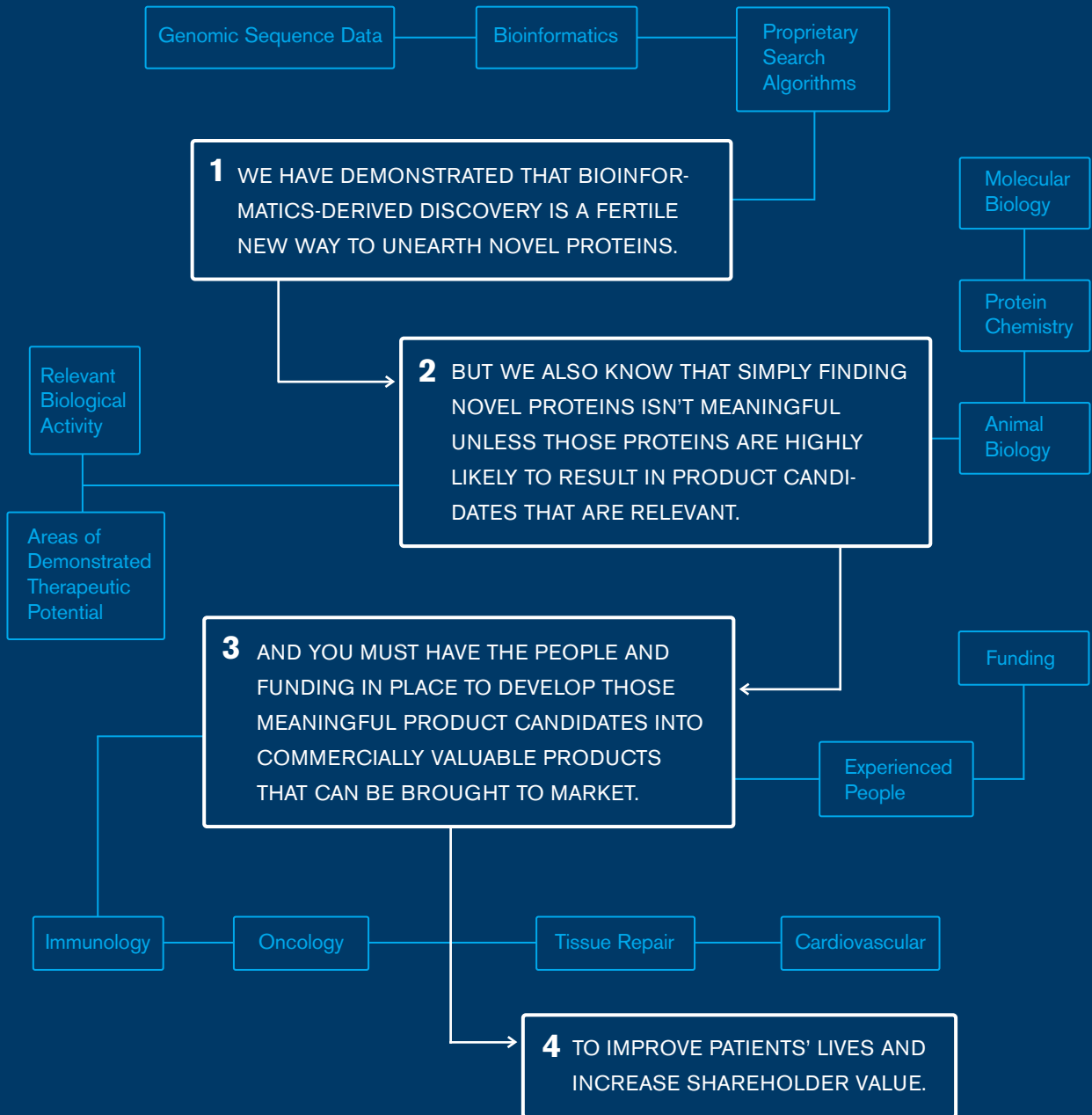


This is good.



V F N T F L R C L G I P A R I T V T N  
H S Q H V F L A P Q Q A R S L L  
Q R V R R A N T F L E E V R K G N  
R Y E R N I E K I S M L E K I Y I H  
P R Y N W R E N L D R D I A L M K  
L K K P V A F S D Y I H P V C L P  
N C A E G L G T N Y R G H V N I T  
C N H Q S Q R T C A A F C R S L S  
K R K P P S T N A G R R Q K H  
L T C P S C D S Y E K K P P

# This is very good.

**Our focus.** Sequencing the human genome has opened up a vast and largely unrealized area for the discovery of potential new protein therapies for the treatment of human disease. We pursue a focused discovery strategy to identify the relatively small subset of proteins that we believe have the highest probability of becoming protein therapeutics.

**Our product candidates.** We combine our bioinformatics-driven discovery approach with our pre-existing strengths in molecular and cellular biology, protein chemistry, and animal pharmacology. We focus on key protein categories that have members with demonstrated therapeutic potential or medically relevant biological activity. As a result, we have established a deep pipeline of novel product candidates with biological activities that span across multiple therapeutic areas.

#### PRODUCT CANDIDATES

##### (1) **rFACTOR XIII** | POST-SURGICAL BLEEDING

**Recombinant version of marketed protein.** Factor XIII is the final enzyme in the blood coagulation cascade. Factor XIII enhances clot strength by cross-linking fibrin strands within the clot and increases resistance to fibrinolysis by cross-linking enzyme inhibitors, such as alpha 2-antiplasmin, into the clot. Clinical experience with plasma-derived Factor XIII, which is currently marketed in a limited number of countries, but not the United States, shows significant therapeutic potential for the prevention and treatment of bleeding complications associated with surgical procedures and for treatment of defects in tissue repair processes associated with congenital and acquired Factor XIII deficiency. ZymoGenetics believes that recombinant human Factor XIII (rFactor XIII) offers several advantages over plasma-based Factor XIII therapies. In 2003, ZymoGenetics initiated clinical studies with rFactor XIII in patients who are congenitally deficient for Factor XIII and in healthy volunteers. The Company intends to extend its rFactor XIII clinical development activities into indications associated with acquired Factor XIII deficiency, such as the treatment of bleeding complications associated with cardiopulmonary bypass procedures.

##### (2) **rhTHROMBIN** | HEMOSTASIS

**Recombinant version of marketed protein.** ZymoGenetics is developing recombinant human thrombin (rhThrombin) as a topical hemostat to control surgical bleeding. Thrombin is applied locally to surgical incisions, sutures, and burns to help stop bleeding. Currently, the only stand-alone thrombin product available in the United States is derived from bovine blood. The presence of other proteins in commercial thrombin preparations can lead to the formation of antibodies to bovine and human blood proteins. This finding has raised safety concerns about the bovine product. ZymoGenetics is developing rhThrombin as an alternative to bovine-derived thrombin. We plan to file an Investigational New Drug Application (IND) with the FDA in the second half of this year to evaluate rhThrombin as a stand-alone topical hemostat. The Company is also evaluating other potential indications, including the use of rhThrombin as a component in surgical sealants.

1 VFNTFLRCLGIPARIVTN

2 RYERNIEKISMLEKIYIH  
PRYNWRENLDRIALMK  
LKKPVAFSDYIHPVCLP

3 CNHQSQRTCAAFCSLS

4 KRKPPSTNAGRROKH  
LTCPSCDSEKPP

# Even better.

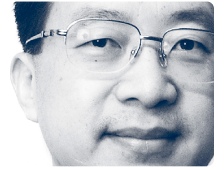
This discovery strategy provides a smooth and progressive flow from research to development to ensure a rich product pipeline. This effort has led to four product candidates that we are advancing into clinical development. We believe that our discoveries to date demonstrate the value of this approach in our search for the drugs of tomorrow.

## (3) TACI-Ig | AUTOIMMUNE DISEASE

**Genomics-derived candidate.** TACI-Ig is a soluble fusion protein that links part of a novel cytokine receptor named TACI to the Fc portion of human immunoglobulin (Ig). TACI-Ig is being developed as a therapy for autoimmune diseases such as systemic lupus erythematosus (SLE). TACI-Ig has been shown to bind to and neutralize BLYS, a cytokine that stimulates B-cell growth and the production of auto-antibodies. Over-production of BLYS correlates with the onset and severity of autoimmune disease in animal models and elevated levels of BLYS have been found in the blood of patients with SLE and other autoimmune diseases, suggesting that an inhibitor of BLYS may have therapeutic value. Functioning as an inhibitor protein, TACI-Ig may be able to remove excess BLYS from the blood stream. ZymoGenetics entered into an agreement with Serono S.A. for the development and commercialization of TACI-Ig for treatment of autoimmune diseases. ZymoGenetics and Serono intend to initiate TACI-Ig clinical studies in the second half of 2003 with SLE as an initial clinical indication.

## (4) INTERLEUKIN 21 | CANCER

**Genomics-derived candidate.** Interleukin 21 (IL-21), a protein discovered by ZymoGenetics, has been shown to activate key classes of immune cells, including cytotoxic T cells and natural killer cells. These cell types destroy malignant or infected cells. Based on the ability of IL-21 to inhibit tumor growth in a number of animal models, ZymoGenetics is developing IL-21 for the treatment of cancer, with metastatic melanoma and renal cell carcinoma as the first two targeted indications. ZymoGenetics has retained the commercialization rights for IL-21 in North America and has licensed the commercialization rights outside of North America to Novo Nordisk A/S. ZymoGenetics and Novo Nordisk have agreed to collaborate on research and development activities leading up to the filing of an IND by ZymoGenetics in the United States. The Company anticipates initiating clinical studies with IL-21 in the first half of 2004.



**Our people.** We have a team of dedicated individuals who have brought us to where we are today and are leading us into the future. As an independent biopharmaceutical company, we have expanded and strengthened our employee base with individuals who have direct experience in developing protein products. Sharing an intense commitment to finding new drugs for people suffering serious



#### COMPANY PROFILE

ZymoGenetics (Nasdaq: ZGEN) is a biopharmaceutical company focused on the discovery, development, and commercialization of therapeutic proteins for the prevention or treatment of human diseases. Using a product discovery engine comprising genomics, bioinformatics, molecular biology, protein chemistry, and preclinical biology, ZymoGenetics has generated a broad pipeline of proprietary product candidates that span a wide array of clinical opportunities, including cardiovascular disease, autoimmune disease, cancer, and tissue repair. ZymoGenetics intends to



# The best.

illnesses, we actively support and, likewise, depend upon each other to foster an energetic, open, and respectful atmosphere in which inquisitiveness, innovation, and collaborative work are prized. Valuing our responsibility to the larger community, we devote many hours of public service to the communities where we work and live.



commercialize these product candidates through internal development, collaborations with biopharmaceutical partners, and out-licensing of its extensive patent portfolio. rFactor XIII, the first of three protein product candidates that the Company intends to advance into clinical studies this year, highlights the Company's transformation from a research subsidiary to an independent biopharmaceutical company focused on the development of therapeutic products.

We are proud to say that 2002, our first year as a publicly traded company, was an extremely good one for ZymoGenetics. As an independent biopharmaceutical company, we achieved numerous key business objectives and ended the year in a strong financial position. Entering 2003, we are well positioned to aggressively pursue our business strategy of discovering, developing, and commercializing protein therapeutics.

# To our shareholders,

During the year, ZymoGenetics made a number of significant advances in product development and other important business areas. We:

- Completed our initial public offering, raising \$120 million.
- Filed an IND for recombinant human Factor XIII (rFactor XIII) and initiated clinical studies in both the United States and Europe.
- Designated Interleukin 21 (IL-21) as our fourth product development candidate.
- Signed agreements with multiple companies, including Amgen, Wyeth, Novo Nordisk, Regeneron, Arriva, and BioMimetic Pharmaceuticals, that provided substantial revenues to the Company.
- Settled the patent infringement lawsuit we had filed against Immunex Corporation, now owned by Amgen.
- Completed a sale and leaseback of our corporate headquarters buildings, raising over \$50 million.

These achievements are strong evidence of our progress in advancing our product development pipeline and building commercial value from our extensive patent portfolio.

PRECLINICAL PRODUCT CANDIDATES

**ZSIG37** | ANTI-THROMBOTIC

**IL-29** | ANTI-VIRAL

**IL-20 ANTAGONIST** | PSORIASIS

We remain dedicated to our strategy to discover, develop, and commercialize protein therapeutics. Our strategy for success includes two important platforms. In the near term, we are developing recombinant versions of marketed protein therapeutics that are currently isolated from human or animal blood. In the long term, using our genomics-based discovery effort, we are building a portfolio of novel proteins that we expect to lead us into the future. We believe that the near-term approach, developing recombinant versions of marketed blood proteins, provides lower-risk opportunities that balance the higher risks and higher potential rewards of our novel genomics-derived product candidates.

**High-Value Recombinant Versions of Marketed Proteins.** The biotechnology industry has a history of success in developing recombinant versions of proteins previously derived from human or animal sources. We played a key role in the commercialization of recombinant forms of two proteins marketed today by Novo Nordisk, human insulin and glucagon. We intend to build on our success in this area with the development and commercialization of rFactor XIII and recombinant human thrombin (rhThrombin). But this time we will do it for the direct benefit of ZymoGenetics.

We are developing rFactor XIII, our most advanced product candidate, for both congenital and acquired Factor XIII deficiencies. We began clinical studies with this protein early in 2003 in both healthy volunteers and in patients congenitally deficient (CD) for Factor XIII. We plan to complete the study in CD patients this year, and begin studies with rFactor XIII in the second half of the year in patients that have an acquired Factor XIII deficiency, such as patients undergoing cardiopulmonary bypass procedure.

rhThrombin is being developed for use as a topical hemostat to stop bleeding during surgery. The only thrombin sold today in the United States as a stand-alone product is isolated from cow's blood. It has been observed that antibodies may develop against the bovine-derived thrombin preparation that cross-react with human blood proteins. This observation has raised safety concerns about the use of bovine thrombin. We are developing rhThrombin as an alternative to the bovine-derived product, and plan to file an IND with the FDA in the second half of this year.

