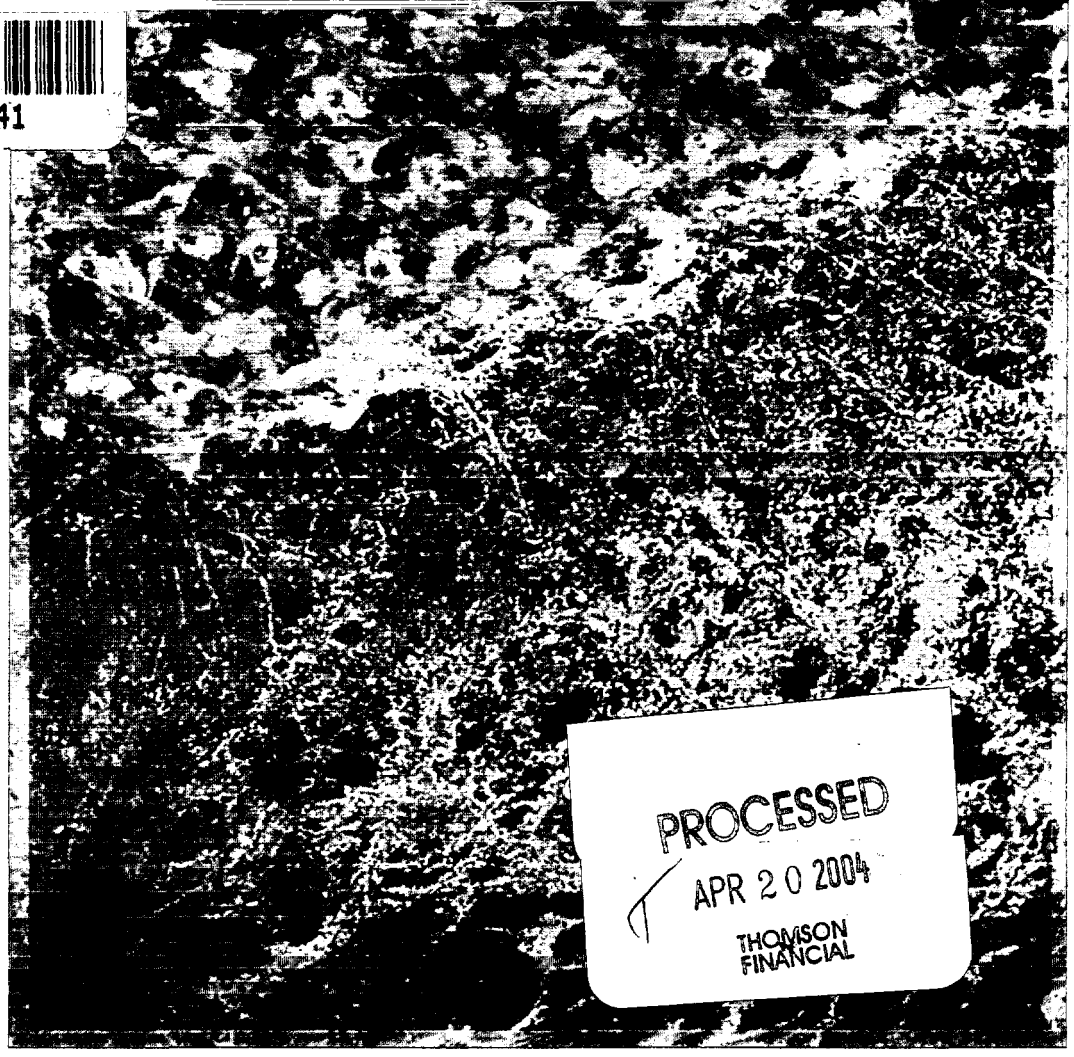
LEXICON GENETICS 2003 Annual Report



ACCELERATING *the course of* DRUG DISCOVERY AND DEVELOPMENT

identified a new potential drug target, present in neurons identified by fluorescent
brain stalk, that appears to interact with dopamine pathways in the brain and may
provide a better means to treat certain diseases of the central nervous system.

LEXICON GENETICS is a biopharmaceutical company focused on the discovery of breakthrough treatments for human disease. We are systematically discovering the physiological and behavioral functions of genes to identify potential points of therapeutic intervention, or drug targets. We make our discoveries using our proprietary technology to knock out, or disrupt, the function of genes in mice. Our gene knockout technology allows us to model, on a genome-wide scale, the effects on physiology that could be expected from prospective drugs directed against novel targets. For targets that we believe have high pharmaceutical value, we engage in programs for the discovery and development of small molecule drugs, therapeutic antibodies and therapeutic proteins. We have advanced more than 40 knockout-validated targets into drug discovery programs in six therapeutic areas: diabetes and obesity, cardiovascular disease, cancer, immune system disorders, ophthalmic disease, and psychiatric and neurological disorders. We are working both independently and through strategic collaborations and alliances to accelerate the development and commercialization of our discoveries. Our physiology-based approach to understanding gene function and our use of knockouts to model expected drug action are designed to identify new ways to treat major human diseases. Lexicon's common stock is traded on the Nasdaq National Market under the symbol LEXG.

ACCELERATING DISCOVERY AND DEVELOPMENT

FINANCIAL HIGHLIGHTS

(in thousands, except per share data)	Year ended December 31, 2003	2002	2001
Revenues	$ 42,838	$ 35,200	$ 30,577
Research and development expenses[1]	82,198	74,859	53,355
Loss from operations[2]	62,593	62,893	43,639
Interest and other income, net	1,471	3,223	8,467
Net loss[2][3]	64,198	59,670	35,172
Net loss per share[2][3]	1.13	1.14	0.70
Weighted average shares outstanding	56,820	52,263	50,213
Capital expenditures	4,824	19,766	13,471

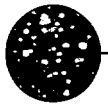
	As of December 31, 2003	2002	2001
Cash, cash equivalents and investments[4]	161,001	123,096	166,840
Stockholders' equity	166,216	169,902	218,372

[1] Includes non-cash, stock-based compensation of $5,048, $5,155 and $5,539 in 2003, 2002 and 2001, respectively.

[2] Includes non-cash, stock-based compensation of $10,115, $10,268 and $10,770 in 2003, 2002 and 2001, respectively.

[3] The 2003 net loss includes the cumulative effect of a change in accounting principle resulting in a one time, non-cash charge of $3,076 related to accumulated depreciation through December 31, 2003 on properties under Lexicon's synthetic lease.

