 1991 whereby the Company was reimbursed for 110% of its research and development costs and an appropriate allocation of general and administrative expenses incurred in connection with approved projects. The agreement was terminated effective January 1, 2000, and accordingly, no research and development contract revenues were recorded in 2000 or 2001. Revenue related to the agreement was approximately $63.7 million for the year ended December 31, 1999.

During 2000, Novo Nordisk paid approximately $90.1 million to the Company, $76.4 million of which was in return for assignment of all rights and obligations with respect to NovoSeven (Factor VII) and $13.7 million for the grant of a perpetual license to the technology relating to analogues of human insulin, including the technology underlying Novo Nordisk's product, NovoRapid. Also, the Company paid $35.7 million to Novo Nordisk to purchase its rights outside the United States to the Company's portfolio of patents, patent applications and related intellectual property that had been developed pursuant to the research and development agreement described above. Concurrently, Novo Nordisk contributed to the Company the rights to this intellectual property in the United States. Because these transactions were consummated when the Company was controlled by Novo Nordisk, they were recorded as capital transactions. On August 4, 2000, the Company entered into a loan in the amount of $35.7 million with Novo Nordisk to fund the purchase of the intellectual property described above. The loan accrued interest of 6.94% per annum and, together with the principal, was paid in full on October 13, 2000. Various other loans were arranged with Novo Nordisk with annual interest rates ranging from 6.82% to 6.87% and with full repayment occurring within seven days of origination. There were no loan obligations due to Novo Nordisk as of December 31, 2000 or 2001.

The Company earns royalties on several products marketed and sold by Novo Nordisk, including Novolin (recombinant insulin) and GlucaGen (recombinant glucagon). Royalties are based on contracts predating the Company's acquisition by Novo Nordisk. Minimum royalties were collected through 1999; however, an analysis completed in 2000 showed additional royalties due the Company for Novolin and GlucaGen of approximately $12.1 million and $3.1 million, respectively. These amounts plus an interest charge of approximately $2.3 million were recorded in 2000 when collectability was assured, and the amounts were fixed and determinable. Including the aforementioned royalty amounts, the Company earned total royalties from Novo Nordisk of approximately $5.2 million, $29.3 million and $5.7 million for the years ended December 31, 2001, 2000 and 1999, respectively.

During 2000, the Company entered into a cross-license agreement with Novo Nordisk which provides non-exclusive licenses to each party to conduct research using the other party's intellectual property relating to Kunitz domains and Kunitz proteins. In addition, the Company has entered into other cross-licensing agreements with Novo Nordisk relating to certain other technologies.

During 1999, the Company entered into an agreement with Novo Nordisk (China) Investment Company Ltd. (NNIC), which was at that time a wholly owned subsidiary of Novo Nordisk, whereby NNIC would perform research for the Company. Payments totaling $150,000 were made to NNIC during 1999.

Pursuant to the private placement of Series B mandatorily redeemable convertible preferred stock, and subject to certain conditions, Novo Nordisk agreed to invest up to $100 million in the Company in any qualified private placement of shares completed during the four-year period ending November 10, 2006. The amount of Novo Nordisk's investment will be limited to the amount invested by the holders of Series B mandatorily redeemable preferred stock in such private placement. Any such purchase will be structured to ensure that Novo Nordisk owns no more than 49% of the Company's outstanding shares of voting securities. As described in Note 15, in February 2002, the Company completed its initial public offering, which terminated this agreement.

All amounts related to research and development contracts and royalty agreements have been processed through intercompany accounts that are settled quarterly. Amounts receivable from Novo Nordisk and related entities were approximately $449,000 and $3.4 million at December 31, 2001 and 2000, respectively. Amounts payable to Novo Nordisk and related entities were $0 and approximately $279,000 at December 31, 2001 and 2000, respectively.

6. NOVO NORDISK STOCK APPRECIATION RIGHTS

In 1988, the Company adopted a plan providing that officers and other key employees be granted rights to the appreciation in the market value of a stated number of shares of common stock of Novo Nordisk listed on the New York Stock Exchange. The rights became exercisable over three- and five-year periods and had a life of ten years. The exercise price of the rights ranged from 85% to 90% of Novo Nordisk's common stock price on the date of the grant. Expenses were charged or credited for the aggregate appreciation or depreciation of the rights during each reporting period. Changes in the value of outstanding rights resulted in compensation expense of approximately $1.5 million for the year ended December 31, 2000 and a reduction in compensation expense of approximately $208,000 for the year ended December 31, 1999. As of December 31, 2000, all such rights had been exercised and none remained outstanding.