**Novel Genomics-Derived Product Candidates.** We remain a firm believer in the use of genomics as a foundation to discover protein therapeutics. Genomics has provided us the opportunity to identify novel proteins that were not readily detectable using other methods. With novelty comes the opportunity to obtain exclusive patent protection for new protein therapeutics.

We search for proteins that could themselves become drugs, rather than targets for the development of medicinal chemistry drugs. In addition, we narrow our search criteria to find novel proteins with structures similar to the protein drugs already on the market or to other known proteins having biology suggestive of clinical utility. This approach has yielded a broad pipeline of product candidates that include potential treatments for autoimmune disease, cardiovascular disease, tissue repair, and oncology.

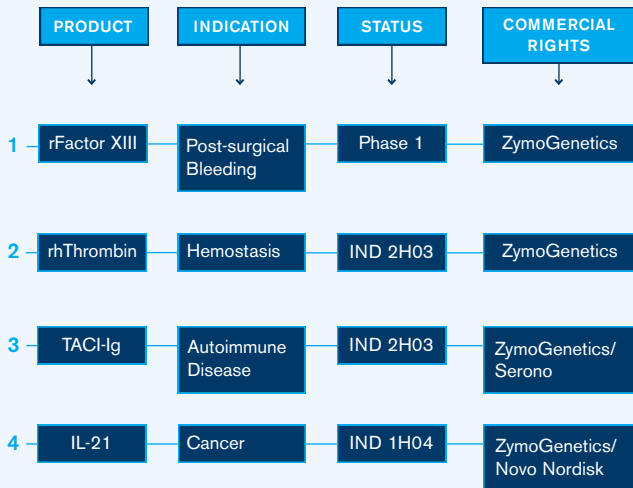
The first of our genomics-derived product development candidates to be tested in clinical trials is TACI-Ig, for the treatment of autoimmune diseases, followed by IL-21, for the treatment of cancer. These proteins provide novel mechanisms to address diseases with poor treatment options.

Our collaborative efforts with Serono S.A., our partner for TACI-Ig, have met all of our expectations and we are on track for TACI-Ig to enter clinical development in the second half of this year. IL-21, a cytokine with potent effects on a variety of immune cells involved in the body's host defense system, is on track for initiation of clinical studies in the first half of 2004.

**Expanding Patent Portfolio and Partnerships.** We continue to receive issued patents on our genomics-derived proteins, demonstrating the strength of our patent filings. In total, we now have over 240 issued U.S. patents, including thirty-five that were issued in 2002. These patents strengthen our product development pipeline, and position us to establish strategic partnerships for co-development relationships and out-licensing agreements. We believe that we will end up with one of the strongest patent portfolios of any company working with protein therapeutics.

During the past year we continued to leverage our patent estate for our commercial benefit by establishing a number of key relationships with both pharmaceutical and biotechnology companies. Additionally, in December of this past year we settled a patent infringement lawsuit with Amgen and its marketing partner Wyeth, who took a nonexclusive license to our immunoglobulin fusion protein patents.

**PRODUCT CANDIDATE PIPELINE**



**Scientific Excellence.** This past year, our scientific staff continued to distinguish the Company as a center for scientific excellence with numerous research publications and presentations at medical conferences highlighting our successes in the discovery and characterization of proteins identified through our genomics efforts. Our ability to determine the biology of these proteins in such diverse areas as cardiovascular biology, cartilage repair, autoimmune disease, psoriasis, and oncology is a strong statement regarding the depth and breadth of biology expertise within ZymoGenetics.

**Strong Financials.** ZymoGenetics entered 2003 with \$285 million in cash and investments, and no debt. These funds, together with anticipated future revenues from royalties, licenses, and milestone payments, should allow us to move our business forward.

The completion of the sale and leaseback of our headquarters facilities netted ZymoGenetics over \$50 million. Additionally, the buyer committed to provide most of the funding necessary for an expansion adding approximately 45,000 square feet of additional research and development space. Included in this space will be manufacturing suites suitable for the production of products under GMP conditions for use in human clinical studies. We initiated construction of this strategically important expansion in the second quarter of 2003.

**The Year Ahead.** 2003 is positioned to be another good year for ZymoGenetics. We expect to move three product candidates into clinical trials this year, demonstrating our commitment to develop our own products. While this is an aggressive development plan, we believe that we have the financial and technical resources to deliver on this goal.

We at ZymoGenetics are excited about the future of the Company, and I am proud to be at the helm of an organization with such dedicated employees. Each day, they offer insightful contributions, foresee problems, and create innovative solutions. We know that significant work lies ahead of us to turn our discoveries into marketed products. As a group, we relish the challenge and look forward to the task.

In closing, I would like to point out that in two years we have transformed ourselves from a research affiliate of Novo Nordisk to an independent company capable of discovering and developing our own drugs. Our past research has contributed to multimillion dollar products for other companies. Our efforts now are to re-create this success for ourselves and for our shareholders who have shown their confidence in us.



**BRUCE L. A. CARTER, PH.D.**  
 PRESIDENT AND CHIEF EXECUTIVE OFFICER  
 APRIL 11, 2003



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

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**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, 2002**

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

Commission File Number 0-33489

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**ZYMOGENETICS, INC.**

(exact name of registrant as specified in its charter)

**Washington**  
(State or other jurisdiction of  
incorporation or organization)

**91-1144498**  
(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**

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

Yes  No

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

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

Yes  No

The aggregate market value of the common equity held by non-affiliates computed by reference to the price at which the common equity was last sold as of June 28, 2002 was: \$115,558,379.

Common stock outstanding at March 14, 2003: 45,900,680 shares.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the Company's definitive Proxy Statement for the annual meeting of shareholders to be held on June 12, 2003, are incorporated by reference in Part III.

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**PART I****Item 1. Business**

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

**Overview**

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 voting interest to less than 50%.

We have contributed to the discovery or development of five marketed recombinant protein products. These products include recombinant versions of proteins previously made from human or animal sources (Novolin<sup>®</sup> (insulin) and GlucaGen<sup>®</sup> (glucagon), marketed by Novo Nordisk) and novel proteins that come from our discoveries (NovoSeven<sup>®</sup> (Factor VIIa) marketed by Novo Nordisk, Regranex<sup>®</sup> (platelet-derived growth factor), marketed by Ortho-McNeil Pharmaceuticals, Inc., a Johnson & Johnson company, and Cleactor<sup>™</sup> (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 increases our research efficiency and maximizes our chances of commercial success. Based on our analysis of published European patent filings, we believe that we have been one of the most successful companies in the world at discovering and filing patent applications for novel proteins within these categories.

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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 240 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, rFactor XIII and rhThrombin, are recombinant versions of proteins that are currently marketed in forms derived from human and cow blood. Our intent is to replace the currently marketed versions, building on our earlier experience with insulin and glucagon. rFactor XIII is a blood-clotting agent for the treatment of bleeding complications following cardiopulmonary bypass surgery, and rhThrombin is a hemostatic agent for the control of bleeding during surgical procedures. We began clinical trials of rFactor XIII in early 2003, and we expect to begin clinical development of rhThrombin in the second half of 2003.

Our other internal product candidates have resulted from our bioinformatics efforts, which in combination with our biology expertise, has yielded proteins with potential medical relevance. Our most advanced bioinformatics-derived product candidates are TACI-Ig and recombinant human interleukin-21 (IL-21). TACI-Ig is a soluble receptor with potential applications for the treatment of autoimmune diseases, which we are developing with Serono S.A., a leading global biotechnology company. IL-21 is a protein with potential applications for the treatment of cancer, which we are developing in North America and which we have licensed to Novo Nordisk for development in the rest of the world. We plan to begin clinical development of TACI-Ig and IL-21 in the second half of 2003 and the first half of 2004, respectively.

## **Business Strategy**

Our long-term 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 focus exclusively on therapeutic proteins. We use bioinformatics to identify the relatively small subset of genes that we believe have the highest probability of coding for proteins with therapeutic potential. Specifically, we focus on key protein categories that have members with demonstrated therapeutic potential or medically relevant biological activity. Once we have identified a protein candidate with relevant biological activity, we intend to develop the therapeutic protein directly, or, where appropriate, develop a monoclonal antibody or soluble receptor that targets the protein.
- *Pursue comprehensive intellectual property protection.* We intend to establish proprietary product opportunities by establishing patent priority for our gene and protein discoveries at the earliest possible time. Data generated from bioinformatics and exploratory biology enhances our patent applications. Our research teams work closely with our intellectual property department to prepare detailed patent applications on full-length genes and their corresponding proteins at an early stage in the discovery process. We augment initial filings with supporting data as it becomes available.
- *Leverage diverse biology expertise.* We 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.
- *Focus initially on lower-risk product candidates.* We intend to mitigate the risk of drug development by concentrating our initial product development efforts on product candidates that have a more favorable risk profile than more recently discovered proteins. Our two most advanced internal product

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development candidates are rFactor XIII and rhThrombin, recombinant versions of proteins intended to replace currently marketed plasma-derived proteins.

- *Pursue a diversified commercialization strategy.* Because we expect to generate more product candidates than we have the capacity to develop on our own in the near term, we are pursuing a three-pronged commercialization strategy. We intend to internally develop and commercialize some product candidates where we believe the clinical trials and sales force requirements are manageable. We intend to partner with other companies to co-develop and co-promote product candidates in cases where we do not have access to the infrastructure required for development and commercialization. Finally, we intend to out-license other product candidates and intellectual property that do not fit within our future commercial focus.
- *Phased acquisition of manufacturing capabilities.* For our existing development candidates, we intend to use third-party contractors or collaborative partners to manufacture both clinical and commercial product. We expect to begin construction in 2003 of small-scale dedicated GMP manufacturing suites, which we intend to use as a source of clinical product supply beginning in 2004. Over the long term, we intend to acquire larger-scale commercial manufacturing capabilities to allow us to control directly all critical elements of product development and commercialization.

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### Products and Product Pipeline

Our track record in the field of therapeutic proteins includes contributions to the discovery or development of five recombinant protein products currently being marketed by Novo Nordisk or other companies. Our current focus is the development of a pipeline of internal product candidates. We also have out-licensed several product candidates outside our areas of interest. The following table summarizes the marketed products and out-licensed product candidates, as well as our most advanced product candidates for internal development or co-development. 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
<b>Internal Candidates</b>			
rFactor XIII	Major cardiac surgery; congenital Factor XIII deficiency; acquired Factor XIII deficiencies	Internal development	Phase 1
rhThrombin	Surgical & critical care hemostat; surgical sealant	Internal development	Pre-IND
TACI-Ig	Systemic lupus erythematosus; other autoimmune diseases	Co-development with Serono S.A.	Pre-IND
IL-21	Cancer; viral infections	Internal development in North America; Novo Nordisk outside North America	Pre-IND
<b>Marketed Products</b>			
Novolin <sup>®</sup> and NovoRapid <sup>®</sup> (Insulin)	Diabetes	Out-licensed to Novo Nordisk	Marketed
NovoSeven <sup>®</sup> (Factor VIIa)	Hemophilia	Out-licensed to Novo Nordisk	Marketed
Regranex <sup>®</sup> (Platelet-derived Growth Factor)	Wound healing	Out-licensed to Johnson & Johnson	Marketed
GlucaGen <sup>®</sup> (Glucagon)	Hypoglycemia; gastrointestinal motility inhibition	Out-licensed to Novo Nordisk	Marketed
Cleactor <sup>™</sup> (tPA Analog)	Myocardial infarction	Out-licensed to Eisai Co., Ltd.	Marketed
<b>Licensed Products</b>			
Platelet-derived Growth Factor	Periodontal disease	Out-licensed to BioMimetic Pharmaceuticals, Inc.	Pivotal
	Bone repair	Out-licensed to BioMimetic Pharmaceuticals, Inc.	Pre-development
Platelet-derived Growth Factor Receptor Antibody	Cancer	Out-licensed to Celltech Group plc	Phase 2

In the table above, Phase 1 refers to clinical trials designed primarily to determine safety and toxicology in human beings; Phase 2 refers to clinical trials in a limited patient population to evaluate preliminary efficacy, dosing and side effects; Pivotal refers to clinical trials in a broad patient population with the intention of

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generating statistical evidence of efficacy and safety to support product approval. Pre-IND refers to the stage in which we have completed pre-development activities, have generated a commercial hypothesis for the product candidate and have begun the process leading to the filing of an investigational new drug application and the initiation of Phase 1 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.

- Novolin<sup>®</sup> and NovoRapid<sup>®</sup> (insulin), recombinant human insulin products marketed by Novo Nordisk worldwide for the treatment of diabetes. In collaboration with Novo Nordisk, we developed a process for the production of recombinant human insulin in yeast that is used by Novo Nordisk.
- NovoSeven<sup>®</sup> (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<sup>®</sup> (platelet-derived growth factor), a growth factor marketed by Ortho-McNeil Pharmaceuticals, Inc., a Johnson & Johnson company, for the treatment of non-healing diabetic ulcers. We cloned the gene that codes for platelet-derived growth factor and demonstrated the importance of this protein in stimulating wound healing.
- GlucaGen<sup>®</sup> (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<sup>™</sup> (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.