[4] Includes restricted cash and investments of $57,514, $57,710 and $43,338 in 2003, 2002 and 2001, respectively.



NEUROSCIENCE

LG617 – Alzheimer's/Cognition
LG726 – Depression
LG324 – Depression
LG527 – Depression
LG487 – Depression
LG915 – Anxiety
LG852 – Anxiety/Stress
LG317 – Parkinson's Disease
LG752 – Pain
LG470 – Pain
LG262 – Psychosis/Schizophrenia
LG351 – Psychosis/Schizophrenia
LG451 – Sleep/Circadian Rhythm
LG590 – Sleep/Circadian Rhythm

IMMUNOLOGY

LG293 – Rheumatoid Arthritis
LG688 – Inflammation
LG253 – Inflammation
LG126 – Arthritis
LG169 – Inflammation
LG512 – Autoimmune Disease
LG148 – Autoimmune Disease
LG267 – Autoimmune Disease
LG347 – Autoimmune Disease
LG111 – Asthma

METABOLISM

LG653 – Obesity/Diabetes
LG314 – Obesity/Diabetes
LG747 – Obesity/Diabetes
LG767 – Obesity/Hyperlipidemia
LG222 – Obesity/Diabetes
LG842 – Obesity/Diabetes
LG519 – Obesity
LG425 – Diabetes
LG881 – Osteoporosis
LG123 – Osteoporosis

2003 was a year of significant scientific and corporate achievements at Lexicon Genetics as we work to accelerate the pace of drug discovery and development:

- We now have more than 40 drug discovery programs;
- We expanded our therapeutic areas of focus to six fields of medicine with the addition of ophthalmology;
- We have completed the physiological and behavioral analysis of more than 1,500 genes, or 30% of the pharmaceutically important genes in our Genome5000™ program;
- We established a landmark alliance with Bristol-Myers Squibb Company for the discovery, development and commercialization of drugs in the neuroscience field. The alliance covers significant disease areas, including depression, anxiety, schizophrenia, pain and Alzheimer's disease;
- We achieved the first performance milestone under our drug discovery alliance with Genentech, Inc.;
- We broadened our gene targeting patent estate to a total of eight issued U.S. patents with two new patent issuances in late 2003 and early 2004;
- We grew revenues by 22% to $42.8 million in 2003, marking our eighth consecutive year of revenue growth;
- We completed a public offering of 10.2 million shares of common stock, raising a net amount of $50.1 million; and
- We published an important study in the *Proceedings of the National Academy of Science* identifying a novel gene target for the control of high blood pressure with a direct link to human hypertension.[1]

WORLD-CLASS COLLABORATION:

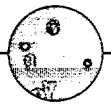
BRISTOL-MYERS SQUIBB COMPANY

Depression is estimated to affect 19 million people in the United States and currently accounts for over $11 billion of annual pharmaceutical sales. Schizophrenia affects one percent of the world's population – two million people in the United States alone – and accounts for over $3 billion in annual drug sales in the United States. With an aging U.S. population, Alzheimer's disease and other cognitive and neurodegenerative disorders represent a growing medical problem. Lexicon's alliance with Bristol-Myers Squibb is designed to accelerate the pace of drug discovery in these disease areas.

[1] Brian P. Zambrowicz *et al.* Wnk1 kinase deficiency lowers blood pressure in mice: A gene-trap screen to identify potential targets for therapeutic intervention. *PNAS.* **100**, 14109–14114 (November 25, 2003).

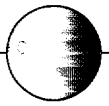
CARDIOLOGY

LG914 – Atherosclerosis
LG101 – Thrombosis
LG110 – Thrombosis
LG844 – Hypertension
LG105 – Hypertension



CANCER

LG152 – Solid Tumors
LG934 – Solid Tumors
LG195 – Solid Tumors
LG247 – Solid Tumors
LG792 – Solid Tumors
LG406 – Solid Tumors



OPHTHALMOLOGY

LG339 – Retinal Degeneration

EXPANDING DRUG DISCOVERY PROGRAMS

The Genome5000 – The Race For Discoveries

We are using our proprietary gene knockout technology to rapidly discover the functions of the most pharmaceutically important genes in the human genome – 5,000 genes that have characteristics suggesting a small molecule, antibody or protein could be developed to modulate their function. We believe our unique ability to systematically determine the physiological and behavioral function of genes provides us with a strategic advantage in the race to discover future breakthrough therapeutics. Our physiology-based approach is designed to enable Lexicon to select the best new targets for its drug discovery programs, thereby accelerating the development of safer and more effective treatments for major human diseases.

Our Genome5000 program is 30% complete and has already produced more than 40 drug discovery programs in six therapeutic areas – diabetes and obesity, cardiovascular disease, cancer, immune system disorders, ophthalmic disease, and psychiatric and neurological disorders. Our most advanced programs include:

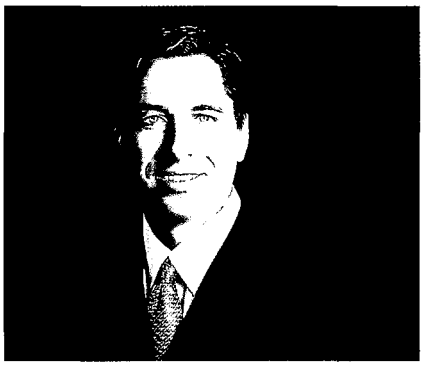
- **LG653 for obesity** – knocking out LG653 results in mouse models that have significantly lower body fat without undesirable side effects. Lower body fat is maintained even in the face of a high-fat diet and increasing age. Lexicon is developing orally available therapeutics directed against the human version of LG653 as a potential treatment for obesity;
- **LG617 for Alzheimer's disease and cognition** – knocking out LG617, a gene expressed in the brain, improves learning and memory in mice. Lexicon is developing orally available therapeutics directed against the human version of LG617 as a potential treatment for Alzheimer's disease and other cognitive disorders;
- **LG152 for solid tumors** – knocking out LG152 reduces cell proliferation rates. The human version of LG152 is expressed at abnormally high levels in certain human tumors. Lexicon is developing therapeutics directed against the human version of LG152 as a potential treatment for cancer.

WORLD-CLASS COLLABORATION: GENENTECH

With drugs like Rituxan® Herceptin® and Avastin™ Genentech is on the forefront of the fight against cancer. Lexicon's drug discovery alliance with Genentech uses Lexicon's target validation technologies to discover therapies based on the functions of secreted proteins and antibody targets identified through Genentech's drug discovery research.