7. NOVO NORDISK SHARE OFFERING PLAN

During 1999, Novo Nordisk implemented the Novo Nordisk 1999 Share Offering Plan (the NSOP). The NSOP provided all eligible employees a one-time grant of options to purchase shares of common stock of Novo Nordisk for $11.05 per share based on their years of service with the Company. The options were fully vested when granted on March 23, 1999 and all options expired on April 5, 1999. A total of 8,920 shares were granted, of which, 100 were forfeited and 8,820 were exercised in 1999. The market value of the stock at the date of grant was approximately $106 per share.

The Company was required to pay Novo Nordisk for the difference between the exercise price and the market value of the options at the date of grant. Accordingly, the Company recognized compensation expense of approximately $821,000 for the year ended December 31, 1999.

The Company applied APB 25 in accounting for the NSOP. Accordingly, compensation cost has been recognized using the intrinsic value based model. Had compensation for the NSOP been determined based on the fair value at the grant date of the award consistent with the fair value method of SFAS 123, the Company's net income would not have been significantly different.

8. EMPLOYEE INCENTIVE PLAN

The Company adopted a Key Employee Incentive Plan (KEIP) to promote the achievement of its short-and long-term objectives. Participation in the KEIP was limited to employees approved by the Company's management committee. The plan period for the KEIP was January 1, 1999 through December 31, 2000. The KEIP awards for the 1999 plan year were based on the number of protein lead product candidates and investigational new drug applications achieved. The awards for the 2000 plan year were based on determining therapeutic utility and initiating preclinical efficacy studies for proteins. The Company accrued and expensed approximately $572,000

and $486,000 for the years ended December 31, 2000 and 1999, respectively. The accrued bonuses as of December 31, 2000 were paid in full during 2001. The KEIP plan was terminated effective January 1, 2001.

9. 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 $1.7 million, $1.6 million and $1.3 million for the years ended December 31, 2001, 2000 and 1999, respectively.

DEFERRED COMPENSATION PLAN

The Company has a Deferred Compensation Plan (the 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. The DCP provides for discretionary contributions by the Company; such contributions were approximately $0, $96,000 and $108,000 for the years ended December 31, 2001, 2000 and 1999, respectively. At December 31, 2001 and 2000, approximately $2.9 million and $3.1 million, respectively, was deferred under the DCP and was recorded as other noncurrent liabilities.

10. INCOME TAXES

At December 31, 2001, the Company had net operating loss carryforwards of approximately $43.7 million, a research and development tax credit carryforward of $12.9 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 losses, research and development tax credit and rehabilitation tax credit will expire in the years 2008 to 2021. The alternative minimum tax credit will carry forward indefinitely. The Company has provided a valuation allowance at December 31, 2001 and 2000 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. No valuation allowance was provided at December 31, 1999, as the Company filed its tax returns with Novo Nordisk's and realization of deferred tax assets was certain. 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 the income tax expense (benefit) were as follows for the years ended December 31:

	2001	2000	1999
Current	**$(89,606)**	$ (7,838,003)	$ 4,196,276
Deferred	—	13,731,405	(1,742,762)
	$(89,606)	$ 5,893,402	$ 2,453,514

Deferred tax assets and liabilities, which arise from temporary differences, were as follows for the years ended December 31:

	2001	2000
Deferred tax assets:		
Net operating loss carryforwards	**$ 15,305,000**	$ 2,071,000
Research and development tax credit carryforwards	**12,868,000**	10,691,000
Alternative minimum tax credit carryforwards	**1,242,000**	1,242,000
Rehabilitation tax credit carryforwards	**1,507,000**	1,507,000
Intellectual property purchased from Novo Nordisk	**9,996,000**	11,246,000
Other	**3,343,000**	2,493,000
	44,261,000	29,250,000
Deferred tax liabilities:		
Deferred revenue	**(2,625,000)**	(2,260,000)
	41,636,000	26,990,000
Less: Valuation allowance	**(41,636,000)**	(26,990,000)
Net deferred tax asset	**$ –**	$ –

On October 20, 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 million. As of December 31, 2001, the Company has research and development tax credit carryforwards of $12.9 million which begin to expire in 2008.