### *Internal Product Candidates*

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

*rFactor XIII.* Factor XIII 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 tissue repair. Acquired Factor XIII deficiency, a transient drop in Factor XIII levels, is much more common. It is thought to be a major cause of bleeding and failure to heal after surgeries and clinical procedures of many types, including cardiopulmonary bypass surgery. Acquired Factor XIII deficiency has also been reported in diseases, such as graft versus host disease of the gut following stem cell transplant and inflammatory bowel disease.

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Human plasma-derived Factor XIII is produced by Aventis Behring GmbH and is marketed as Fibrogammin<sup>®</sup> P in Japan, Germany, Austria and South Africa. However, Fibrogammin<sup>®</sup> P is not approved for use in the United States and many European countries. Clinical studies have shown that normal levels of Factor XIII activity can be restored in patients with a congenital or acquired deficiency by intravenous administration of plasma-derived Factor XIII. Our market research indicates that physicians in some countries are currently using plasma-derived Factor XIII not only for the treatment of congenital Factor XIII deficiency, but for other medical conditions associated with acquired Factor XIII deficiency. According to industry statistics and our own analysis, current annual sales of plasma-derived Factor XIII in the few countries in which it is sold are estimated at less than \$50 million.

In patients undergoing cardiopulmonary bypass surgery, there is significant illness and death associated with post-operative bleeding. Multiple transfusions with plasma and other blood products are often used to compensate for blood loss, but there are adverse health risks and costs associated with these transfusions. In some cases, surgeries must be redone, at significant cost and risk to the patient, to address uncontrolled bleeding. Studies have indicated that levels of Factor XIII 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 could decrease or eliminate the potential 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 rFactor 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 rFactor 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 rFactor XIII development, including replacement therapy for congenital Factor XIII deficiency and treatment of acquired Factor XIII deficiency such as in graft versus host disease of the gut following stem cell transplant and 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 rFactor XIII than with other recombinant human protein products that are not being developed as replacement products.

rFactor XIII is manufactured in yeast cells. The initial supply of rFactor XIII product for use in clinical testing has been manufactured for us by Avecia Limited. We filed an IND with the Food and Drug Administration, or FDA, in September 2002, and we began Phase 1 clinical trials in both congenitally deficient patients and healthy subjects in early 2003.

*rhThrombin.* Thrombin is a specific blood-clotting enzyme that converts fibrinogen to fibrin. Fibrin is the primary protein contained in newly formed blood clots. Thrombin also promotes clot formation by activating Factor XIII, which crosslinks the fibrin molecules and strengthens the newly forming clot. In addition, thrombin stimulates platelet aggregation and acts as a potent cell activator.

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Profuse bleeding is a serious complication of major surgeries. Surgeons try to limit bleeding during surgery to control blood loss, limit the use of transfused blood products and maintain visibility in the operating field. Thrombin is widely used to stop diffuse bleeding occurring during surgical procedures, either as a stand-alone hemostat or as a component of other hemostatic products, 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 glues or 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 of plasma derived products. It would also alleviate concerns associated with products of bovine origin, including the potential risk of contamination with the pathogen that causes the human form of "mad cow" disease. 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 can cross-react with human Factor V, creating a condition that is particularly difficult to manage and is potentially fatal in patients who develop severe bleeding conditions. Use of bovine plasma-derived thrombin in patients with antibodies to bovine clotting factors may result in abnormal clotting time, post-operative complications, clotting disorders and the resulting higher treatment costs.

We intend to develop rhThrombin as a replacement product for the currently marketed human and bovine plasma-derived thrombin products. Current sales of plasma-derived thrombin as a stand-alone product are estimated at \$100 million annually in the United States and \$150 million annually worldwide. It is estimated that plasma-derived thrombin is used in more than 500,000 surgical procedures annually in the United States. As with plasma-derived thrombin, rhThrombin would be used in the clinical setting to control bleeding. Primary applications would include a wide range of surgeries, trauma and burn injuries. We believe the market for rhThrombin could be further expanded by providing it to other companies for inclusion in a variety of surgical hemostats, fibrin sealants and vascular sealing devices.

We have developed a patent-protected method we believe will enable us to cost-effectively manufacture rhThrombin in a two-step process. First, prethrombin is produced in mammalian cells, and then using an enzyme activation step, prethrombin is converted to rhThrombin. Currently, we are producing prethrombin internally, and a third-party manufacturer is performing the activation and purifying the resulting rhThrombin. We expect to have product for clinical use available later this year and to begin clinical development of rhThrombin in the second half of 2003.

*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

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collagen-induced model of rheumatoid arthritis, TACI-Ig has been shown to inhibit the incidence of disease. Taken together, these data indicate that TACI-Ig acts by inhibiting the production of mature B cells and decreasing autoantibody levels.

Based on positive data from animal models, 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. Although estimates on prevalence vary widely, there are believed to be over 300,000 patients treated for systemic lupus erythematosus in the United States, a disease which primarily affects women. 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.

In addition, rheumatoid arthritis appears to be a promising potential 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. Serono has manufactured clinical grade materials in quantities adequate to supply initial clinical trials. Toxicology and pharmacology studies are underway in appropriate animal species, and we expect to begin clinical development in the second half of 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. IL-21 shares both structural and genetic sequence similarity with interleukin-2 (IL-2), a cytokine approved as a therapy for malignant melanoma and renal cell carcinoma. We have shown that IL-21 regulates the proliferation and functional activity of several populations of immune cells, including cytotoxic T cells (CTL) and natural killer (NK) cells, both of which are thought to be critical in eliminating malignant or virally infected cells from the body. Preclinical studies have indicated that IL-21 is an effective therapy in a number of animal models of cancer.

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

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

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

We intend to pursue malignant melanoma and renal cell carcinoma, the two approved indications for IL-2, as initial indications for IL-21. There are 100,000 new cases of melanoma per year worldwide with approximately 50% of the cases occurring in North America. Melanoma is the cause of 8,000 deaths per year in North America and has become one of the leading cancers in women between the ages of 25-34. There are approximately 100,000 new cases of renal cell carcinoma per year worldwide with 36,000 new cases in North America. Renal cell carcinoma results in approximately 12,000 deaths per year in North America. There is a demonstrated need for new and improved therapies for both types of cancer. Subject to the outcome of the initial clinical studies, we intend to expand the IL-21 clinical program into additional cancer indications and, potentially, into the treatment of viral diseases.

Novo Nordisk has licensed the rights to IL-21 outside North America and we have retained all rights within North America. In December 2002, we entered into a collaborative preclinical development agreement with Novo Nordisk. Under our agreement, we will share all costs of the IL-21 preclinical development program with Novo Nordisk through the filing of an investigational new drug application in the U.S., which is currently planned for the first half of 2004.

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

#### *Bioinformatics*

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

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

- private databases, including Incyte Genomics' LifeSeq database;
- public EST and DNA sequences;

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- our own internal EST sequences, where we have eliminated transcripts of highly expressed genes to concentrate on sequences of rarely-expressed genes; and
- genomic sequences published daily by the Human Genome Project.

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

### *Exploratory Biology*

We use a diverse set of tools to identify the biological functions of the genes and proteins we discover. Throughout our exploratory biology effort, we use a variety of in-house approaches, including physiological screens of mice in which the gene of interest has either been genetically over-expressed from birth, otherwise known as transgenic mice, or temporarily over-expressed in adult mice using an adenovirus containing the gene. We also conduct screens of mice in which the gene of interest has been eliminated from birth, otherwise known as knockout mice. In addition, we conduct analyses of disease models using a variety of laboratory tests, or assays, to detect changes in behavior, physiology and biochemistry. We also use hundreds of in-house assays to investigate biological activities of our novel proteins. To obtain additional information, our scientists either adapt or create *in vivo* laboratory models that mimic human diseases to determine the cause of disease and response to treatment. For certain ligands, we can also apply laboratory techniques to clone the receptors for the ligand present in a tissue or cell. In addition to providing a marker for tissues that should respond to the protein, the receptors themselves can have therapeutic potential. We also rely on an external network of collaborators to investigate biology and conduct additional tests that we do not perform in-house.

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

### **Collaborative Relationships**

#### *Novo Nordisk Option Agreement*

As part of our separation from Novo Nordisk, we granted Novo Nordisk options to license certain rights to potential therapeutic proteins pursuant to an option agreement. Under this agreement, we retain exclusive rights

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to these proteins in North America, and Novo Nordisk may obtain exclusive rights in the rest of the world. However, Novo Nordisk has the option to obtain exclusive worldwide rights to any licensed protein that acts to generate, expand or prevent the death of insulin-producing beta cells, which are involved in diabetes, a core business focus of Novo Nordisk. The option agreement also provides that:

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

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

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

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

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

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

To date, Novo Nordisk has exercised options to license IL-21, IL-20 and IL-20 receptor pursuant to this agreement.

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In December 2002, we announced that we had signed a collaborative agreement with Novo Nordisk for the preclinical development of IL-21. Under the terms of the agreement, ZymoGenetics and Novo Nordisk will collaborate on all research and development activities leading up to the filing of an IND in the United States. Novo Nordisk will reimburse us for a portion of our costs incurred prior to the agreement, and the two companies will equally share all costs of the program going forward. In total, we could receive up to \$11 million in payment or services under the agreement.

### *Serono S.A.*

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

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

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

The term of the agreement began on August 30, 2001 and will continue for 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.

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### *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, a growth factor that stimulates the growth of a variety of cell types. We have out-licensed this growth factor to BioMimetic Pharmaceuticals, Inc. (BMPI), originally for the treatment of periodontal disease and bone defects of the head and face, and more recently for the treatment of all other bone defects. BMPI has initiated a pivotal study of platelet-derived growth factor in periodontal disease.
- Platelet-derived growth factor receptor antibody, an antibody that blocks the binding of platelet-derived growth factor to its beta receptor, which we have out-licensed to Celltech Group plc. Celltech has designated the product candidate CDP 860, and initiated Phase 2 clinical trials of CDP 860 in 2002 for the treatment of cancer.

### *Other Collaborations*

We recognize external collaborations as an important aspect of our success in analyzing and characterizing protein function. Where possible, we establish collaborations with experts in the field who have a depth of knowledge on a select protein, protein category or disease state that is related to the understanding of our gene and protein discoveries. These collaborations serve to accelerate the rate at which we can assess the biological functions of proteins and confirm medical hypotheses. In addition, throughout our history, we have collaborated actively with the University of Washington, a leading biomedical research institution, to explore the biological function of proteins. The University's significant resources and expertise, together with its geographic proximity to us, have made it a valuable partner on a number of our projects.

### **Manufacturing**

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

For rFactor XIII, which is made in yeast, large-scale manufacturing of preclinical and clinical grade product is being performed by Avecia Limited. We have made arrangements with Pentapharm for the conversion of internally produced prethrombin to rhThrombin. We are in the process of identifying a contract manufacturing organization for the production of rhThrombin at commercial scale. Serono will manufacture TACI-Ig, which is made in mammalian cells, under the terms of our collaborative development and marketing agreement. IL-21 is manufactured in E. coli; we intend to use Avecia Limited as our contract manufacturer for the initial production runs of IL-21.

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.

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### **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 rFactor XIII, rhThrombin 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 240 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

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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 rFactor XIII or rhThrombin, 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

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available, to the third-party patents or to develop or obtain alternative technology. Responding to challenges initiated by third parties may require significant expenditures and divert the attention of our management and key personnel from other business concerns. In addition, enforcing our patents against third parties may require significant expenditures regardless of the outcome of such efforts.

In addition, third parties may independently develop intellectual property similar to our patented intellectual property, which could result in, among other things, interference proceedings in the United States Patent and Trademark Office to determine priority of invention. An interference proceeding is an administrative proceeding to determine which party was first to invent the contested subject matter. Our product candidate rFactor XIII is currently the subject of an interference proceeding with Aventis Behring. Although we recently obtained a license to Aventis Behring's Factor XIII patents for the development of rFactor XIII, other product candidates may in the future be the subject of similar proceedings.

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

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

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

## **Government Regulation**

Regulation by government authorities in the United States, Europe, Japan and other countries is a significant consideration in our ongoing research and product development activities and in the manufacture and marketing of our potential products. The FDA and comparable regulatory bodies in other countries currently regulate therapeutic proteins and related pharmaceutical products as biologics. Biologics are subject to extensive pre- and

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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 GMP 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.

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

The results of pharmaceutical development, 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 GMP 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

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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 sophisticated bioinformatics technologies to discover genes, including Genentech, Inc., Human Genome Sciences, Inc., Curagen, Inc. and Amgen Inc. We also face competition from entities using more traditional methods to discover genes related to particular diseases, including other large biotechnology and pharmaceutical companies. We expect that competition in our field will continue to be intense.

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

We believe the principal competitive factors affecting our markets are rights to develop and commercialize therapeutic protein-based products, including appropriate patent and proprietary rights; safety and effectiveness of therapeutic protein-based products; the timing and scope of regulatory approvals; the cost and availability of these products; the availability of appropriate third-party reimbursement programs; and the availability of alternative therapeutic products or treatments. Although we believe that we are well positioned to compete adequately with respect to these factors in the future, our future success is currently difficult to predict because we are an early stage company; nearly all of our internal product candidates are in 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, 2002, we had 364 full-time employees, 82 of whom hold degrees at the doctoral level. Currently, we have approximately 246 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.

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### **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 our bioinformatics-based therapeutic protein discovery strategy will yield commercially valuable products because we are in the early stages of development. For most of our corporate existence, we relied on exploratory biology to study particular diseases and medical conditions and to find potential treatments. We shifted our emphasis to bioinformatics-based discovery relatively recently. Bioinformatics is the use of high-powered computers, software and analytical tools to interpret DNA sequence data and to assist in identifying those genes and proteins that are likely to play a meaningful role in human health. We use bioinformatics to discover genes and their corresponding proteins in genomic databases, with the goal of developing therapeutic protein-based products based on these discoveries. We have 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 successful development or commercialization of any products.