Building Strategic Alliances

Lexicon is working both independently and through strategic collaborations and alliances to accelerate the development of its drug discoveries. We have numerous alliances with leading pharmaceutical and biotechnology companies, as well as collaborations with research and academic institutions. We expect to form new alliances to complement our internal capabilities and further accelerate the development and commercialization of our drug discovery programs.



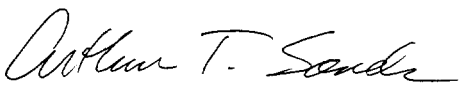
ARTHUR T. SANDS, M.D., PH.D. President and Chief Executive Officer

In December 2003, Lexicon and Bristol-Myers Squibb Company formed a broad alliance for the discovery, development and commercialization of drugs in the neuroscience field. In the alliance, we are contributing a number of potentially breakthrough neuroscience drug discovery programs at various stages of development. In addition, we will continue to use our gene knockout technology to identify novel drug targets with promise in neuroscience. We receive significant research funding from Bristol-Myers Squibb and will also receive clinical and regulatory milestone payments and royalties for each drug Bristol-Myers Squibb develops under the alliance. By combining Lexicon's ability to discover the physiological functions and pharmaceutical utility of genes with Bristol-Myers Squibb's clinical and commercial expertise, we believe our respective strengths will create a lasting leadership position in the treatment of neurological and psychiatric disorders.

In another exciting alliance, we have been working closely with Genentech, Inc. since December 2002 to discover the functions of 500 secreted proteins and potential antibody targets identified through Genentech's internal drug discovery research. Our alliance with Genentech has progressed rapidly, with the achievement of the first performance milestone in 2003.

Accelerating Drug Discovery And Development

Lexicon's gene knockout technologies allow us to discover the key switches that control our physiology, with the promise of accelerating the development of breakthrough therapies for human disease. In 2003, Lexicon established an important corporate alliance and made remarkable scientific discoveries. In 2004, we look forward to advancing our lead drug discovery programs through pre-clinical development and forming valuable new corporate alliances. We will continue to apply the knowledge we gain from our exploration of the human genome to invent the next generation of drugs.



ARTHUR T. SANDS, M.D., PH.D.
President and Chief Executive Officer

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

FORM 10-K

(Mark One)

☑ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the Fiscal Year Ended December 31, 2003

or

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

For the Transition Period from _____ to _____

Commission File Number: 000-30111

Lexicon Genetics Incorporated

(Exact Name of Registrant as Specified in its Charter)

Delaware	76-0474169
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification Number)
8800 Technology Forest Place The Woodlands, Texas 77381 (Address of Principal Executive Offices and Zip Code)	(281) 863-3000 (Registrant's Telephone Number, Including Area Code)

Securities registered pursuant to Section 12(b) of the Act: None

Securities registered pursuant to Section 12(g) of the Act:
Common Stock, par value $0.001 per share

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 amendment to this Form 10-K. ☑

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes ☑ No ☐

The aggregate market value of voting stock held by non-affiliates of the registrant as of the last day of the registrant's most recently completed second quarter was approximately $198.3 million, based on the closing price of the common stock on the Nasdaq National Market on June 30, 2003 of $6.60 per share. For purposes of the preceding sentence only, all directors, executive officers and beneficial owners of ten percent or more of the registrant's common stock are assumed to be affiliates. As of March 8, 2004, 63,312,972 shares of common stock were outstanding.

Documents Incorporated by Reference

Certain sections of the registrant's definitive proxy statement relating to the registrant's 2004 annual meeting of stockholders, which proxy statement will be filed under the Securities Exchange Act of 1934 within 120 days of the end of the registrant's fiscal year ended December 31, 2003, are incorporated by reference into Part III of this annual report on Form 10-K.

Lexicon Genetics Incorporated

Table of Contents

In this annual report on Form 10-K, "Lexicon Genetics," "Lexicon," "we," "us" and "our" refer to Lexicon Genetics Incorporated.

Factors Affecting Forward Looking Statements

This annual report on Form 10-K contains forward-looking statements. These statements relate to future events or our future financial performance. We have attempted to identify forward-looking statements by terminology including "anticipate," "believe," "can," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "should" or "will" or the negative of these terms or other comparable terminology. These statements are only predictions and involve known and unknown risks, uncertainties and other factors, including the risks outlined under "Item 1. Business – Risk Factors," that may cause our or our industry's actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. We are not under any duty to update any of the forward-looking statements after the date of this annual report on Form 10-K to conform these statements to actual results, unless required by law.

PART I

Item 1. *Business*

Overview

Lexicon Genetics is a biopharmaceutical company focused on the discovery of breakthrough treatments for human disease. We are systematically discovering the physiological and behavioral functions of genes to identify those that encode potential targets for therapeutic intervention, or drug targets. We make our discoveries using our proprietary technology to knock out, or disrupt, the function of genes in mice to model the effects on physiology that could be expected from prospective drugs directed against those targets. For targets that we believe have high pharmaceutical value, we engage in programs for the discovery and development of potential small molecule drugs, therapeutic antibodies and therapeutic proteins. We focus our discovery efforts in six therapeutic areas – diabetes and obesity, cardiovascular disease, psychiatric and neurological disorders, cancer, immune system disorders and ophthalmic disease – and we have advanced targets into drug discovery programs in each of these areas with potential for addressing large medical markets.

We make our discoveries using proprietary technology to knock out genes in mice, analyze the resulting effects on physiology and behavior, and identify those genes that exhibit a favorable therapeutic profile in mouse models. Using this information, we select potential targets encoded by the corresponding human genes for our drug discovery programs. . Our physiology-based approach to understanding gene function and our use of mouse models in our drug discovery efforts allow us to make highly-informed decisions throughout the drug discovery and development process, which we believe will increase our likelihood of success in discovering breakthrough therapeutics.

The scope of our gene knockout technology, combined with the size and sophistication of our facilities and our evaluative technologies, provides us with what we believe to be a significant competitive advantage. We are using these technologies in our Genome5000 program to discover the physiological and behavioral functions of 5,000 genes from the human genome that belong to gene families that we consider to be pharmaceutically important. We have completed our analysis of more than 30% of these genes, and we expect to complete the analysis of the remaining genes by the end of 2007. Through February 2004, we have advanced into drug discovery programs more than 40 targets, each of which we have validated in living mammals, or *in vivo*.