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:

	2001	2000	1999
Federal income tax rate	**(35)%**	(35)%	35 %
Research and development tax credits	**(6)**	–	(14)
Nondeductible expenses	**–**	–	(1)
Valuation allowance	**39**	62	–
Other	**2**	(3)	1
Effective tax rate	**0 %**	24 %	21 %

11. COMMITMENTS

The Company leases certain office and laboratory space, some of which has been subleased to a third party.

On November 9, 2001, the Company entered into a lease agreement for additional office space. The lease commences on the earlier of February 1, 2002 or the date of occupancy. The lease term is 10 years with options to renew for up to two additional terms, each of sixty months. The lease also provides the Company a First Right of Refusal to lease additional space within the next few years.

Future minimum rental payments under noncancelable operating leases with initial or remaining terms in excess of one year are as follows:

YEAR ENDING DECEMBER 31,	
2002	$ 2,337,379
2003	652,122
2004	532,332
2005	550,179
2006	555,731
Thereafter	3,084,161
	7,711,904
Less: Future sublease income	(2,077,511)
Net future minimum rental payments	$ 5,634,393

In addition to the above, the Company may be obligated to lease additional office space. In such a case, the minimum rental payments under that lease could range from approximately $444,000 to $630,000 per year beginning February 2004 and ending January 2012.

Gross rental expense for the years ended December 31, 2001, 2000, and 1999 was approximately $1.9 million, $1.8 million and $2.3 million respectively. Cash received under the sublease agreements for the subleased office space was approximately $2.0 million, $1.8 million and $856,000 for the years ended December 31, 2001, 2000, and 1999 respectively.

The Company maintains a severance plan, which provides salary and health insurance for up to 40 weeks from notice of termination. In addition, certain key employees have employment agreements with the Company providing certain additional severance benefits. As of December 31, 2001 and 2000, approximately $179,000 and $193,000 respectively, was payable under the plan and employment agreements.

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. The Company will accrete the net proceeds, using the effective interest method, to the liquidation value on the earliest mandatory redemption date of November 10, 2007.

In November 2000, 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 dividend was computed at $37.39 per share of Series A mandatorily redeemable convertible preferred stock.

Mandatorily redeemable convertible preferred stock at December 31, 2001 consisted of the following:

	SHARES			AMOUNT, NET OF UNAMORTIZED ISSUANCE COST
	DESIGNATED	ISSUED AND OUTSTANDING	LIQUIDATION PREFERENCE	
Series A	2,528,000	2,528,000	$103,148,879	$103,148,879
Series B	4,011,768	4,011,768	163,690,417	157,391,508
	6,539,768	6,539,768	$266,839,296	$260,540,387

CONVERSION

Each share of Preferred Stock is convertible into 3.6 shares of common stock at any time at the option of the holder. Series B preferred shares convert into voting common stock. Series A preferred shares convert into non-voting common stock. As described in Note 15, subsequent to December 31, 2001, the outstanding shares of mandatorily redeemable convertible preferred stock were converted to common stock.

LIQUIDATION

Upon any liquidation, dissolution or winding up of the Company, the holders of Preferred Stock shall be entitled to be paid out of any assets of the Company legally available an amount equal to the greater of $37.39 per share plus all accrued and unpaid dividends (the Liquidation Value) or the pro rata portion of the assets of the Company available for distribution that the holders of Preferred Stock would be entitled to receive on an as-converted basis together with the holders of common stock. If the assets of the Company are insufficient to permit payment in full, the assets of the Company available for distribution will be distributed ratably among the holders of Preferred Stock in proportion to the full amount to which they would otherwise be entitled.

MANDATORY REDEMPTION

On November 10, 2007 or a later date consented to in writing by the holders of a majority of the shares of Series B mandatorily redeemable convertible preferred stock, the Company must redeem, from any source of funds legally available, all outstanding shares of Series A and B preferred stock. Redemption is to be effected through payment of cash in the amount of the Liquidation Value in exchange for each outstanding share of Preferred Stock.