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

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

*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

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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.

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

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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 rFactor XIII or rhThrombin, 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.

*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. 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

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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 3 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

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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 2 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 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.

*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;

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- 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 GMP 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

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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 GMP regulations in the manufacture of therapeutic proteins. Assuming we successfully complete construction of our planned small-scale GMP manufacturing suites, we will need to hire and train employees to staff them. These initial manufacturing suites will not provide us with the capability to produce drug materials for commercial sale. To develop this capability we would need to acquire larger manufacturing facilities. If any of our future facilities cannot pass a pre-approval plant inspection, the FDA 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 any 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.

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

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

*We anticipate incurring additional losses and may not achieve profitability.*

As of December 31, 2002, we had an accumulated deficit of \$141.5 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

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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 were 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 sophisticated bioinformatics technologies to discover genes, including Genentech, Inc., Human Genome Sciences, Inc., Curagen, Inc. and Amgen, Inc. We also face competition from entities using more traditional methods to discover genes related to particular diseases, including other large biotechnology and pharmaceutical companies. 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;

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- 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 maintain product liability insurance, our coverage 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;

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

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

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

Novo Nordisk, together with Warburg, Pincus Equity Partners, L.P. and entities affiliated with Apax Partners, Inc., beneficially own an aggregate of approximately 70% of our outstanding 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 to 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.

### **Website Access to Our SEC Reports**

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

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### **Item 2. Properties**

We are headquartered in Seattle, Washington, where we lease two buildings containing approximately 160,000 square feet. In 2003, construction is expected to begin on an expansion of one of these buildings that will add approximately 45,000 square feet of additional laboratory and office space. We own land adjacent to one of the existing buildings on which we originally intended to construct a pilot manufacturing plant. We are holding this land for potential expansion in the future. 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, planned and potential expansion space, will be adequate to fulfill our needs for the foreseeable future.

### **Item 3. Legal Proceedings**

None.

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

No matters were submitted to a vote of our shareholders during the fourth quarter of our fiscal year ended December 31, 2002.

## **PART II**

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

Our common stock began trading on the Nasdaq Stock Market under the symbol ZGEN on February 1, 2002. As of March 14, 2003, we had approximately 80 shareholders of record. We have never paid cash dividends and do not anticipate paying them in the foreseeable future.

The following table sets forth, for the fiscal periods indicated, the range of high and low closing sales prices of our common stock as quoted on the Nasdaq Stock Market for the year 2002:

	<u>High</u>	<u>Low</u>
1 <sup>st</sup> Quarter (from February 1, 2002)	\$ 12.05	\$ 8.70
2 <sup>nd</sup> Quarter	12.94	7.05
3 <sup>rd</sup> Quarter	8.78	5.37
4 <sup>th</sup> Quarter	10.64	6.16

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, without par value. Net proceeds of approximately \$110 million have been invested in short-term, investment-grade, interest bearing instruments.

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### Item 6. Selected Financial Data

The following selected financial data should be read in conjunction with the financial statements and notes to the financial statements and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” contained elsewhere in this Form 10–K. The selected Statements of Operations and Balance Sheet data for, and as of the years ended December 31, 2002, 2001 and 2000 have been derived from our audited financial statements appearing elsewhere in this Form 10–K. The selected Statements of Operations and Balance Sheet data for, and as of the years ended December 31, 1999 and 1998 have been derived from our audited financial statements that are not included in this Form 10–K. Historical results are not necessarily indicative of future results.

	Years Ended December 31,				
	2002	2001	2000	1999	1998
	(in thousands, except per share data)				
<b>Statement of Operations Data:</b>					
Revenues	\$ 52,775	\$ 17,828	\$ 32,464	\$ 69,675	\$ 66,744
Operating expenses:					
Research and development(1)	66,469	48,052	49,337	48,415	49,886
General and administrative(2)	16,925	10,475	12,069	9,550	9,339
Noncash stock-based compensation expense	7,188	3,507	—	—	—
Total operating expenses	90,582	62,034	61,406	57,965	59,225
Income (loss) from operations	(37,807)	(44,206)	(28,942)	11,710	7,519
Other income (expense):					
Interest income	6,772	7,152	5,417	274	29
Interest expense	(8)	(13)	(848)	(56)	(485)
Other, net	627	98	(111)	(52)	(72)
Income (loss) before provision for income taxes	(30,416)	(36,969)	(24,484)	11,876	6,991
Benefit (provision) for income taxes	—	90	(5,893)	(2,454)	(1,273)
Net income (loss)	(30,416)	(36,879)	(30,377)	9,422	5,718
Preferred stock dividend and accretion	(1,718)	(20,610)	(2,903)	—	—
Net income (loss) attributable to common shareholders	\$ (32,134)	\$ (57,489)	\$ (33,280)	\$ 9,422	\$ 5,718
Basic net income (loss) per share	\$ (0.75)	\$ (4.85)	\$ (3.38)	\$ 1.11	\$ 0.68
Diluted net income (loss) per share	\$ (0.75)	\$ (4.85)	\$ (3.38)	\$ 0.80	\$ 0.48
Weighted-average shares used in computing basic net income (loss) per share	42,578	11,846	9,846	8,455	8,455
Weighted-average shares used in computing diluted net income (loss) per share	42,578	11,846	9,846	11,793	11,793
<b>Balance Sheet Data:</b>					
Cash, cash equivalents and short-term investments	\$ 285,438	\$ 147,077	\$ 172,976	\$ 19,648	\$ 5,738
Working capital	271,276	138,493	166,245	19,504	12,566
Total assets	312,233	205,435	228,637	91,914	83,473
Mandatorily redeemable convertible preferred stock	—	260,540	239,930	—	—
Total shareholders’ equity (deficit)	269,268	(79,402)	(27,269)	77,687	68,265

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

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

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

#### Overview

We are a biopharmaceutical company focused on 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

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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 \$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 will 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 will earn royalties on sales of any resulting products. To date, Novo Nordisk has exercised options to license three proteins pursuant to this agreement.

In February 2002, we completed our initial public offering. Upon the completion of the initial public offering, each share of Series A and B preferred stock held by Novo Nordisk and other investors converted into 3.6 shares of non-voting and voting common stock, respectively. In June 2002, all shares of non-voting common stock were converted into the same number of shares of voting common stock. As of December 31, 2002, Novo Nordisk's ownership percentage was 47.5%.

After termination of the funding agreement with Novo Nordisk, we incurred net losses of \$30.4 million, \$36.9 million and \$30.4 million for the years ended December 31, 2000, 2001 and 2002, respectively. As of December 31, 2002, we had an accumulated deficit of \$141.5 million. The accumulated deficit resulted from the net losses and certain capital transactions with Novo Nordisk. We expect our net losses to increase in the future as we continue to expand our product development activities, including clinical trials, and 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, 2002, revenues from royalties were \$8.0 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 with Novo Nordisk and Serono S.A. As of December 31, 2002 we had deferred revenues aggregating \$16.8 million, of which \$10.3 million are expected to be recognized in 2003. 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

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substantial portion of our revenues for the foreseeable future will depend on the establishment of new agreements and the achievement of development-related milestones, our results of operations could 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 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 development-related milestones, which may not be achieved.

Our 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, costs of consumables, facility costs and contracted services. 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 expand our product development activities. We expect that a large percentage of our research and development expenses in 2003 will be incurred in support of our internal product development programs for rFactor XIII, rhThrombin, TACI-Ig and IL-21. It is not unusual for the clinical development of these types of products to take five years or more to complete, and to cost well over \$100 million per product candidate. 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 were granted in 2000 with exercise prices equal to the estimated fair value of the common stock at the date of grant. In 2001 and early 2002, prior to the completion of our initial public offering, stock options were granted to employees and directors at exercise prices below the estimated fair value of the common stock on the date of grant. As a result, we recorded total deferred stock-based compensation of \$29.0 million through December 31, 2002. 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. We amortized noncash stock-based compensation expense of \$3.5 million in 2001, \$7.2 million in 2002, and expect to amortize \$7.2 million in 2003, \$7.2 million in 2004 and \$3.9 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. Although we have no intention of doing so, the amount could increase if future options are granted with exercise prices below the estimated fair value of the common stock on the date of the grant.

Other income (expense) 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. As a result of the sale leaseback transaction completed in October 2002, we recorded a deferred gain of \$14.4 million, which will be recognized as other income on a straight-line basis over the 15-year initial lease term.

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, 2002, we had net operating loss carryforwards of \$52.5 million, research and development tax credit carryforwards of \$15.0 million, a rehabilitation tax credit carryforward of \$1.5

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million, and alternative minimum tax credit carryforwards of \$1.2 million. These credits will expire during the period from 2008 through 2022. 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 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.

As a result of our separation from Novo Nordisk in November 2000, and the subsequent evolving nature of our business, we believe that certain 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, 2002 and 2001*

**Revenues.** Revenues increased by \$35.0 million, from \$17.8 million in 2001 to \$52.8 million in 2002. This increase was due primarily to a one-time license fee payment of \$30.0 million received in December 2002, which resulted from the granting of a license to our Ig-fusion protein patents. As a result of the agreement, the patent infringement lawsuit filed by us in March 2002 against Immunex Corporation (now owned by Amgen) was terminated by all parties. The revenue increase was also due to increased revenues from licensing arrangements and milestone payments based on the achievement of development-related milestones. These increases were partially offset by a decrease in product royalties in 2002.

**Research and development expenses.** Research and development expenses, exclusive of noncash stock-based compensation expense of \$2.1 million in 2001 and \$4.5 million in 2002, increased by \$18.4 million, from \$48.1 million in 2001 to \$66.5 million in 2002. A significant portion of the increase was due to increased expenses for contract manufacturing to support the development of two of our lead internal product candidates, rFactor XIII and rhThrombin. Additionally, an increase in personnel, primarily in areas supporting product development, resulted in an increase in salaries and related costs. We anticipate that research and development expenses, particularly with respect to clinical trials, will increase in the foreseeable future as we continue to advance our internal development programs. Annual rent expense of \$6.6 million resulting from the sale leaseback transaction, of which the majority will be classified as research and development expense, will also contribute to future increases.

**General and administrative expenses.** General and administrative expenses, exclusive of noncash stock-based compensation expense of \$1.4 million in 2001 and \$2.6 million in 2002, increased by \$6.4 million from \$10.5 million in 2001 to \$16.9 million in 2002. The increase reflects added administrative personnel, resulting in an increase in salaries and related costs; an increase in legal costs associated with the recently settled lawsuit with Amgen; and increased expenses related to our operation as a public company. Additionally, our decision to postpone construction of a dedicated pilot manufacturing facility resulted in the write-off of design and engineering costs totaling \$1.6 million in 2002.

**Noncash stock-based compensation expense.** Noncash stock-based compensation expense increased by \$3.7 million from \$3.5 million in 2001 to \$7.2 million in 2002. The increase resulted from the granting of options during the second half of 2001 and the beginning of 2002 with estimated fair values exceeding the exercise prices of the options.

**Other income (expense).** Other income (expense) increased by \$0.2 million from \$7.2 million in 2001 to \$7.4 million in 2002. The increase resulted from recognition of \$0.2 million of gain on the sale leaseback transaction. Although our average cash invested in 2002 was greater than in the comparable period in 2001, the average interest rate earned on our investments in 2002 was lower than the average interest rate in 2001.

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*Benefit (provision) for income taxes.* 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 either 2001 or 2002 due to the uncertainty of realization.

### *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 decrease was attributable 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 collectibility 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 devoted to research and development.

*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.

*Noncash stock-based compensation expense.* Noncash stock-based compensation expense was \$3.5 million in 2001; none was recorded 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 the 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. We incurred this interest on various loans from Novo Nordisk, which were fully repaid by the end of 2000.

*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 due to the uncertainty of realization.

## **Liquidity and Capital Resources**

Over the three years ended December 31, 2002, 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;

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- net proceeds of \$142.5 million from our November 2000 private equity financing;
- net proceeds of \$110.7 million from our initial public offering in February 2002;
- net proceeds of \$50.5 million from the sale and leaseback transaction completed in October 2002;
- revenues earned from royalties, option fees, license fees and milestone payments; and
- investment income.

As of December 31, 2002, we had cash, cash equivalents and short-term investments of \$285.4 million, which increased from \$147.1 million as of December 31, 2001. 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 \$38.0 million in 2000, \$18.9 million in 2001 and \$11.8 million in 2002. 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. Cash used in operating activities for each of the years 2001 and 2002 was less than our net loss due to non-cash items, such as depreciation and amortization and stock-based compensation expense, and revenues received but deferred to future periods. 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 and through clinical trials.

Net cash used in investing activities was \$5.6 million in 2000, \$117.7 million in 2001 and \$80.3 million in 2002. 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. Net cash used in investing activities in 2002 included \$120.9 million for purchases of short-term investments, net of proceeds from sales and maturities, and \$9.9 million for capital expenditures, partially offset by the receipt of \$50.5 million of net proceeds from the completion of the sale leaseback transaction, which is described below. In October 2002, pursuant to an earlier commitment, we purchased the final parcel of land originally intended for the construction of a pilot manufacturing facility. Earlier in 2002 we decided to defer the construction of this facility to an undetermined date in the future. The acquired land is being held for future expansion.

Cash provided by financing activities was \$196.9 million in 2000, \$28,000 in 2001 and \$111.3 million in 2002. 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. Financing activities in 2002 included the net proceeds of \$110.7 million from the completion of our initial public offering and \$0.6 million of net proceeds from the exercise of stock options.