We are working both independently and through strategic collaborations and alliances to commercialize our technology and turn our discoveries into drugs. We have established multiple collaborations with leading pharmaceutical and biotechnology companies, as well as research institutes and academic institutions. We are working with Bristol-Myers Squibb Company to discover and develop novel small molecule drugs in the neuroscience field. We are working with Genentech, Inc. to discover the functions of secreted proteins and potential antibody targets identified through Genentech's internal drug discovery research. We are also working with Abgenix, Inc. to discover and develop therapeutic antibodies for drug targets identified in our own research. In addition, we have established collaborations and license agreements with many other leading pharmaceutical and biotechnology companies under which we receive fees and, in many cases, are eligible to receive milestone and royalty payments, in return for granting access to some of our technologies and discoveries for use in such companies' own drug discovery efforts.

Lexicon Genetics was incorporated in Delaware in July 1995, and commenced operations in September 1995. Our corporate headquarters are located at 8800 Technology Forest Place, The Woodlands, Texas 77381, and our telephone number is (281) 863-3000.

Our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 are made available free of charge on our corporate website located at www.lexicon genetics.com as soon as reasonably practicable after the filing of those reports with the Securities and Exchange Commission. Information found on our website should not be considered part of this annual report on Form 10 K.

Our Drug Discovery Process

Our drug discovery process begins with our Genome5000 program, in which we are using our gene knockout technology to discover the physiological and behavioral functions of 5,000 human genes through analysis of the corresponding knockout mouse models. Our Genome5000 efforts are focused on the discovery of the functions in mammalian physiology of proteins encoded by gene families that we consider to be pharmaceutically important, such as G-protein coupled, or GPCRs, and other receptors, kinases, ion channels, other key enzymes and secreted proteins. We have already completed our physiology- and behavior-based analysis of more than 30% of these 5,000 genes, and we expect to complete the analysis of the remaining genes by the end of 2007.

We use knockout mice – mice whose DNA has been altered to disrupt, or knock out, the function of the altered gene – to discover the physiological and behavioral effects that result from loss of functioning protein encoded by the disrupted gene. Historically, the study of such loss of function genetic alterations in mice has been a very powerful tool for understanding human genes because of the close similarity of gene function and physiology between mice and humans. With the genomic sequence of both organisms now available, it is noteworthy that approximately 99% of all human genes have a counterpart in the mouse genome. Our patented gene trapping and gene targeting technologies enable us to rapidly generate these knockout mice by altering the DNA of genes in a special variety of mouse cells, called embryonic stem cells, which can be cloned and used to generate mice with the altered gene. We employ an integrated platform of advanced medical technologies to systematically discover, *in vivo*, the physiological and behavioral functions and pharmaceutical utility of the genes we have knocked out and the potential drug targets they encode.

We believe that the power of our technology has been described in a large body of scientific literature which was summarized in a retrospective analysis that we performed of the 100 best selling drugs of 2001 and their targets, as modeled by the physiological characteristics of knockout mice. This analysis was published in the January 2003 issue of *Nature Reviews Drug Discovery*, a peer-reviewed scientific journal. In this analysis we concluded that in most cases there was a direct correlation between the physiological characteristics, or phenotypes, of knockout mice and the therapeutic effect of the 100 best-selling drugs of 2001.

We are working to discover potential small molecule drugs, therapeutic antibodies and therapeutic proteins for those *in vivo*-validated drug targets that we consider to have high pharmaceutical value. We have established an internal small molecule drug discovery program, in which we use our own sophisticated libraries of drug-like chemical compounds in high-throughput screening assays to identify "hits," or chemical compounds demonstrating activity, against these targets. We then employ our industrialized medicinal chemistry platform to optimize the potency and selectivity of these hits and to identify lead compounds for potential development. Our compound libraries include chemical scaffolds and building blocks that we designed based on analyses of the characteristics of drugs that have proven safe and effective in the past. When we identify a hit, we can rapidly reassemble these building blocks to create hundreds or thousands of variations around the structure of the initial compound, enabling us to accelerate our medicinal chemistry efforts.

In all of our drug discovery programs, we use the same physiological analysis technology platform that we use in the discovery of gene function to analyze the *in vivo* efficacy and safety profiles of drug candidates in mice. We believe that by focusing on the physiological functions and pharmaceutical utility of genes at the outset of the drug discovery process, we will increase our likelihood of success in discovering breakthrough treatments for human disease.

Our Technology

The scope of our gene knockout and evaluative technologies allows us to create and analyze knockout mice at a rate and on a scale that we believe is unmatched by our competitors. Combined with our state-of-the-art facilities, which are among the largest and most sophisticated of their kind in the world, these technologies provide us with what we believe to be a significant competitive advantage. The core elements of our technology platform include our patented technologies for the generation of knockout mice, our integrated platform of advanced medical technologies for the systematic and comprehensive biological analysis of *in vivo* physiology and our industrialized approach to medicinal chemistry and the generation of high-quality, drug-like compound libraries.

Gene Knockout Technologies

Gene Targeting. Our gene targeting technology, which is covered by eight issued patents that we have licensed, enables us to generate highly specific alterations in targeted genes. The technology uses a vector to replace DNA of a gene in a mouse embryonic stem cell through a process known as homologous recombination to disrupt the function of the targeted gene, permitting the generation of knockout mice. By using this technology in combination with one or more additional technologies, we are able to generate alterations that selectively disrupt, or conditionally regulate, the function of the targeted gene for the analysis of the gene's function in selected tissues, at selected stages in the animal's development or at selected times in the animal's life. We can also use this technology to replace the targeted gene with its corresponding human gene for use for preclinical research in our therapeutic discovery programs.

Gene Trapping. Our gene trapping technology, which is covered by six issued patents that we own, is a high-throughput method of generating knockout mouse clones that we invented. The technology uses genetically engineered retroviruses that infect mouse embryonic stem cells in vitro, integrate into the chromosome of the cell and disrupt the function of the gene into which it integrates, permitting the generation of knockout mice. This process also stimulates transcription of a non-protein producing portion of the trapped gene, using the cell's own splicing machinery to extract this transcript from the chromosome for automated DNA sequencing. This allows us to identify and catalogue each embryonic stem cell clone by DNA sequence from the trapped gene and to select embryonic stem cell clones by DNA sequence for the generation of knockout mice.