DIVIDENDS

Subject to the rights of other holders of preferred stock that may be issued with dividend rights equal or superior to the rights of Series A or B holders, the holders of Series A and B mandatorily redeemable convertible preferred stock (Preferred Stock) are entitled to receive a cumulative dividend of 8% per annum on the then current liquidation value. Dividends accrue on a quarterly basis effective November 10, 2000 and are payable only when and if declared by the Company's board of directors. No dividends can be paid to holders of common stock unless all accrued but unpaid dividends are first paid to the holders of Preferred Stock.

VOTING RIGHTS

Each holder of Series B mandatorily redeemable convertible preferred stock is entitled to the number of votes equal to the number of shares of common stock into which such holder's shares are convertible. The Series A mandatorily redeemable convertible preferred stock is non-voting. However, the holders of Series A preferred stock have the right to appoint two of the Company's nine directors.

13. 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 will collaborate with Serono to develop biopharmaceutical products based on two receptors, TACI and BCMA. Additionally, 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. 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 will have 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 will be responsible for manufacturing all products for both clinical trials and commercial sale. The Company has received a $7.5 million payment from Serono which is being amortized over the estimated term of the development program, approximately nine years.

14. SHAREHOLDERS' EQUITY (DEFICIT)

The Company's authorized capital stock consists of 130,000,000 shares of no par value voting common stock, 30,000,000 no par value non-voting common stock and 30,000,000 shares of no par value preferred stock. Prior to the filing of amended articles of incorporation in November 2000, the common stock had a par value of $0.01 per share. As described in Note 15, subsequent to December 31, 2001, the Company approved an increase of 20,000,000 shares of authorized no par value voting common stock.

COMMON STOCK

In August 2000, Novo Nordisk converted 420,000 shares of Class A convertible preferred stock and 506,976 shares of Class B convertible preferred stock to 3,337,114 shares of common stock. At December 31, 2001, 23,543,159 shares of authorized common stock were reserved for issuance upon conversion of preferred stock.

STOCK OPTIONS

In March 2000, the Company adopted the 2000 Stock Incentive Plan (the Plan). The Plan provides 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 has reserved a total of 8,820,000 shares of common stock for issuance under the Plan, of which 1,241,828 are available for future grant at December 31, 2001. The Company's board of directors is responsible for administration of the Plan 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. Options to purchase 144,000 shares that are immediately exercisable have been granted to certain board members. Upon completion of the Company's initial public offering, described in Note 15, the 2000 Stock Incentive Plan was suspended and the 2001 Stock Incentive Plan (the 2001 Plan) became effective. The 2001 Plan 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. The first annual increase under the 2001 Plan occurred upon completion of the Company's initial public offering. Any shares from the 2000 Stock Incentive Plan that are not actually issued shall continue to be available for issuance under the 2001 Plan. As of the effective date of the initial public offering, 9,423,180 shares of common stock are authorized for issuance under the 2001 Plan and the 2000 Stock Incentive Plan.

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

	OPTIONS	WEIGHTED-AVERAGE EXERCISE PRICE	WEIGHTED-AVERAGE FAIR VALUE AT GRANT DATE
Balance, January 1, 2000	—	$ —	
Granted	4,331,520	2.78	$ 2.78
Exercised	—	—	
Canceled	(20,520)	2.78	
Balance, December 31, 2000	4,311,000	$2.78	
Granted	3,629,066	3.94	$11.72
Exercised	(271,080)	2.78	
Canceled	(361,894)	3.03	
Balance, December 31, 2001	7,307,092	$3.35	

The exercise price of options granted in 2000 was equal to the estimated fair value of the Company's shares at the date of grant. The exercise price of options granted in 2001 was less than the fair value of the Company's shares at the date of grant.

The following table summarizes information about options outstanding at December 31, 2001:

	OPTIONS OUTSTANDING			OPTIONS EXERCISABLE	
EXERCISE PRICE	WEIGHTED-AVERAGE EXERCISE PRICES	NUMBER OF OPTIONS	WEIGHTED-AVERAGE REMAINING CONTRACTUAL LIFE (IN YEARS)	NUMBER OF OPTIONS	WEIGHTED-AVERAGE EXERCISE PRICES
$2.78	$2.78	4,897,471	8.7	2,458,545	$2.78
3.89	3.89	226,890	9.5	36,000	3.89
4.44	4.44	1,213,974	9.6	—	—
4.72	4.72	968,757	9.9	—	—
	$3.35	7,307,092	9.1	2,494,545	$2.79

The following table presents net loss and per share amounts for the years ended December 31, 2001 and 2000 as if the Company had accounted for its stock options granted to employees under the fair value method prescribed by Statement 123.