On October 4, 2002, we completed a sale and leaseback transaction involving our headquarter buildings located in Seattle, Washington. The three buildings were sold for a total purchase price of \$52.3 million. Simultaneously, we agreed to lease the buildings from the purchaser for a period of 15 years, subject to four five-year renewal options. Net proceeds from this transaction amounted to \$50.5 million and a gain on the sale of \$14.4 million will be deferred and will be recognized ratably over the initial lease term. The initial rental payment of \$5.1 million per year will increase by 3.5% each year during the initial term. We will recognize rent expense of \$6.6 million per year, which is the average annual rent over the initial lease term. We have retained an option to expand one of the leased buildings. Planning is underway to pursue this option in 2003. If this expansion project is pursued, we expect the project to cost approximately \$26 million, including all related equipment costs. The purchaser has agreed to finance a substantial portion of these costs. To date, we have made no material financial commitments related to the facility expansion.

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We expect to incur substantial costs as we continue to expand our research and development programs, particularly as we move product candidates into clinical trials. We expect these expenditures to increase 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, including the net proceeds of \$50.5 million from the sale leaseback transaction completed in October 2002, will provide sufficient funding to support our operations for at least the next three years. If we are successful in completing additional collaborative development transactions, which would generate both revenues and cost reductions, we believe that our cash resources will fund our programs for at least four years. If, at any time, our prospects for financing these programs decline, we may decide to reduce our ongoing investment in our development programs. We could reduce our investment by discontinuing our funding under existing co-development arrangements, establishing new co-development arrangements for other product candidates to provide additional funding sources or out-licensing product candidates that we might otherwise develop internally. Additionally, we could consider delaying or discontinuing development of product candidates to reduce the level of our related expenditures.

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

- the costs involved in filing, prosecuting, enforcing and defending patent claims;
- the results 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 would be reduced, and these securities could have rights superior to those of our common stock. If we are unable to raise additional funds when we need them, we could be required to delay, scale back or eliminate expenditures for some of our development programs or expansion plans, or grant rights to third parties to develop and market product candidates that we would prefer to develop and market internally, with license terms that are not favorable to us.

## Contractual Obligations

We are contractually obligated to make payments as follows:

Contractual Obligations	Payments Due by Period				
	Total	1 Year	2-3 Years	4-5 Years	After 5 Years
	(Amounts in thousands)				
Operating leases	\$ 103,257	\$ 5,860	\$ 12,024	\$ 12,856	\$ 72,517

Operating lease terms range from one to fifteen years with certain renewal provisions at our option.

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### **Critical Accounting Policies**

Our critical accounting policies are as follows:

#### *Revenue Recognition*

To date, our revenue has been generated primarily from three different sources: option fees, product royalties and license and milestone 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 to pay us the \$7.5 million annual payments. 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 six months to ten years. For certain license agreements, which require no performance on our part, license fee revenue has been recognized immediately upon execution of the agreement. 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. We exercised our judgment in determining the fair value of our stock with share prices varying from \$9.09 to \$15.11 for options granted during 2001 through January 2002. Deferred compensation is amortized over the vesting period of the individual options, using the straight-line method.

### **Recent Accounting Pronouncements**

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 and will adopt the standard the first quarter of fiscal 2003.

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In 2002, the FASB issued Statement of Financial Accounting Standards No. 145, Rescission of FASB Statements No. 4, 44 and 64, Amendment to FASB Statement No. 13, and Technical Corrections (SFAS 145). SFAS 145 eliminates the requirement in Statement of Financial Accounting Standards No. 4 (SFAS 4) that gains and losses from the extinguishments of debt be aggregated and classified as extraordinary items, net of the related income tax. The rescission of SFAS 4 is effective for fiscal years beginning after May 15, 2002. We do not expect that the rescission of SFAS 4 will have a material impact on our results of operations, cash flows or financial condition.

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

In November 2002, the Emerging Issues Task Force (EITF) finalized its tentative consensus on EITF Issue No. 00–21 (EITF 00–21), *Revenue Arrangements With Multiple Deliverables*, which provides guidance on the timing and method of revenue recognition for sales agreements that include delivery of more than one product or service. EITF 00–21 is effective prospectively for arrangements entered into in fiscal periods beginning after June 15, 2003. We are currently assessing the impact of EITF 00–21 on our financial statements and will adopt the new guidance prospectively beginning in the first quarter of 2004.

In December 2002, the FASB issued Interpretation No. 45, *Guarantor's Accounting and Disclosure Requirements for Guarantees, Including Indirect Guarantees of Indebtedness of Others* (FIN 45). FIN 45 expands on the accounting guidance of SFAS 5, 57 and 107 and incorporates without change the provisions of FASB Interpretation No. 34. FIN 45 provides guidance for the initial recognition and measurement, applicable prospectively to all guarantees issued or modified after December 31, 2002, and disclosure requirements effective for financial statements of interim and annual reporting periods ending after December 15, 2002. Our December 2002 financial statements include the disclosures required by FIN 45. Adoption of this interpretation is not expected to have a material impact on our results of operations, cash flows or financial condition.

In December 2002, the FASB issued SFAS No. 148, *Accounting for Stock-Based Compensation—Transition and Disclosure—An Amendment of FASB Statement No. 123* (SFAS 148). This Statement amends SFAS No. 123, *Accounting for Stock-Based Compensation*, to provide alternative methods of transition for a voluntary change to the fair value based method of accounting for stock-based employee compensation. In addition, this statement amends the disclosure requirements of SFAS 123 to require prominent disclosures in both annual and interim financial statements about the method of accounting for stock-based employee compensation and the effect of the method used on reported results. This statement requires that companies having a year-end after December 15, 2002 follow the prescribed format and provide the additional disclosures in their annual reports. Our financial statements include the disclosures required by SFAS 148.

In January 2003, the FASB issued Interpretation No. 46, *Consolidation of Variable Interest Entities* (FIN 46). FIN 46 clarifies the application of Accounting Research Bulletin No. 51, *Consolidated Financial Statements*, to certain entities in which equity investors do not have (i) the characteristics of a controlling financial interest or (ii) sufficient at-risk equity. FIN 46 applies to a broad range of unconsolidated investee entities (e.g. joint ventures, partnerships and cost basis investments) and, effective for financial statements issued after January 31, 2003, adds certain disclosure requirements. We are currently assessing the impact of FIN 46 on our financial statements.

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**Table of Contents****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**

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**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, 2002 and 2001, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2002 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.

/s/ PRICEWATERHOUSECOOPERS LLP  
Seattle, Washington  
January 31, 2003

**Table of Contents****ZYMOGENETICS, INC.****BALANCE SHEETS**

	December 31,	
	2002	2001
<b>Assets</b>		
Current assets		
Cash and cash equivalents	\$ 55,578,707	\$ 36,393,551
Short-term investments	229,858,985	110,683,392
Receivables		
Related party	388,655	449,314
Interest and other receivables	3,328,028	3,606,421
Prepaid expenses and other assets	2,252,879	2,291,270
	<u>291,407,254</u>	<u>153,423,948</u>
Total current assets	291,407,254	153,423,948
Property and equipment, net	17,252,932	49,128,094
Other assets	3,572,806	2,882,522
	<u>312,232,992</u>	<u>205,434,564</u>
Total assets	\$ 312,232,992	\$ 205,434,564
<b>Liabilities, Mandatorily Redeemable Convertible Preferred Stock and Shareholders' Equity (Deficit)</b>		
Current liabilities		
Accounts payable	\$ 3,172,193	\$ 4,109,382
Accrued liabilities	5,689,066	3,150,220
Deferred gain on sale of assets	959,860	—
Deferred revenue	10,310,064	7,671,521
	<u>20,131,183</u>	<u>14,931,123</u>
Total current liabilities	20,131,183	14,931,123
Deferred gain on sale of assets	13,205,812	—
Deferred revenue	6,524,039	6,482,416
Other noncurrent liabilities	3,103,942	2,882,522
<b>Commitments</b>		
Mandatorily redeemable convertible preferred stock, no par value, 30,000,000 shares authorized		
Series A, 2,528,000 shares authorized, issued and outstanding at December 31, 2001	—	103,148,879
Series B, 4,011,768 shares authorized, issued and outstanding at December 31, 2001	—	157,391,508
Shareholders' equity (deficit)		
Common stock, no par value, 150,000,000 shares authorized, 45,815,031 and 12,063,600 issued and outstanding at December 31, 2002 and 2001, respectively	427,009,984	55,855,870
Non-voting common stock, no par value, 30,000,000 shares authorized	—	—
Notes receivable from shareholders	(725,000)	(725,000)
Deferred stock compensation	(18,290,550)	(25,234,712)
Accumulated deficit	(141,535,635)	(111,119,557)
Accumulated other comprehensive income	2,809,217	1,821,515
	<u>269,268,016</u>	<u>(79,401,884)</u>
Total shareholders' equity (deficit)	269,268,016	(79,401,884)
Total liabilities, mandatorily redeemable convertible preferred stock and shareholders' equity (deficit)	\$ 312,232,992	\$ 205,434,564

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

**Table of Contents****ZYMOGENETICS, INC.****STATEMENTS OF OPERATIONS**

	Year ended December 31,		
	2002	2001	2000
Revenues			
Royalties			
Related parties	\$ 4,985,538	\$ 5,151,347	\$ 29,310,940
Other	3,009,781	3,962,881	2,111,640
Option fee from related party	7,500,000	7,500,000	1,041,667
Ig-fusion protein license fee	30,000,000	—	—
License fees, milestones and other	7,280,065	1,213,870	—
Total revenues	52,775,384	17,828,098	32,464,247
Operating expenses			
Research and development (excludes noncash stock-based compensation expense of \$4,542,568 in 2002 and \$2,109,246 in 2001)	66,469,252	48,051,456	49,336,648
General and administrative (excludes noncash stock-based compensation expense of \$2,645,056 in 2002 and \$1,398,106 in 2001)	16,925,391	10,474,904	12,069,226
Noncash stock-based compensation expense	7,187,624	3,507,352	—
Total operating expenses	90,582,267	62,033,712	61,405,874
Loss from operations	(37,806,883)	(44,205,614)	(28,941,627)
Other income (expense)			
Interest income	6,772,352	7,152,351	5,417,089
Interest expense	(8,075)	(13,489)	(848,040)
Other, net	626,528	97,838	(111,080)
Loss before provision for income taxes	(30,416,078)	(36,968,914)	(24,483,658)
Benefit (provision) for income taxes	—	89,606	(5,893,402)
Net loss	(30,416,078)	(36,879,308)	(30,377,060)
Preferred stock dividend and accretion	(1,717,865)	(20,610,216)	(2,903,535)
Net loss attributable to common shareholders	\$ (32,133,943)	\$ (57,489,524)	\$ (33,280,595)
Net loss per share—basic and diluted	\$ (0.75)	\$ (4.85)	\$ (3.38)
Weighted-average number of shares used in computing basic and diluted net loss per share	42,578,029	11,846,093	9,845,870

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

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**ZYMOGENETICS, INC.**

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

	Shareholders' equity (deficit)											
	Mandatorily redeemable convertible preferred stock		Convertible preferred stock		Common stock		Additional paid-in capital	Notes receivable from shareholders	Deferred stock compensation	Accumulated earnings (deficit)	Accumulated other comprehensive income	Total
	Shares	Amount	Shares	Amount	Shares	Amount						
Balance at January 1, 2000	—	\$ —	926,976	\$ 9,270	8,455,406	\$ 84,554	\$ 49,780,733	\$ —	\$ —	\$ 27,812,875	\$ —	\$ 77,687,432
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	(30,377,060)	—	(30,377,060)
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 reliability of tax benefits related to purchase of intellectual property from related party	—	—	—	—	—	—	—	—	—	(11,245,499)	—	(11,245,499)
Balance at December 31, 2000	6,539,768	239,930,171	—	—	11,792,520	46,971,022	—	—	—	(74,240,250)	—	(27,269,228)
Comprehensive loss:												
Net loss	—	—	—	—	—	—	—	—	—	(36,879,307)	—	(36,879,307)
Unrealized gain on short-term investments	—	—	—	—	—	—	—	—	—	—	1,821,515	1,821,515
Total comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	(35,057,792)
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 stock options:												
Grants	—	—	—	—	—	28,742,064	—	—	(28,742,064)	—	—	—
Amortization	—	—	—	—	—	—	—	—	3,507,352	—	—	3,507,352
Accretion on mandatorily redeemable	—	1,048,462	—	—	—	(1,048,462)	—	—	—	—	—	(1,048,462)

convertible preferred stock												
Dividends accrued on mandatorily redeemable convertible preferred stock	—	19,561,754	—	—	—	(19,561,754)	—	—	—	—	—	(19,561,754)
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)
Comprehensive loss:												
Net loss	—	—	—	—	—	—	—	—	—	(30,416,078)	—	(30,416,078)
Unrealized gain on short-term investments, net of reclassification adjustment	—	—	—	—	—	—	—	—	—	—	987,702	987,702
Total comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	(29,428,376)
Common stock issued in connection with stock option exercises	—	—	—	—	208,272	596,059	—	—	—	—	—	596,059
Deferred stock compensation related to stock options:												
Grants	—	—	—	—	—	483,390	—	—	(483,390)	—	—	—
Forfeitures	—	—	—	—	—	(239,928)	—	—	239,928	—	—	—
Amortization	—	—	—	—	—	—	—	—	7,187,624	—	—	7,187,624
Accretion and dividends on mandatorily redeemable convertible preferred stock	—	1,717,865	—	—	—	(1,717,865)	—	—	—	—	—	(1,717,865)
Conversion of Series A and B mandatorily redeemable convertible preferred stock	(6,539,768)	(262,258,252)	—	—	23,543,159	262,258,252	—	—	—	—	—	262,258,252
Net proceeds from issuance of common stock (net of offering costs of \$10,225,794)	—	—	—	—	10,000,000	109,774,206	—	—	—	—	—	109,774,206
Balance at December 31, 2002	—	\$ —	—	\$ —	45,815,031	\$427,009,984	\$ —	\$ (725,000)	\$ (18,290,550)	\$ (141,535,635)	\$ 2,809,217	\$269,268,016