Physiological Analysis Technologies

We employ an integrated platform of advanced medical examinations to rapidly and systematically discover and catalogue the physiological and behavioral effects resulting from loss of gene function in the mouse knockouts we have generated using our gene trapping and gene targeting technologies. These examinations include many of the most sophisticated diagnostic technologies and tests currently available, many of which might be found in a major medical center. The following are included among the many tests we use::

- CAT-scans;
- magnetic resonance imaging, or MRI;
- complete blood cell analysis, including red and white blood cell counts;
- fluorescently activated cell sorting, or FACS, analysis;
- automated behavior analyses;
- nuclear magnetic resonance, or NMR, analysis; and.
- dual energy X-ray absorptiometry.

Each of these technologies has been adapted specifically for the analysis of mouse physiology. This state-of-the-art technology platform enables us to assess the consequences of loss of gene function in a living mammal across a wide variety of parameters relevant to human disease.

We believe that our medical center approach and the technology platform that makes it possible provide us with substantial advantages over other approaches to discover gene function and identify novel drug targets. In particular, we believe that the comprehensive nature of this approach allows us to uncover functions within the context of mammalian physiology that might be missed by more narrowly focused efforts. We also believe our approach is more likely to reveal those side effects that may be a direct result of inhibiting or otherwise modulating the drug target. Such target-related side effects might limit the utility of potential therapeutics directed at the drug target or prove to be unacceptable in light of the potential therapeutic benefit. We believe these advantages will contribute to better target selection and, therefore, to the success of our drug discovery and development efforts.

We employ the same physiological analysis technology platform that we use in the discovery of gene function to analyze the *in vivo* efficacy and safety profiles of therapeutic candidates in mice. We believe that this

approach will allow us, at an early stage, to identify and optimize therapeutic candidates for further preclinical and clinical development that demonstrate *in vivo* efficacy and to distinguish side effects caused by a specific compound from the target-related side effects that we defined using the same comprehensive series of tests.

Production and Analysis Infrastructure

Our facilities, which are among the largest and most sophisticated of their kind in the world, enable us to capitalize on our gene knockout and physiological analysis technologies by generating knockout mice and analyzing the physiological function of genes on an expansive scale. We are able to generate knockout mice for the large number of genes that we believe may be pharmaceutically important and analyze the physiology of each of those knockout mice by utilizing our broad range of medical technologies. Our state-of-the-art animal facilities, occupying a total of approximately 100,000 square feet, are designed to allow us to generate and analyze approximately 1,000 knockout mice per year. These facilities, completed in 1999 and 2002, respectively, were custom designed for the generation and analysis of knockout mice and are accredited by AAALAC International, or Association for Assessment and Accreditation of Laboratory Animal Care.

Our facilities also enable us to maintain in-house control over our entire *in vivo* validation process, from the generation of embryonic stem cell clones through the completion of *in vivo* analysis, in a specific pathogen-free environment. As part of our Genome5000 program, we have already examined the physiological functions of more than 1,500 genes and expect to complete our analysis of an aggregate of 5,000 genes by the end of 2007. We are not aware of any study approaching either the magnitude or breadth of our Genome5000 program, and we believe that the investment of significant resources over a period of several years would be required for any competitor to duplicate our gene knockout and physiological analysis capabilities. The scope of our gene knockout technology, combined with the size and sophistication of our facilities and our evaluative technologies, provides us with what we believe to be a significant competitive advantage.

Medicinal Chemistry Technology

We use solution-phase chemistry to generate diverse libraries of optically pure compounds that are targeted against the same pharmaceutically relevant gene families that we address in our Genome5000 program. These libraries are built using highly robust and scalable organic reactions that allow us to generate compound collections of great diversity and to specially tailor the compound collections to address various therapeutic target families. We design these libraries by analyzing the chemical structures of drugs that have been proven safe and effective against human disease and using that knowledge in the design of scaffolds and chemical building blocks for the generation of large numbers of new drug-like compounds. We can rapidly reassemble these building blocks to generate optimization libraries when we identify a hit against one of our *in vivo*-validated targets, enabling us to rapidly optimize those hits and accelerate our medicinal chemistry efforts.

Our medicinal chemistry technology is housed in a state-of-the-art 76,000 square foot facility in Hopewell, New Jersey. Our lead optimization chemistry groups are organized around specific discovery targets and work closely with their pharmaceutical biology counterparts in our facilities in The Woodlands, Texas. The medicinal chemists optimize lead compounds in order to select clinical candidates with the desired absorption, distribution, metabolism, excretion and physicochemical characteristics. We have the capability to profile our compounds using the same battery of *in vivo* assays that we use to characterize our drug discovery targets. This provides us with valuable detailed information relevant to the selection of the highest quality compounds for clinical development.

OmniBank Library and LexVision Database

We have capitalized on these core elements of our technology platform by developing our OmniBank library of gene knockout clones and our LexVision database cataloging the functions of certain *in vivo*-validated drug targets.

OmniBank Library. We have used our gene trapping technology in an automated process to create our OmniBank library of more than 200,000 frozen gene knockout embryonic stem cell clones, each identified by DNA sequence in a relational database. Each OmniBank mouse clone contains a single genetic mutation that can be used to produce knockout models of gene function. We estimate that our OmniBank library currently contains embryonic stem cell clones representing more than half of all genes in the mammalian genome and believe it is the largest

library of its kind. We believe our OmniBank library permits us to generate knockout mice at a significantly higher rate than is possible using other methods and, therefore, provides us with a significant strategic advantage in the discovery of *in vivo* gene function and the identification of novel drug targets.

LexVision Database. Our LexVision database is a comprehensive, relational database *of in vivo*-validated drug targets that catalogs the physiological functions of genes that we have knocked out using our gene targeting and gene trapping technologies. Our LexVision collaborators obtain non-exclusive access to the LexVision database for the discovery of small molecule drugs. We are committed to include 1,250 *in vivo*-validated drug targets in our LexVision database over a period of five years. As of December 31, 2003, we had deposited a total of 750 such targets in our LexVision database.

Research and Development Expenses

In 2003, 2002 and 2001, respectively, we incurred expenses of $82.2 million, $74.9 million and $53.4 million in company-sponsored research and development activities, including $5.0 million, $5.2 million, and $5.5 million, respectively, of stock-based compensation expense.