	2001	2000
Net loss attributable to common shareholders, as reported	**$(57,489,523)**	$(33,280,595)
Net loss attributable to common shareholders, pro forma	**$(55,072,543)**	$(34,070,766)
Basic net loss per share, as reported	**$ (4.85)**	$ (3.38)
Basic net loss per share, pro forma	**$ (4.65)**	$ (3.46)

Net income and per share amounts for the year ended December 31, 1999 are excluded from the above table as stock options were first granted during the year ended December 31, 2000.

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 below for the years ended December 31, 2001 and 2000. For options granted subsequent to September 10, 2001, the same assumptions were utilized except that volatility was assumed to be 70%.

	2001	2000
Expected dividend yield	0%	0%
Expected stock price volatility	0%	0%
Risk-free interest rate	4.48%	5.58%
Expected life of options	5 years	5 years

On September 14, 2001, the Company made loans of $400,000 to Bruce L.A. Carter, our President, Chief Executive Officer and a director, $150,000 to James A. Johnson, our Senior Vice President, Chief Financial Officer and Treasurer and $175,000 to Patrick J. O'Hara, our Vice President of Biomolecular Informatics, pursuant to promissory notes in connection with the purchase of shares of common stock upon the exercise of non-qualified stock options by Dr. Carter, Mr. Johnson and Dr. O'Hara. 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 loans 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.

15. SUBSEQUENT EVENTS

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. Also in January, the Company's shareholders approved a 20,000,000 share increase in authorized no par voting common stock and the adoption of the 2001 Stock Incentive Plan.

On February 1, 2002, the Company sold 10,000,000 shares of common stock in an initial public offering. 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. Upon completion of the initial public offering, the increase in authorized shares of common stock and the 2001 Stock Incentive Plan became effective. Net proceeds from the initial offering amounted to approximately $110 million.

On March 7, 2002, the Company filed a patent infringement lawsuit against Immunex Corporation in the United States District Court for the Western District of Washington in Seattle. The lawsuit charges Immunex of directly and willfully infringing United States Patent Numbers 5,843,725, 6,018,026, 6,291,212 B1, 6,291,646 B1, 6,300,099 B1 and 6,323,323 B1 through the manufacture, importation and sale of Enbrel®, a dimeric fusion protein. While it is impossible to predict accurately or to determine the eventual outcome of this matter, the Company believes that the outcome will not have a material adverse effect on its financial position or results of operations.

16. QUARTERLY FINANCIAL RESULTS (UNAUDITED)

Operating results for each quarter of 2001 and 2000 are summarized as follows (in thousands):

	Q1	Q2	Q3	Q4
Year ended December 31, 2001:				
Revenue	$ 5,092	$ 3,458	$ 4,346	$ 4,932
Net loss	$ (6,230)	$ (9,666)	$ (9,726)	$(11,257)
Net loss attributable to common shareholders	$(11,382)	$(14,818)	$(14,879)	$(16,410)
Net loss per common share:				
Basic	$ (0.97)	$ (1.26)	$ (1.26)	$ (1.37)
Diluted	$ (0.97)	$ (1.26)	$ (1.26)	$ (1.37)
Year ended December 31, 2000:				
Revenue	$ 17,085	$ 1,825	$ 2,068	$ 11,486
Net income (loss)	$ 4,764	$ (9,233)	$ (7,745)	$(18,163)
Net income (loss) attributable to common shareholders	$ 4,764	$ (9,233)	$ (7,745)	$(21,067)
Net income (loss) per common share:				
Basic	$ 0.56	$ (1.09)	$ (0.73)	$ (1.79)
Diluted	$ 0.40	$ (1.09)	$ (0.73)	$ (1.79)

ITEM 9. *CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE*

None

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 section captioned "Proposal 1: Election of Directors" and the section captioned "Section 16(a) Beneficial Ownership Reporting Compliance" in the proxy statement for our annual meeting of shareholders to be held on June 21, 2002. We will file the proxy statement within 120 days of December 31, 2001, 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" and the section captioned "Section 16(a) Beneficial Ownership Reporting Compliance" in the proxy statement for our annual meeting of shareholders to be held on June 21, 2002.