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

**Table of Contents**
**ZYMOGENETICS, INC.**
**STATEMENTS OF CASH FLOWS**

	Year ended December 31,		
	2002	2001	2000
<b>Cash flows from operating activities</b>			
Net loss	\$ (30,416,078)	\$ (36,879,307)	\$ (30,377,060)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation and amortization	5,508,144	5,404,635	5,689,451
Net (gain) loss on disposition of property and equipment	(44,775)	77	111,080
Provision for deferred income taxes	—	—	13,731,405
Income taxes on future royalty payments from related party	—	—	(31,524,691)
Noncash stock-based compensation	7,187,624	3,507,352	—
Net realized gain on sale of short-term investments	(581,613)	(94,748)	—
Amortization of premium on short-term investments	2,448,197	786,834	—
Changes in			
Receivables	339,052	380,588	2,850,238
Prepaid expenses and other assets	(705,333)	(365,751)	(220,556)
Accounts payable	(937,188)	2,148,826	521,860
Related party payables	—	(278,975)	(4,281,414)
Accrued liabilities	2,538,846	(995,546)	1,731,110
Stock appreciation plan liability, net of cash distributions	—	—	(3,712,369)
Deferred revenue	2,680,166	7,695,604	6,458,333
Other noncurrent liabilities	221,419	(249,846)	1,032,166
Net cash used in operating activities	(11,761,539)	(18,940,257)	(37,990,447)
<b>Cash flows from investing activities</b>			
Purchase of property and equipment	(9,942,665)	(8,181,492)	(5,617,038)
Purchase of short-term investments	(305,516,569)	(207,700,172)	—
Proceeds from sale of property and equipment	50,520,130	64,780	60,789
Proceeds from sale and maturity of short-term investments	184,613,093	98,146,209	—
Net cash used in investing activities	(80,326,011)	(117,670,675)	(5,556,249)
<b>Cash flows from financing activities</b>			
Net proceeds from sale of Series B mandatorily redeemable convertible preferred stock (net of offering costs of \$7,495,290)	—	—	142,504,716
Net proceeds from issuance of common stock	110,676,647	—	—
Proceeds from exercise of stock options	596,059	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	111,272,706	28,000	196,875,262
Net increase (decrease) in cash and cash equivalents	19,185,156	(136,582,932)	153,328,566
Cash and cash equivalents at beginning of period	36,393,551	172,976,483	19,647,917
Cash and cash equivalents at end of period	\$ 55,578,707	\$ 36,393,551	\$ 172,976,483
Cash paid to related party during the period for interest	\$ —	\$ —	\$ 844,629
Cash paid during the period for interest	\$ 8,075	\$ 13,489	\$ 3,411
Cash paid during the period for income taxes	\$ —	\$ —	\$ 29,196,276
<b>Noncash financing activities</b>			
Accretion on Series B mandatorily redeemable convertible preferred stock	\$ 87,719	\$ 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	\$ 1,630,146	\$ 19,561,754	\$ 2,755,617
Recognition of prepaid offering costs	\$ 902,441	\$ —	\$ —
Deferred gain on sale leaseback transaction	\$ 14,165,672	\$ —	\$ —

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

**NOTES TO FINANCIAL STATEMENTS****1. Organization and summary of significant accounting policies****Nature of operations**

ZymoGenetics, Inc. (the Company) was incorporated in the state of Washington in June 1981 and operated independently until it was acquired in 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 independent from Novo Nordisk upon completion of a private placement of Series B mandatorily redeemable convertible preferred stock with an investor consortium. On February 1, 2002, the Company completed an initial public offering of common stock, at which time all Series A and B mandatorily redeemable convertible preferred stock held by Novo Nordisk was converted to common stock. As of December 31, 2002, Novo Nordisk's ownership percentage was 47.50%.

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 with an original maturity of three months or less at the date of purchase 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). Interest on securities classified as available-for-sale is included in interest income. 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.

**Fair value of financial instruments**

The carrying values of cash and cash equivalents, accounts receivable, accounts payable and accrued liabilities approximate their respective fair values due to their relative short maturities.

**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 40 years for buildings. Expenditures for repairs and maintenance are charged to expense as incurred.

**NOTES TO FINANCIAL STATEMENTS—(Continued)**

Leasehold improvements are amortized evenly over either their estimated useful lives or the term of the lease, whichever is shorter. At December 31, 2002, the Company amortized its leasehold improvements over ten and fifteen year periods.

**Impairment of long-lived assets**

The Company periodically determines whether any property and equipment have been impaired. 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, 2002.

**Patents and licensing agreements**

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

**Revenue recognition**

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 are recognized when the milestone is achieved and amounts are due and payable.

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

**Research and development costs**

Research and development costs are expensed as incurred.

**Income taxes**

The Company records a provision for income taxes in accordance with Statement of Financial Accounting Standards No. 109, *Accounting for Income Taxes* (SFAS 109), which 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

**NOTES TO FINANCIAL STATEMENTS—(Continued)**

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 with respect to 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 underlying individual options, using the straight-line method.

The following table illustrates the effect on net income and earnings per share as if the fair value based method had been applied to all outstanding and unvested awards for each of the years ended December 31:

	<u>2002</u>	<u>2001</u>	<u>2000</u>
Net loss attributable to common shareholders, as reported	\$ (32,133,943)	\$ (57,489,524)	\$ (33,280,595)
Add: stock-based compensation included in reported net loss	7,187,624	3,507,352	—
Deduct: total stock-based compensation expense determined under the fair value method	(2,144,953)	(965,558)	(359,473)
Net loss attributable to common shareholders, pro forma	<u>\$ (27,091,272)</u>	<u>\$ (54,947,729)</u>	<u>\$ (33,640,068)</u>
Basic and diluted net loss per share, as reported	<u>\$ (0.75)</u>	<u>\$ (4.85)</u>	<u>\$ (3.38)</u>
Basic and diluted net loss per share, pro forma	<u>\$ (0.64)</u>	<u>\$ (4.64)</u>	<u>\$ (3.42)</u>

**Other comprehensive loss**

Comprehensive loss is comprised of net loss and unrealized gains and losses on short-term investments.

**Use of estimates**

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

**Loss per share**

Basic and diluted net loss per share are computed based on net loss available to common shareholders and the weighted-average number of common shares outstanding during the applicable period. Common stock equivalents are excluded from the computation of diluted net loss per share because they are antidilutive. Shares subject to repurchase have been excluded from the denominator for both the basic and diluted computations.

**ZYMOGENETICS, INC.**

**NOTES TO FINANCIAL STATEMENTS—(Continued)**

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

	2002	2001	2000
Net loss attributable to common shareholders	\$ (32,133,943)	\$ (57,489,524)	\$ (33,280,595)
Weighted-average shares used in computing basic and diluted net loss per share	42,578,029	11,846,093	9,845,870
Net loss per share—basic and diluted	\$ (0.75)	\$ (4.85)	\$ (3.38)
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	8,267,397	7,307,092	4,311,000
Shares subject to repurchase	6,750	87,750	—
	8,274,147	30,938,001	27,854,159

**Recent accounting pronouncements**

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 and will adopt the standard the first quarter of fiscal 2003.

In 2002, the FASB issued Statement of Financial Accounting Standards No. 145, *Rescission of FASB Statements No. 4, 44 and 64, Amendment to FASB Statement No. 13, and Technical Corrections* (SFAS 145). SFAS 145 eliminates the requirement in Statement of Financial Accounting Standards No. 4, (SFAS 4) that gains and losses from the extinguishments of debt be aggregated and classified as extraordinary items, net of the related income tax. The rescission of SFAS 4 is effective for fiscal years beginning after May 15, 2002. The Company does not expect that the rescission of SFAS 4 will have a material impact on its results of operations, cash flows or financial condition.

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

In November 2002, the Emerging Issues Task Force (EITF) finalized its tentative consensus on EITF Issue No. 00-21, *Revenue Arrangements With Multiple Deliverables* (EITF 00-21), which provides guidance on the timing and method of revenue recognition for sales agreements that include delivery of more than one product or service. EITF 00-21 is effective prospectively for arrangements entered into in fiscal periods beginning after June 15, 2003. The Company is currently assessing the impact of EITF 00-21 on its financial statements and will adopt the new guidance prospectively beginning in the first quarter of 2004.

**ZYMOGENETICS, INC.**

**NOTES TO FINANCIAL STATEMENTS—(Continued)**

In December 2002, the FASB issued Interpretation No. 45, *Guarantor's Accounting and Disclosure Requirements for Guarantees, Including Indirect Guarantees of Indebtedness of Others* (FIN 45). FIN 45 expands on the accounting guidance of FASB No. 5, 57 and 107 and incorporates without change the provisions of FASB Interpretation No. 34. FIN 45 provides guidance for the initial recognition and measurement, applicable prospectively to all guarantees issued or modified after December 31, 2002, and disclosure requirements effective for financial statements of interim and annual reporting periods ending after December 15, 2002. The Company's December 2002 financial statements include the disclosures required by FIN 45. Adoption of this interpretation is not expected to have a material impact on the Company's results of operations, cash flows or financial condition.

In December 2002, the FASB issued SFAS No. 148, *Accounting for Stock-Based Compensation—Transition and Disclosure—An Amendment of FASB Statement No. 123* (SFAS 148). This Statement amends SFAS 123, *Accounting for Stock-Based Compensation*, to provide alternative methods of transition for a voluntary change to the fair value based method of accounting for stock-based employee compensation. In addition, this statement amends the disclosure requirements of SFAS 123 to require prominent disclosures in both annual and interim financial statements about the method of accounting for stock-based employee compensation and the effect of the method used on reported results. This statement requires that companies having a year-end after December 15, 2002 follow the prescribed format and provide the additional disclosures in their annual reports. The Company's financial statements include the disclosures required by SFAS 148.

In January 2003, the FASB issued Interpretation No. 46, *Consolidation of Variable Interest Entities* (FIN 46). FIN 46 clarifies the application of Accounting Research Bulletin No. 51, *Consolidated Financial Statements*, to certain entities in which equity investors do not have (i) the characteristics of a controlling financial interest or (ii) sufficient at-risk equity. FIN 46 applies to a broad range of unconsolidated investee entities (e.g. joint ventures, partnerships and cost basis investments) and, effective for financial statements issued after January 31, 2003, adds certain disclosure requirements. The Company is currently assessing the effect of the adoption of FIN 46 on its financial position and results of operations.

**2. Short-term investments**

Short-term investments consisted of the following at:

	December 31, 2002			
	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Estimated Fair Value
Type of security:				
Commercial paper and money market	\$ 4,660,089	\$ —	\$ —	\$ 4,660,089
Corporate debt securities	55,625,685	908,468	(470)	56,533,683
Asset-backed securities	48,332,210	370,805	(4,144)	48,698,871
U.S. government and agency securities	113,545,537	1,450,080	—	114,995,617
Foreign government securities	4,886,246	84,479	—	4,970,725
	<b>\$ 227,049,767</b>	<b>\$ 2,813,832</b>	<b>\$ (4,614)</b>	<b>\$ 229,858,985</b>

## ZYMOGENETICS, INC.

## NOTES TO FINANCIAL STATEMENTS—(Continued)

	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
	<u>\$ 108,861,877</u>	<u>\$ 1,867,388</u>	<u>\$ (45,873)</u>	<u>\$ 110,683,392</u>

The following table summarizes contractual maturity information for the securities at:

	Estimated Fair Value	Amortized Cost
December 31, 2002:		
Maturity date:		
Less than one year	\$ 100,821,898	\$ 99,923,568
Due in 1–3 years	129,037,087	127,126,199
	<u>\$ 229,858,985</u>	<u>\$ 227,049,767</u>
December 31, 2001:		
Maturity date:		
Less than one year	\$ 22,040,421	\$ 21,808,678
Due in 1–3 years	88,642,971	87,053,199
	<u>\$ 110,683,392</u>	<u>\$ 108,861,877</u>

Realized gains were \$863,000 and \$132,000 for the years ended December 31, 2002 and 2001, respectively. Realized losses were \$281,000 and \$37,000 for the years ended December 31, 2002 and 2001, respectively. Reclassification adjustments reflected in other comprehensive income for net realized gains and losses were \$595,000 for the year ended December 31, 2002.

### 3. Property and equipment

Property and equipment consisted of the following at December 31:

	2002	2001
Land and buildings	\$ 4,443,983	\$ 49,344,651
Leasehold improvements	6,248,220	5,737,412
Furniture and equipment	39,590,449	36,830,103
Construction in progress	1,463,016	710,248
	<u>51,745,668</u>	<u>92,622,414</u>
Less: Accumulated depreciation and amortization	(34,492,736)	(43,494,320)
	<u>\$ 17,252,932</u>	<u>\$ 49,128,094</u>

**NOTES TO FINANCIAL STATEMENTS—(Continued)**

**4. Accrued liabilities**

Accrued liabilities consisted of the following at December 31:

	2002	2001
Vacation pay	\$ 2,021,754	\$ 1,737,960
Incentive compensation	171,539	134,668
Contract services	2,756,170	744,573
City and state taxes	255,376	25,280
Severance payments	73,189	179,167
Other	411,038	328,572
	\$ 5,689,066	\$ 3,150,220

**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 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, 2002 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 collectibility was assured, and the amounts were fixed and determinable.