Our Commercialization Strategy

We are working both independently and through strategic collaborations and alliances with leading pharmaceutical and biotechnology companies, research institutes and academic institutions to commercialize our technology and turn our discoveries into drugs. Consistent with this approach, we intend to develop and commercialize certain of our drug discovery programs internally and retain exclusive rights to the benefits of such programs and to collaborate with third parties with respect to the development and commercialization of other drug discovery programs.

We apply our internal resources to our drug discovery programs in order to commercialize our technology and turn our discoveries into drugs. As we advance targets into our drug discovery programs, we allocate our internal resources in a manner designed to maximize our ability to commercialize opportunities presented by these programs. Our prioritization and allocation of internal resources among these programs are based on our expectations regarding their relative likelihood of success and the relevant medical market, as well as progress realized in our drug discovery efforts for the program. We revise our prioritization and resource allocation among programs as necessary in order to capitalize on new discoveries and opportunities.

Our collaboration and alliance strategy involves drug discovery alliances to discover and develop therapeutics based on our drug target discoveries, particularly when the alliance enables us to obtain access to technology and expertise that we do not possess internally or is complementary to our own. These strategic collaborations, as well as our licenses with pharmaceutical and biotechnology companies, research institutes and academic institutions, enable us to generate near-term revenues in exchange for access to some of our technologies and discoveries for use by these third parties in their own drug discovery efforts. These collaborations and licenses also offer us the potential, in many cases, to receive milestone payments and royalties on products that our collaborators and licensees develop using our technology.

Alliances, Collaborations and Licenses

Drug Discovery Alliances

We have entered into the following alliances for the discovery and development of therapeutics based on our *in vivo* drug target discovery efforts:

Bristol-Myers Squibb Company. We established a drug discovery alliance with Bristol-Myers Squibb in December 2003 to discover, develop and commercialize small molecule drugs in the neuroscience field. In the alliance, we are contributing a number of neuroscience drug discovery programs at various stages of development. We will continue to use our gene knockout technology to identify additional drug targets with promise in the neuroscience field. For those targets that are selected for the alliance, we and Bristol-Myers Squibb will work together, on an exclusive basis, to identify, characterize and carry out the preclinical development of small molecule drugs, and will share equally both in the costs and in the work attributable to those efforts. As drugs resulting from

the alliance enter clinical trials, Bristol-Myers Squibb will have the first option to assume full responsibility for clinical development and commercialization.

We received an upfront payment under the agreement and are entitled to receive research funding during the initial three years of the agreement. We may receive additional cash payments if we exceed specified research productivity levels. We will also receive clinical and regulatory milestone payments for each drug target for which Bristol-Myers Squibb develops a drug under the alliance and royalties on sales of drugs commercialized by Bristol-Myers Squibb. The target discovery portion of the alliance has a term of three years, subject to Bristol-Myers Squibb's option to extend the discovery portion of the alliance for an additional two years in exchange for further research funding payments.

Genentech, Inc. We established a drug discovery alliance with Genentech in December 2002 to discover novel therapeutic proteins and antibody targets. Under the alliance agreement, we are using our target validation technologies to discover the functions of secreted proteins and potential antibody targets identified through Genentech's internal drug discovery research. Genentech will have exclusive rights to the discoveries resulting from the collaboration for the research, development and commercialization of therapeutic proteins and antibodies. We will retain certain other rights to those discoveries, including non-exclusive rights, along with Genentech, for the development and commercialization of small molecule drugs. We received an up-front payment and are entitled to receive performance payments for our work in the collaboration as it is completed. We are also entitled to receive milestone payments and royalties on sales of therapeutic proteins and antibodies for which Genentech obtains exclusive rights. The agreement has an expected collaboration term of three years.

Abgenix, Inc. We established a drug discovery alliance with Abgenix in July 2000 to discover novel therapeutic antibodies using our target validation technologies and Abgenix's technology for generating fully human monoclonal antibodies. We and Abgenix expanded and extended the alliance in January 2002, with the intent of accelerating the selection of *in vivo* validated antigens for antibody discovery and the development and commercialization of therapeutic antibodies based on those targets. Under the alliance agreement, we and Abgenix will each have the right to obtain exclusive commercialization rights, including sublicensing rights, for an equal number of qualifying therapeutic antibodies, and will each receive milestone payments and royalties on sales of therapeutic antibodies from the alliance that are commercialized by the other party or a third-party sublicensee. Each party bears its own expenses under the alliance. The expanded alliance also provides us with access to Abgenix's XenoMouse® technology for use in some of our own drug discovery programs. The collaboration period, as extended, expires in July 2004, subject to the right of the parties to extend the term by mutual agreement for up to three additional one-year periods.

Incyte Corporation. We established a drug discovery alliance with Incyte in June 2001 to discover novel therapeutic proteins using our target validation technologies in the discovery of the functions of secreted proteins identified in Incyte's LifeSeq® Gold database. The alliance agreement provides that up to 250 secreted proteins will be jointly selected for functional characterization, and we expect 150 to be selected in the first three years. Under the alliance agreement, we receive research funding from Incyte during the term of the collaboration. In addition, we and Incyte will each have the right to obtain exclusive commercialization rights, including sublicensing rights, for an equal number of qualifying therapeutic proteins, and will each receive milestone payments and royalties on sales of therapeutic proteins from the alliance that are commercialized by the other party or a third-party sublicensee. The collaboration period will terminate on June 27, 2004.

LexVision Collaborations

We have entered into the following collaborations for access to our LexVision database of *in vivo*-validated drug targets:

Bristol-Myers Squibb Company. We established a LexVision collaboration with Bristol Myers Squibb in September 2000, under which Bristol-Myers Squibb has non-exclusive access to our LexVision database and OmniBank library for the discovery of small molecule drugs. We receive annual access fees under this agreement and are entitled to receive milestone payments and royalties on products Bristol-Myers Squibb develops using our technology. The collaboration period extends through December 31, 2005, although either party may terminate the collaboration period on December 31, 2004.

Incyte Corporation. We established a LexVision collaboration with Incyte in June 2001, under which Incyte has non-exclusive access to our LexVision database and OmniBank library for the discovery of small molecule drugs. We receive annual access fees under this agreement, and are entitled to receive milestone payments and royalties on products Incyte develops using our technology. The collaboration period will terminate on June 27, 2004.