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" and the section captioned "Employment Contracts, Termination of Employment and Change-in-Control Arrangements" in the proxy statement for our annual meeting of shareholders to be held on June 21, 2002.

ITEM 12. *SECURITY OWNERSHIP OF BENEFICIAL OWNERS AND MANAGEMENT*

The information required by this item with respect to beneficial ownership is incorporated by reference from 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 21, 2002.

ITEM 13. *RELATIONSHIPS AND RELATED TRANSACTIONS*

The information required by this item is incorporated by reference from the section labeled "Certain Transactions" in the proxy statement for our annual meeting of shareholders to be held on June 21, 2002.

PART IV

ITEM 14. *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. (Exhibit 3.1)	(A)
3.2	Amended and Restated Bylaws. (Exhibit 3.2)	(A)
9.1	Voting Agreement, dated October 20, 2000, by and between Warburg, Pincus Equity Partners, L.P. and Ernesto Bertarelli. (Exhibit 9.1)	(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. (Exhibit 9.2)	(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. (Exhibit 9.3)	(A)
10.1	Employment Agreement, dated November 9, 2000, between ZymoGenetics, Inc. and Bruce L.A. Carter. (Exhibit 10.1)	(A)
10.2	Employment Agreement, dated March 21, 2001, between ZymoGenetics, Inc. and Jan K. Öhrström. (Exhibit 10.4)	(A)
10.3	Employment Agreement, dated March 23, 2001, between ZymoGenetics, Inc. and Patrick J. O'Hara. (Exhibit 10.3)	(A)
10.4	Employment Agreement, dated April 23, 2001, between ZymoGenetics, Inc. and Frank D. Collins. (Exhibit 10.2)	(A)
10.5	Employment Agreement, dated April 30, 2001, between ZymoGenetics, Inc. and James A. Johnson. (Exhibit 10.5)	(A)
10.6	Employment Agreement, dated January 2, 2002, between ZymoGenetics, Inc. and Mark D. Young. (Exhibit 10.35)	(A)
10.7	Employment Agreement, dated January 28, 2002, between ZymoGenetics, Inc. and Robert S. Whitehead.	
10.8	Employment Agreement, dated February 12, 2002, between ZymoGenetics, Inc. and Suzanne Shema.	
10.9	Amended and Restated 2000 Stock Incentive Plan. (Exhibit 10.11)	(A)
10.10	2001 Stock Incentive Plan. (Exhibit 10.29)	(A)
10.11	Stock Option Grant Program for Nonemployee Directors under the ZymoGenetics 2001 Stock Incentive Plan. (Exhibit 10.30)	(A)
10.12	Incentive Compensation Plan Summary. (Exhibit 10.12)	(A)
10.13	Deferred Compensation Plan for Key Employees. (Exhibit 10.14)	(A)
10.14	Form of Promissory Note, dated September 14, 2001, between ZymoGenetics, Inc. and the executive officers listed on Schedule A thereto. (Exhibit 10.31)	(A)