**NOTES TO FINANCIAL STATEMENTS—(Continued)**

Including the aforementioned royalty amounts, the Company earned total royalties from Novo Nordisk of approximately \$5.0 million, \$5.2 million and \$29.3 million for the years ended December 31, 2002, 2001 and 2000, respectively. All amounts related to royalty agreements are settled quarterly.

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.

On February 1, 2002, the Company completed its initial public offering. Upon the completion of the initial public offering each share of Series A and Series B mandatorily redeemable convertible preferred stock held by Novo Nordisk, converted to 3.6 shares of non-voting and voting common stock, respectively. Effective June 24, 2002, all shares of non-voting common stock were converted into the same number of shares of voting common stock.

In December 2002, the Company completed a collaborative agreement with Novo Nordisk for the preclinical development of Interleukin 21. Under the terms of the agreement, the Company and Novo Nordisk will collaborate on all research and development activities leading up to the filing of an Investigational New Drug application (IND) in the United States. Upon signing, Novo Nordisk paid \$4.0 million to the Company as reimbursement of a portion of the Company's costs incurred prior to the agreement. This amount has been deferred and will be recognized as revenue ratably over the estimated period leading to the IND filing. Novo Nordisk also agreed to pay the Company up to \$7.0 million for its 50% share of Interleukin 21 development costs incurred from the date of the agreement through the filing of the IND. This amount will be recorded as an offset to development costs.

Amounts receivable from Novo Nordisk and related entities were approximately \$389,000 and \$449,000 at December 31, 2002 and 2001, 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. All rights under this plan were fulfilled as of December 31, 2000.

**7. 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 \$2.1 million, \$1.7 million and \$1.6 million for the years ended December 31, 2002, 2001 and 2000, respectively.

**NOTES TO FINANCIAL STATEMENTS—(Continued)**

**Deferred compensation plan**

The Company has a Deferred Compensation Plan (DCP) for key employees. Eligible plan participants are designated by the Company's board of directors. The DCP allows participants to defer up to 15% of their annual compensation and up to 100% of any bonus. The DCP provides for discretionary contributions by the Company; such contributions were \$96,000 for the year ended December 31, 2000. There were no such contributions in 2002 and 2001. At December 31, 2002 and 2001, approximately \$2.7 million and \$2.9 million, respectively, was deferred under the DCP and was recorded both as a noncurrent asset and a noncurrent liability.

**8. Income taxes**

At December 31, 2002, the Company had net operating loss carryforwards of approximately \$52.5 million, a research and development tax credit carryforward of \$15.0 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 2022. The alternative minimum tax credit will carry forward indefinitely. The Company completed an initial public offering on February 1, 2002 and pursuant to the provisions of Internal Revenue Code Section 382 the offering may qualify as a change in ownership. Accordingly, a portion of the net operating loss carryforwards may be limited.

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

	<u>2002</u>	<u>2001</u>	<u>2000</u>
Current	\$ —	\$ (89,606)	\$ (7,838,003)
Deferred	—	—	13,731,405
	<u>\$ —</u>	<u>\$ (89,606)</u>	<u>\$ 5,893,402</u>

Deferred tax assets and liabilities arise from temporary differences between financial and tax reporting. The Company has provided a valuation allowance at December 31, 2002 and 2001 to offset the excess of deferred tax assets over the deferred tax liabilities, due to the Company's status as a stand-alone taxpayer and the uncertainty of realizing the benefits of the net deferred tax asset. Deferred tax and liabilities were as follows for the years ended December 31:

	<u>2002</u>	<u>2001</u>
Deferred tax assets:		
Net operating loss carryforwards	\$ 18,382,000	\$ 15,305,000
Research and development tax credit carryforwards	14,953,000	12,868,000
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	8,747,000	9,996,000
Deferred gain on sale of assets	4,958,000	—
Other	6,180,000	3,343,000
	<u>55,969,000</u>	<u>44,261,000</u>
Deferred tax liabilities:		
Deferred revenue	(3,938,000)	(2,625,000)
	<u>52,031,000</u>	<u>41,636,000</u>
Less: Valuation allowance	(52,031,000)	(41,636,000)
Net deferred tax asset	<u>\$ —</u>	<u>\$ —</u>

**NOTES TO FINANCIAL STATEMENTS—(Continued)**

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.

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:

	<u>2002</u>	<u>2001</u>	<u>2000</u>
Federal income tax rate	(35)%	(35)%	(35)%
Research and development tax credits	(7)	(6)	—
Valuation allowance	34	39	62
Other	8	2	(3)
	<u>          </u>	<u>          </u>	<u>          </u>
Effective tax rate	0%	0%	24%
	<u>          </u>	<u>          </u>	<u>          </u>

**9. Commitments**

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

In November 2001, the Company entered into a lease agreement for additional office space. The lease began on February 1, 2002. The lease term is 10 years with options to renew for up to two additional terms of five years each. Annual lease payments will range from \$0.4 million to \$0.5 million. The lease also provides the Company a right of first refusal through February 1, 2004 to lease additional space in the building.

In October 2002, the Company completed a sale and leaseback transaction involving its headquarter buildings located in Seattle, Washington. The three buildings were sold for a total purchase price of \$52.3 million. Net proceeds from this transaction amounted to \$50.5 million, and a gain of \$14.4 million has been deferred and will be recognized ratably over the lease term. Simultaneously, the Company agreed to lease the buildings from the purchaser for a period of 15 years, subject to four five-year renewal options. The Company has provided the lessor a security deposit in the form of pledged securities equal to two months base rent. The Company has accounted for this transaction as a sale and leaseback in accordance with the criteria of SFAS 98. The lease of the building has been classified as an operating lease in accordance with SFAS 13. The initial rental payment of \$5.1 million per year will increase by 3.5% each year during the term. The Company will recognize rent expense of \$6.6 million per year, which is the average annual rent over the initial lease term. Rent for the renewal terms will be the greater of fair market value or 90% of the rent for the last year prior to renewal. The Company has retained an option to expand one of the leased buildings. Planning is underway to pursue this option in 2003. If this expansion project is pursued, it is expected to cost approximately \$26 million, including all related equipment costs. The purchaser has agreed to finance a substantial portion of these costs, in return for increased rent payments. To date, no material financial commitments have been made related to the facility expansion.

**NOTES TO FINANCIAL STATEMENTS—(Continued)**

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

<u>Year ending December 31,</u>		
2003	\$	5,860,235
2004		5,909,817
2005		6,114,653
2006		6,311,868
2007		6,544,573
Thereafter		72,516,449
		<hr/>
		103,257,595
Less: Future sublease income		(120,969)
		<hr/>
Net future minimum rental payments	\$	103,136,626

In addition to the above minimum rental payments, 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 \$368,000 to \$476,000 per year beginning February 2004 and ending January 2012.

Gross rental expense for the years ended December 31, 2002, 2001, and 2000 was approximately \$4.2 million, \$1.9 million and \$1.8 million, respectively. Cash received under the sublease agreements for the subleased office space was approximately \$2.0 million, \$2.0 million and \$1.8 million for the years ended December 31, 2002, 2001, and 2000 respectively.

Certain key employees have employment agreements with the Company providing certain severance benefits.

**10. 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 in 2001, which is being amortized over the estimated term of the development program, approximately nine years.

**NOTES TO FINANCIAL STATEMENTS—(Continued)**

**11. Mandatorily redeemable convertible preferred stock**

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

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

**12. Shareholders' equity (deficit)**

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

**Common stock**

At December 31, 2001, 23,543,159 shares of authorized common stock were reserved for issuance upon conversion of preferred stock. 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. Effective June 24, 2002, all shares of non-voting common stock were converted into the same number of shares of voting common stock.

**Stock options**

In March 2000, the Company adopted the 2000 Stock Incentive Plan (the 2000 Plan). Upon completion of the Company's initial public offering, in February 2002, the 2000 Plan was suspended and the 2001 Stock Incentive Plan (the 2001 Plan) became effective. Both plans provide for the issuance of incentive stock options and nonqualified stock options to employees, directors, consultants and other independent contractors who provide services to the Company. The Company's board of directors is responsible for administration of the Plans and determines the term of each option, exercise price and the vesting terms. Options generally vest over a four-year period and expire ten years from the date of grant. The 2001 Plan provides for an annual increase effective the first day of each year equal to the least of (i) 2,700,000 shares; (ii) 5% of the outstanding common stock as of the end of the Company's preceding fiscal year; and (iii) a lesser amount as determined by the Board of Directors. The first annual increase under the 2001 Plan occurred upon completion of the Company's initial public offering. Any shares from the 2000 Plan that are not actually issued shall continue to be available for issuance under the 2001 Plan. The Company has reserved a total of 9,423,180 shares of common stock for issuance under the Plan, of which 676,431 are available for future grant at December 31, 2002. Certain board members were granted options to purchase 144,000 shares that are immediately exercisable. Options to purchase 93,464 shares have been granted to certain board members in 2002 that are exercisable as of the one-year anniversary from the grant date.

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**ZYMOGENETICS, INC.**

**NOTES TO FINANCIAL STATEMENTS—(Continued)**

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	\$ .68
Exercised	—	—	
Canceled	(20,520)	2.78	
<b>Balance, December 31, 2000</b>	<b>4,311,000</b>	<b>\$ 2.78</b>	
Granted	3,629,066	\$ 3.94	\$ .79
Exercised	(271,080)	2.78	
Canceled	(361,894)	3.03	
<b>Balance, December 31, 2001</b>	<b>7,307,092</b>	<b>\$ 3.35</b>	
Granted	1,241,410	\$ 8.34	\$ 5.05
Exercised	(208,272)	2.86	
Canceled	(72,833)	3.73	
<b>Balance, December 31, 2002</b>	<b>8,267,397</b>	<b>\$ 4.10</b>	

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 prices of options granted during 2001 and through January 9, 2002 were less than the fair value of the Company's shares at the date of grant. The exercise prices of options granted for the remainder of 2002 were equal to the fair value of the Company's shares at the date of grant.

The following table summarizes information about options outstanding at December 31, 2002:

Exercise Price	Options outstanding			Options exercisable	
	Weighted–average exercise prices	Number of options	Weighted–average remaining contractual life (in years)	Number of options	Weighted–average exercise prices
\$2.77 – \$ 3.77	\$2.78	4,658,035	7.6	3,111,465	\$2.78
\$3.78 – \$ 6.78	4.51	2,453,572	8.6	737,411	4.46
\$6.79 – \$ 9.79	7.73	871,790	9.5	—	—
\$9.80 – \$11.80	11.21	284,000	7.9	—	—
	4.10	8,267,397	8.1	3,848,876	3.10

The weighted average fair values were determined based on the Black–Scholes option–pricing model with the following assumptions:

	2002	2001	2000
Expected dividend yield	0%	0%	0%
Expected stock price volatility	70%	0%	0%
Risk–free interest rate	3.85%	4.48%	5.58%
Expected life of options	5 years	5 years	5 years

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

**ZYMOGENETICS, INC.**

**NOTES TO FINANCIAL STATEMENTS—(Continued)**

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

**13. Quarterly Financial Results (unaudited)**

Operating results for each quarter of 2002 and 2001 are summarized as follows (in thousands):

	<u>Q1</u>	<u>Q2</u>	<u>Q3</u>	<u>Q4</u>
<b>Year ended December 31, 2002:</b>				
Revenue	\$ 5,799	\$ 6,960	\$ 5,925	\$ 34,092
Net income (loss)	(11,803)	(15,132)	(14,466)	10,985
Net income (loss) attributable to common shareholders	(13,521)	(15,132)	(14,466)	10,985
Net income (loss) per common share:				
Basic	(0.41)	(0.33)	(0.32)	0.24
Diluted	(0.41)	(0.33)	(0.32)	0.23
<b>Year ended December 31, 2001:</b>				
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)

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### **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 "Election of Directors" in the proxy statement for our annual meeting of shareholders to be held on June 12, 2003. We will file the proxy statement within 120 days of December 31, 2002, our fiscal year end.

(b) The information required by this item with respect to our executive officers is incorporated by reference to the section captioned "Executive Officers" in the proxy statement for our annual meeting of shareholders to be held on June 12, 2003.

It has been recently announced that Robert S. Whitehead, our Senior Vice President and Chief Business Officer, will leave the Company effective June 30, 2003 to pursue other opportunities.

### **Item 11. Executive Compensation**

The information required by this item with respect to executive compensation is incorporated by reference to the section captioned "Executive Compensation" in the proxy statement for our annual meeting of shareholders to be held on June 12, 2003.

### **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 12, 2003.

The following table provides information regarding our equity compensation plans at December 31, 2002.

<u>Plan category</u>	<u>Number of securities to be issued upon exercise of outstanding options, warrants and rights</u>	<u>Weighted-average exercise price of outstanding options, warrants and rights</u>	<u>Number of securities remaining available for future issuance under equity compensation plans(1)</u>
Equity compensation plans approved by security holders	8,267,397	\$ 4.10	676,431
Equity compensation plans not approved by security holders	—	—	—
<b>Total</b>	<b>8,267,397</b>	<b>\$ 4.10</b>	<b>676,431</b>

(1) Does not include 2,290,752 shares remaining available for issuance under the 2001 Plan on January 1, 2003 pursuant to a provision of the 2001 Plan that provides for an annual increase effective the first day of each year equal to the least of (i) 2,700,000 shares; (ii) 5% of the outstanding common stock as of the end of the Company's preceding fiscal year; and (iii) a lesser amount as determined by the Board of Directors.