Target Validation Collaborations

We have established target validation collaboration agreements with a number of leading pharmaceutical and biotechnology companies. Under these collaboration agreements, we generate and, in some cases, analyze knockout mice for genes requested by the collaborator. In addition, we grant non-exclusive licenses to the collaborator for use of the knockout mice in its internal drug discovery programs and, if applicable, analysis data that we generate under the agreement. Some of these agreements also provide for non-exclusive access to our OmniBank database. We receive fees for knockout mice under these agreements. In some cases, these agreements also provide for annual subscription fees, annual minimum commitments and the potential for royalties on products that our collaborators discover or develop using our technology.

We are generally not pursuing renewals of these agreements as they expire, and are entering into new agreements on a very limited basis.

e-Biology Collaboration Program

We provide access to our OmniBank database through the Internet to subscribing researchers at academic and non-profit research institutions. Our bioinformatics software allows subscribers to mine our OmniBank database for genes of interest, and we permit subscribers to acquire OmniBank knockout mice or embryonic stem cells on a non-exclusive basis in our e-Biology collaboration program. We receive fees for knockout mice or embryonic stem cells provided to collaborators in this program and, with participating institutions, rights to license inventions or to receive royalties on products discovered using our materials. In all cases we retain rights to use the same OmniBank knockout mice in our own gene function research and with commercial collaborators. We have entered into more than 200 agreements under our e-Biology collaboration program with researchers at leading institutions throughout the world.

Technology Licenses

We have granted non-exclusive, internal research-use sublicenses under certain of our gene targeting patent rights to a total of 12 leading pharmaceutical and biotechnology companies. Many of these agreements extend for the life of the patents. Others have terms of one to three years, in some cases with provisions for subsequent renewals. We typically receive up-front license fees and, in some cases, receive additional license fees or milestone payments on products that the sublicensee discovers or develops using our technology.

Patents and Proprietary Rights

We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that those rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. Accordingly, patents and other proprietary rights are an essential element of our business. We seek patent protection for the genes, proteins and drug targets that we discover. Specifically, we seek patent protection for:

- the sequences of genes that we believe to be novel, including full-length human genes and partial human and mouse gene sequences, the proteins they encode and their predicted utility as a drug target or therapeutic protein;
- the utility of genes and the drug targets or therapeutic proteins they encode based on our discoveries of their biological functions using knockout mice;
- drug discovery assays for our *in vivo*-validated targets;
- chemical compounds and their use in treating human diseases and conditions; and

- various enabling technologies in the fields of mutagenesis, embryonic stem cell manipulation and transgenic or knockout mice.

We own or have exclusive rights to six issued United States patents that are directed to our gene trapping technology, 31 issued United States patents that are directed to full-length sequences of potential drug targets identified in our gene discovery programs, and five issued United States patents that are directed to specific knockout mice and discoveries of the functions of genes made using knockout mice. We have licenses under 64 additional United States patents, and corresponding foreign patents and patent applications, directed to gene targeting, gene trapping and genetic manipulation of mouse embryonic stem cells. These include patents to which we hold exclusive rights in certain fields, including a total of eight United States patents directed to the use of gene targeting technologies known as positive-negative selection and isogenic DNA targeting, as well as patents directed to the use of site specific genetic recombination technology known as Cre/lox technology.

We have filed or have exclusive rights to more than 600 pending patent applications in the United States Patent and Trademark Office, the European Patent Office, the national patent offices of other foreign countries or under the Patent Cooperation Treaty, directed to our gene trapping technology, the DNA sequences of genes, the uses of specific drug targets, drug discovery assays, and other products and processes. Collectively, these patent applications are directed to, among other things, approximately 200 full-length human gene sequences, more than 50,000 partial human gene sequences, and more than 45,000 knockout mouse clones and corresponding mouse gene sequence tags. Patents typically have a term of no longer than 20 years from the date of filing.

As noted above, we hold rights to a number of these patents and patent applications under license agreements with third parties. In particular, we license our gene targeting technologies from GenPharm International, Inc. and our Cre/lox technology from DuPont Pharmaceuticals Company. Many of these licenses are nonexclusive, although some are exclusive in specified fields. Most of the licenses, including those from GenPharm and DuPont, have terms that extend for the life of the licensed patents. In the case of our license from GenPharm, the license generally is exclusive in specified fields, subject to specific rights held by third parties, and we are permitted to grant sublicenses.

All of our employees, consultants and advisors are required to execute a proprietary information agreement upon the commencement of employment or consultation. In general, the agreement provides that all inventions conceived by the employee or consultant, and all confidential information developed or made known to the individual during the term of the agreement, shall be our exclusive property and shall be kept confidential, with disclosure to third parties allowed only in specified circumstances. We cannot assure you, however, that these agreements will provide useful protection of our proprietary information in the event of unauthorized use or disclosure of such information.

Competition

The biotechnology and pharmaceutical industries are highly competitive and characterized by rapid technological change. We face significant competition in each of the aspects of our business from for-profit companies such as Human Genome Sciences, Inc., Millennium Pharmaceuticals, Inc. and Exelixis, Inc., among others, many of which have substantially greater financial, scientific and human resources than we do. In addition, the Human Genome Project and a large number of universities and other not-for-profit institutions, many of which are funded by the U.S. and foreign governments, are also conducting research to discover genes and their functions.

While we are not aware of any other commercial entity that is developing large-scale gene trap mutagenesis in ES cells, we face competition from entities using traditional knockout mouse technology and other technologies. Several companies, including Regeneron Pharmaceuticals, Inc. and DNX (a subsidiary of Xenogen Corporation), and a large number of academic institutions create knockout mice for third parties using these more traditional methods, and a number of companies create knockout mice for use in their own research.

Many of our competitors in drug discovery and development have substantially greater research and product development capabilities and financial, scientific, marketing and human resources than we do. As a result, our competitors may succeed in developing products earlier than we do, obtaining approvals from the FDA or other regulatory agencies for those products more rapidly than we do, or developing products that are more effective than those we propose to develop. Similarly, our collaborators face similar competition from other competitors who may

succeed in developing products more quickly, or developing products that are more effective, than those developed by our collaborators. We expect that competition in this field will intensify.

Government Regulation

Regulation of Pharmaceutical Products

The development, manufacture and sale of any pharmaceutical or biological products developed by us or our collaborators will be subject to extensive regulation by United States and foreign governmental authorities, including federal, state and local authorities. In the United States, new drugs are subject to regulation under the Federal Food, Drug and Cosmetic Act and the regulations promulgated thereunder, or the FDC Act, and biological products are subject to regulation both under certain provisions of the FDC Act and under the Public Health Services Act and the regulations promulgated thereunder, or the PHS Act. The FDA regulates, among other things, the development, preclinical and clinical testing, manufacture, safety, efficacy, record keeping, reporting, labeling, storage, approval, advertising, promotion, sale, distribution and export of drugs and biologics. The process of obtaining FDA approval has historically been costly and time-consuming.