EXHIBIT NO.	DESCRIPTION	
10.15	Form of Pledge and Security Agreement, dated September 14, 2001, between ZymoGenetics, Inc. and the executive officers listed on Schedule A thereto. (Exhibit 10.32)	(A)
10.16	Pledge and Security Agreement, dated September 14, 2001, between ZymoGenetics, Inc. and Bruce L.A Carter. (Exhibit 10.33)	(A)
10.17*	Insulin Agreement, dated August 6, 1982, between ZymoGenetics, Inc. and Novo Industri A/S. (Exhibit 10.18)	(A)
10.18*	Letter Agreement, dated March 13, 1987, between ZymoGenetics, Inc. and Novo Industri A/S. (Exhibit 10.19)	(A)
10.19*	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. (Exhibit 10.20)	(A)
10.20*	License Agreement for Analogues of Human Insulin, dated September 28, 2000, between the registrant and Novo Nordisk Health Care AG. (Exhibit 10.21)	(A)
10.21*	License Agreement, dated February 23, 1989, between ZymoGenetics, Inc. and the University of Washington. (Exhibit 10.16)	(A)
10.22*	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. (Exhibit 10.17)	(A)
10.23	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. (Exhibit 10.27)	(A)
10.24*	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. (Exhibit 10.15)	(A)
10.25*	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. (Exhibit 10.22)	(A)
10.26*	Cross-License Agreement, effective November 10, 2000, between ZymoGenetics, Inc. and Novo Nordisk A/S, Enzyme Business. (Exhibit 10.24)	(A)
10.27*	Cross-License Agreement, effective November 10, 2000, between ZymoGenetics, Inc. and Novo Nordisk A/S. (Exhibit 10.25)	(A)
10.28*	Kunitz Protein Agreement, effective November 10, 2000, between ZymoGenetics, Inc. and Novo Nordisk A/S. (Exhibit 10.26)	(A)
10.29*	Collaborative Development and Marketing Agreement, effective August 30, 2001, by and between ZymoGenetics, Inc. and Ares Trading S.A. (Exhibit 10.28)	(A)
10.30	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. (Exhibit 10.7)	(A)
10.31	Series B Co-Sale Agreement by and among ZymoGenetics, Inc. and the persons listed on Schedule A thereto, entered into and effective as of November 10, 2000. (Exhibit 10.8)	(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. (Exhibit 10.9)	(A)
10.33	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. (Exhibit 10.10)	(A)
10.34	Tax Sharing Agreement, effective October 20, 2000, between ZymoGenetics, Inc. and Novo Nordisk of North America, Inc. (Exhibit 10.23)	(A)
10.35	Office Lease Agreement, dated November 9, 2001, between ZymoGenetics, Inc. and 1144 Eastlake LLC. (Exhibit 10.34)	(A)
23.1	Consent of PricewaterhouseCoopers LLP, independent accountants.	

* 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 designated exhibit included with ZymoGenetics' Registration Statement on Form S-1 (No. 333-69190) filed on September 10, 2001, as amended.

(b) Reports on Form 8-K

None.

SIGNATURES

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

ZYMOGENETICS, INC.

By /s/ BRUCE L.A. CARTER

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

Date: March 26, 2002

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 registrant 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 26, 2002
/s/ JAMES A. JOHNSON **James A. Johnson**	Senior Vice President, Chief Financial Officer and Treasurer (Principal Accounting and Financial Officer)	March 26, 2002
/s/ GEORGE B. RATHMANN, PH.D. **George B. Rathmann, Ph.D.**	Chairman of the Board of Directors	March 26, 2002
/s/ DAVID I. HIRSH, PH.D. **David I. Hirsh, Ph.D.**	Director	March 26, 2002
/s/ JONATHAN S. LEFF **Jonathan S. Leff**	Director	March 26, 2002
/s/ KURT ANKER NIELSEN **Kurt Anker Nielsen**	Director	March 26, 2002
/s/ EDWARD E. PENHOET, PH.D. **Edward E. Penhoet, Ph.D.**	Director	March 26, 2002
/s/ LORI F. RAFIELD, PH.D. **Lori F. Rafield, Ph.D.**	Director	March 26, 2002
/s/ LARS REBIEN SORENSEN **Lars Rebien Sorensen**	Director	March 26, 2002

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COMPANY INFORMATION:

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.
Professor and Chairman
Department of Biochemistry and Molecular Biophysics
Columbia University

Jonathan S. Leff
Managing Director
Warburg Pincus LLC

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

Edward E. Penhoet, Ph.D.
Dean, School of Public Health
University of California, Berkeley

Lori F. Rafield, Ph.D.
General Partner
Patricof & Co. Ventures, Inc.

Lars Rebien Sorensen
President and 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

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

Patrick J. O'Hara, Ph.D.
Vice President, Biomolecular Informatics

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

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

Robert S. Whitehead
Senior Vice President
Chief Business Officer

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

COMPANY HEADQUARTERS

ZymoGenetics, Inc.
1201 Eastlake Avenue East
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 National Market under the symbol ZGEN.

ANNUAL MEETING

The annual meeting of shareholders will be held at 8:00 a.m. on Friday, June 21, 2002, 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.