### **Item 13. Relationships and Related Transactions**

The information required by this item is incorporated by reference from the section labeled "Certain Transactions" in the proxy statement for our annual meeting of shareholders to be held on June 12, 2003.

### **Item 14. Controls and Procedures**

Our principal executive officer and principal financial officer, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rules 13a-14(c) and 15d-14(c)) as of a date within ninety days before the filing date of this report, have concluded that, as of such date our disclosure controls and procedures were effective. No significant changes were made to our internal controls or other factors that could significantly affect these controls subsequent to the date of their evaluation.

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**Table of Contents****PART IV****Item 15. Exhibits, Financial Statement Schedule and Reports on Form 8-K**

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

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

	<u>Page in Form 10-K</u>
Report of PricewaterhouseCoopers LLP, Independent Accountants	45
Balance Sheets	46
Statements of Operations	47
Statement of Changes in Mandatorily Redeemable Convertible Preferred Stock and Shareholders' Equity	48
Statements of Cash Flows	49
Notes to Financial Statements	50-63

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*

<u>Exhibit No.</u>	<u>Description</u>	
3.1	Amended and Restated Articles of Incorporation of ZymoGenetics, Inc.	(A)
3.2	Amended and Restated Articles of Incorporation of ZymoGenetics, Inc.	(D)
3.3	Amended and Restated Bylaws.	(A)
9.1	Voting Agreement, dated October 20, 2000, by and between Warburg, Pincus Equity Partners, L.P. and Ernesto Bertarelli.	(A)
9.2	Agreement and Waiver of Co-Sale Rights, dated July 16, 2001, by and among ZymoGenetics, Inc., the holders of Series B Preferred Stock listed on the signature pages thereto and Serono B.V.	(A)
9.3	Share Transfer and Voting Agreement, dated January 2, 2001, by and between Warburg, Pincus Equity Partners, L.P. and Mount Everest Advisors, L.L.C. and acknowledged by ZymoGenetics, Inc.	(A)
10.2	Employment Agreement, dated March 21, 2001, between ZymoGenetics, Inc. and Jan K. Öhrström.	(A)
10.3	Employment Agreement, dated March 23, 2001, between ZymoGenetics, Inc. and Patrick J. O'Hara.	(A)
10.4	Employment Agreement, dated April 23, 2001, between ZymoGenetics, Inc. and Frank D. Collins.	(A)
10.5	Employment Agreement, dated April 30, 2001, between ZymoGenetics, Inc. and James A. Johnson.	
10.6	Employment Agreement, dated January 2, 2002, between ZymoGenetics, Inc. and Mark D. Young.	(A)
10.7	Employment Agreement, dated January 28, 2002, between ZymoGenetics, Inc. and Robert S. Whitehead.	(B)

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<u>Exhibit No.</u>	<u>Description</u>	
10.8	Employment Agreement, dated February 12, 2002, between ZymoGenetics, Inc. and Suzanne Shema.	(B)
10.9	Amended and Restated 2000 Stock Incentive Plan.	(A)
10.10	2001 Stock Incentive Plan.	(A)
10.11	Stock Option Grant Program for Nonemployee Directors under the ZymoGenetics 2001 Stock Incentive Plan.	
10.12	Deferred Compensation Plan for Key Employees.	(A)
10.13	Form of Promissory Note, dated September 14, 2001, between ZymoGenetics, Inc. and the executive officers listed on Schedule A thereto.	(A)
10.14	Form of Pledge and Security Agreement, dated September 14, 2001, between ZymoGenetics, Inc. and the executive officers listed on Schedule A thereto.	(A)
10.15	Pledge and Security Agreement, dated September 14, 2001, between ZymoGenetics, Inc. and Bruce L.A Carter.	(A)
10.16*	Insulin Agreement, dated August 6, 1982, between ZymoGenetics, Inc. and Novo Industri A/S.	(A)
10.17*	Letter Agreement, dated March 13, 1987, between ZymoGenetics, Inc. and Novo Industri A/S.	(A)
10.18*	Amended and Restated Human Glucagon, Analogues of Human Glucagon, Analogues of Human Insulin Letter Agreement, dated September 28, 2000, between ZymoGenetics, Inc. and Novo Nordisk A/S.	(A)
10.19*	License Agreement for Analogues of Human Insulin, dated September 28, 2000, between the registrant and Novo Nordisk Health Care AG.	(A)
10.20*	License Agreement, dated February 23, 1989, between ZymoGenetics, Inc. and the University of Washington.	(A)
10.21*	License Agreement, dated January 18, 1994, including Amendment No. 1, dated January 1, 1997, and Amendment No. 2, dated June 5, 2000, between and among ZymoGenetics, Inc., Novo Nordisk A/S, Johnson & Johnson and Chiron Corporation.	(A)
10.22*	Royalty Agreement pertaining to the January 18, 1994 Agreement Relating to Platelet Derived Growth Factor, dated January 1, 2000, between ZymoGenetics, Inc. and Novo Nordisk.	(A)
10.23*	License Agreement, dated December 31, 1998, as amended on February 4, 1999 and October 23, 2000, between ZymoGenetics, Inc. and St. Jude Children's Research Hospital.	(A)
10.24*	Option and License Agreement, effective November 10, 2000, as amended effective as of June 16, 2000 and October 20, 2000, between ZymoGenetics, Inc. and Novo Nordisk A/S.	(A)
10.25*	Cross-License Agreement, effective November 10, 2000, between ZymoGenetics, Inc. and Novo Nordisk A/S, Enzyme Business.	(A)
10.26*	Cross-License Agreement, effective November 10, 2000, between ZymoGenetics, Inc. and Novo Nordisk A/S.	(A)
10.27*	Kunitz Protein Agreement, effective November 10, 2000, between ZymoGenetics, Inc. and Novo Nordisk A/S.	(A)
10.28*	Collaborative Development and Marketing Agreement, effective August 30, 2001, by and between ZymoGenetics, Inc. and Ares Trading S.A.	(A)
10.29*	Collaborative Agreement for IL-21, dated December 14, 2002, between ZymoGenetics, Inc. and Novo Nordisk A/S.	

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<u>Exhibit No.</u>	<u>Description</u>	
10.30*	Exclusive Patent License Agreement, effective December 18, 2002, between ZymoGenetics, Inc. and Aventis Behring GmbH.	
10.31	Series B Preferred Stock Purchase Agreement, dated October 20, 2000, by and among ZymoGenetics, Inc., Novo Nordisk A/S and the other investors listed on Exhibit A thereto.	(A)
10.32	Shareholders' Agreement by and among ZymoGenetics, Inc., Novo Nordisk A/S, Novo Nordisk Pharmaceuticals, Inc. and the investors listed on Schedule A thereto, effective as of November 10, 2000.	(A)
10.33	First Amendment to Shareholders' Agreement by and among ZymoGenetics, Inc., Novo Nordisk A/S, Novo Nordisk Pharmaceuticals, Inc. and the investors listed on Schedule A thereto, dated as of February 4, 2002.	(C)
10.34	Investors' Rights Agreement by and among ZymoGenetics, Inc., Novo Nordisk Pharmaceuticals, Inc. and the persons listed on Schedule A thereto, effective as of November 10, 2000.	(A)
10.35	Tax Sharing Agreement, effective October 20, 2000, between ZymoGenetics, Inc. and Novo Nordisk of North America, Inc.	(A)
10.36	Office Lease Agreement, dated November 9, 2001, between ZymoGenetics, Inc. and 1144 Eastlake LLC.	(A)
10.37	Office Lease Agreement, dated October 4, 2002, between ZymoGenetics, Inc. and ARE-1201/1208 Eastlake Avenue, LLC.	
10.38	Office Lease Agreement, dated October 4, 2002, between ZymoGenetics, Inc. and ARE-1208 Eastlake Avenue, LLC.	
23.1	Consent of PricewaterhouseCoopers LLP, independent accountants.	
99.1	Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	
99.2	Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	

\* Portions of these exhibits have been omitted based on a request for 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) Incorporated by reference to designated exhibit included with ZymoGenetics Annual Report on Form 10-K for the year ended December 31, 2001.
- (C) Incorporated by reference to designated exhibit included with ZymoGenetics Quarterly Report on Form 10-Q for the quarter ended March 31, 2002.
- (D) Incorporated by reference to designated exhibit included with ZymoGenetics Quarterly Report on Form 10-Q for the quarter ended June 30, 2002.

- (b) Reports on Form 8-K

On October 18, 2002, the Company filed a Current Report on Form 8-K to report the completion of a sale and leaseback transaction involving the Company's headquarter buildings and the issuance of a press release announcing the transaction.

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## SIGNATURES

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

ZYMOGENETICS, INC.

Date: March 25, 2003

By:           /s/ BRUCE L.A. CARTER          

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

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

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

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>          /s/ BRUCE L.A. CARTER, PH.D.          </u> <b>Bruce L.A. Carter, Ph.D.</b>	President, Chief Executive Officer and Director (Principal Executive Officer)	March 25, 2003
<u>          /s/ JAMES A. JOHNSON          </u> <b>James A. Johnson</b>	Senior Vice President, Chief Financial Officer and Treasurer (Principal Accounting and Financial Officer)	March 25, 2003
<u>          /s/ GEORGE B. RATHMANN, PH.D.          </u> <b>George B. Rathmann, Ph.D.</b>	Chairman of the Board of Directors	March 25, 2003
<u>          /s/ DAVID I. HIRSH, PH.D.          </u> <b>David I. Hirsh, Ph.D.</b>	Director	March 25, 2003
<u>          /s/ JONATHAN S. LEFF          </u> <b>Jonathan S. Leff</b>	Director	March 25, 2003
<u>          /s/ KURT ANKER NIELSEN          </u> <b>Kurt Anker Nielsen</b>	Director	March 25, 2003
<u>          /s/ EDWARD E. PENHOET, PH.D.          </u> <b>Edward E. Penhoet, Ph.D.</b>	Director	March 25, 2003
<u>          /s/ LORI F. RAFIELD, PH.D.          </u> <b>Lori F. Rafield, Ph.D.</b>	Director	March 25, 2003
<u>          /s/ LARS REBIEN SØRENSEN          </u> <b>Lars Rebien Sørensen</b>	Director	March 25, 2003

**CERTIFICATIONS**

I, Bruce L.A. Carter, certify that:

1. I have reviewed this annual report on Form 10-K of ZymoGenetics, Inc. (the "Company");
2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;
3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this annual report;
4. The Company's other certifying officers and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-14 and 15d-14) for the Company and we have:
  - a) designed such disclosure controls and procedures to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;
  - b) evaluated the effectiveness of the Company's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report (the "Evaluation Date"); and
  - c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date;
5. The Company's other certifying officers and I have disclosed, based on our most recent evaluation, to the Company's auditors and the audit committee of Company's board of directors (or persons performing the equivalent function):
  - a) all significant deficiencies in the design or operation of internal controls which could adversely affect the Company's ability to record, process, summarize and report financial data and have identified for the Company's auditors any material weaknesses in internal controls; and
  - b) any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal controls; and
6. The Company's other certifying officers and I have indicated in this annual report whether or not there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to the date of our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

Date: March 25, 2003

/s/ BRUCE L.A. CARTER

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Bruce L.A. Carter  
President and Chief Executive  
Officer

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## Table of Contents

I, James A. Johnson, certify that:

1. I have reviewed this annual report on Form 10-K of ZymoGenetics, Inc. (the "Company");
2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;
3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this annual report;
4. The Company's other certifying officers and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-14 and 15d-14) for the Company and we have:
  - a) designed such disclosure controls and procedures to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;
  - b) evaluated the effectiveness of the Company's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report (the "Evaluation Date"); and
  - c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date;
5. The Company's other certifying officers and I have disclosed, based on our most recent evaluation, to the Company's auditors and the audit committee of Company's board of directors (or persons performing the equivalent function):
  - a) all significant deficiencies in the design or operation of internal controls which could adversely affect the Company's ability to record, process, summarize and report financial data and have identified for the Company's auditors any material weaknesses in internal controls; and
  - b) any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal controls; and
6. The Company's other certifying officers and I have indicated in this annual report whether or not there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to the date of our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

Date: March 25, 2003

/s/ JAMES A. JOHNSON

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James A. Johnson  
Senior Vice President and  
Chief Financial Officer

## 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.

Chief Program Officer  
The Gordon and Betty Moore Foundation

### LORI F. RAFIELD, PH.D.

Partner  
Apax Partners, Inc.

### LARS REBIEN SØRENSEN

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.

Senior 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](http://www.zymogenetics.com)

## ANNUAL MEETING

The annual meeting of shareholders will be held at 8:00 a.m. on Thursday, June 12, 2003, at the Company headquarters.

## SHAREHOLDER INQUIRIES

Information about the Company can be found on the Internet at [www.zymogenetics.com](http://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.

# Company Information

## TRANSFER AGENT AND REGISTRAR

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

## GENERAL COUNSEL

Perkins Coie LLP  
Seattle, Washington

## INDEPENDENT ACCOUNTANTS

PricewaterhouseCoopers LLP  
Seattle, Washington

## STOCK LISTING

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

## FORWARD-LOOKING STATEMENTS

This Annual Report contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on the current intent and expectations of the management of ZymoGenetics. These statements are not guarantees of future performance and involve risks and uncertainties that are difficult to predict. ZymoGenetics' actual results and the timing and outcome of events may differ materially from those expressed in or implied by the forward-looking statements because of risks associated with our unproven discovery strategy, preclinical and clinical development, regulatory oversight, intellectual property claims and litigation, reliance on collaboration partners, and other risks detailed in the Company's public filings with the Securities and Exchange Commission, including the Company's Annual Report on Form 10-K for the year ended December 31, 2002. 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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# ZYMOGENETICS

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