FORWARD-LOOKING STATEMENTS

This Annual Report contains forward-looking statements. Forward-looking statements are based on the opinions, assumptions and estimates of management at the time the statements are made and are subject to both known and unknown uncertainties. Our actual results could differ materially from those described or implied by the forward-looking statements for many reasons, including the risks described under "Important Factors That May Affect Our Business, Our Results of Operations and Our Stock Price" in our Annual Report on Form 10-K for the year ended December 31, 2001, and in the filings we make with the Securities and Exchange Commission from time to time. You should not place undue reliance on these forward-looking statements, which speak only as of the date of this Annual Report.

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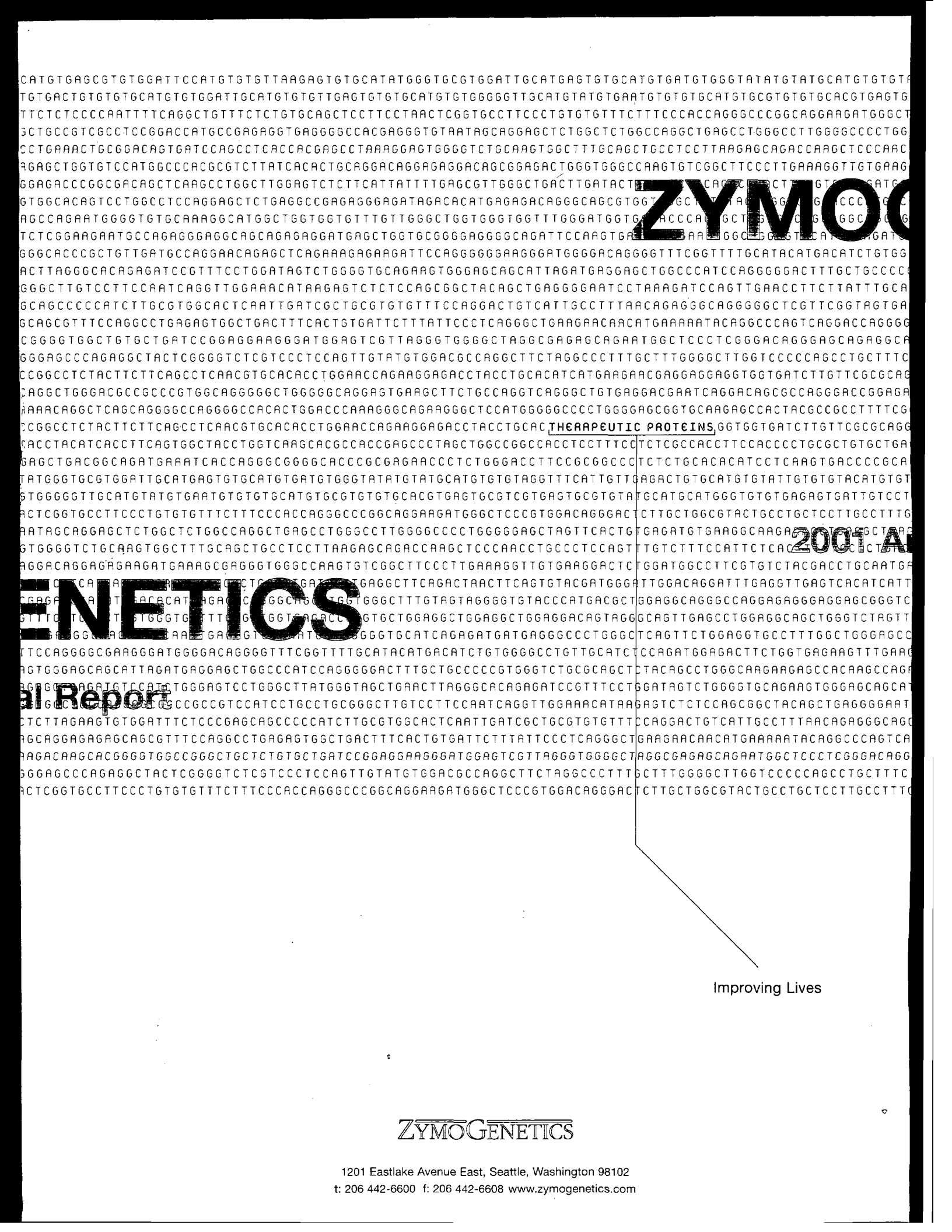

Improving Lives

ZYMOGENETICS

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