The standard process required by the FDA before a pharmaceutical or biological product may be marketed in the United States includes:

- preclinical laboratory and animal tests performed under the FDA's current Good Laboratory Practices regulations;
- submission to the FDA of an Investigational New Drug application, or IND, which must become effective before human clinical trials may commence;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug or biologic in our intended application;
- for drugs, submission of a New Drug Application, or NDA, and, for biologics, submission of a Biologic License Application, or BLA, with the FDA; and
- FDA approval of the NDA or BLA prior to any commercial sale or shipment of the product.

Among other things, the FDA reviews an NDA to determine whether a product is safe and effective for its intended use and a BLA to determine whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued safety, purity and potency.

In addition to obtaining FDA approval for each product, each drug or biologic manufacturing establishment must be inspected and approved by the FDA. All manufacturing establishments are subject to inspections by the FDA and by other federal, state and local agencies and must comply with current Good Manufacturing Practices requirements. Non-compliance with these requirements can result in, among other things, total or partial suspension of production, failure of the government to grant approval for marketing and withdrawal, suspension or revocation of marketing approvals.

Preclinical studies can take several years to complete, and there is no guarantee that an IND based on those studies will become effective to even permit clinical testing to begin. Once clinical trials are initiated, they take years to complete. In addition, the FDA may place a clinical trial on hold or terminate it if, among other reasons, the agency concludes that clinical subjects are being exposed to an unacceptable health risk. After completion of clinical trials of a new drug or biologic product, FDA marketing approval of the NDA or BLA must be obtained. An NDA or BLA, depending on the submission, must contain, among other things, information on chemistry, manufacturing controls and potency and purity, non-clinical pharmacology and toxicology, human pharmacokinetics and bioavailability and clinical data. The process of obtaining approval requires substantial time and effort and there is no assurance that the FDA will accept the NDA or BLA for filing and, even if filed, that approval will be granted. The FDA's approval of an NDA or BLA can take years and can be delayed if questions arise. Limited

indications for use or other conditions could also be placed on any approvals that could restrict the commercial applications of products.

Once the FDA approves a product, a manufacturer must provide certain updated safety and efficacy information. Product changes as well as certain changes in a manufacturing process or facility would necessitate additional FDA review and approval. Other post-approval changes may also necessitate further FDA review and approval. Additionally, a manufacturer must meet other requirements including those related to adverse event reporting and record keeping.

Violations of the FDC Act, the PHS Act or regulatory requirements may result in agency enforcement action, including voluntary or mandatory recall, license suspension or revocation, product seizure, fines, injunctions and civil criminal penalties.

In addition to regulatory approvals that must be obtained in the United States, a drug or biological product is also subject to regulatory approval in other countries in which it is marketed, although the requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary widely from country to country. No action can be taken to market any drug or biological product in a country until the regulatory authorities in that country have approved an appropriate application. FDA approval does not assure approval by other regulatory authorities. The current approval process varies from country to country, and the time spent in gaining approval varies from that required for FDA approval. In some countries, the sale price of a drug or biological product must also be approved. The pricing review period often begins after marketing approval is granted. Even if a foreign regulatory authority approves a drug or biological product, it may not approve satisfactory prices for the product.

Other Regulations

In addition to the foregoing, our business is and will be subject to regulation under various state and federal environmental laws, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act and the Toxic Substances Control Act. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in and wastes generated by our operations. We believe that we are in material compliance with applicable environmental laws and that our continued compliance with these laws will not have a material adverse effect on our business. We cannot predict, however, whether new regulatory restrictions on the production, handling and marketing of biotechnology products will be imposed by state or federal regulators and agencies or whether existing laws and regulations will adversely affect us in the future.

Employees and Consultants

We believe that our success will be based on, among other things, achieving and retaining scientific and technological superiority and identifying and retaining capable management. We have assembled a highly qualified team of scientists as well as executives with extensive experience in the biotechnology industry.

As of March 1, 2004, we employed 637 persons, of whom 136 hold M.D., Ph.D. or D.V.M. degrees and another 86 hold other advanced degrees. We believe that our relationship with our employees is good.

Risk Factors

Our business is subject to risks and uncertainties, including those described below:

Risks Related to Our Business

We have a history of net losses, and we expect to continue to incur net losses and may not achieve or maintain profitability.

We have incurred net losses since our inception, including net losses of $35.2 million for the year ended December 31, 2001, $59.7 million for the year ended December 31, 2002 and $64.2 million for the year ended December 31, 2003. As of December 31, 2003, we had an accumulated deficit of $213.9 million. We are unsure when we will become profitable, if ever. The size of our net losses will depend, in part, on the rate of growth, if any, in our revenues and on the level of our expenses.

We derive substantially all of our revenues from drug discovery alliances, subscriptions to our LexVision database and our OmniBank library and collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice and technology licenses, and will continue to do so for the foreseeable future. Our future revenues from alliances, database subscriptions and collaborations are uncertain because our existing agreements have fixed terms or relate to specific projects of limited duration. Our future revenues from technology licenses are uncertain because they depend, in part, on securing new agreements. Our ability to secure future revenue-generating agreements will depend upon our ability to address the needs of our potential future collaborators and licensees, and to negotiate agreements that we believe are in our long-term best interests. We may determine that our interests are better served by retaining rights to our discoveries and advancing our therapeutic programs to a later stage, which could limit our near-term revenues. Given the early-stage nature of our operations, we do not currently derive any revenues from sales of pharmaceuticals.

A large portion of our expenses is fixed, including expenses related to facilities, equipment and personnel. In addition, we expect to spend significant amounts to fund research and development and to enhance our core technologies. As a result, we expect that our operating expenses will continue to increase significantly in the near term and, consequently, we will need to generate significant additional revenues to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

We will need additional capital in the future and, if it is not available, we will have to curtail or cease operations.

Our future capital requirements will be substantial and will depend on many factors, including:

- our ability to obtain alliance, database subscription, collaboration and technology license agreements;
- the amount and timing of payments under such agreements;
- the level and timing of our research and development expenditures;
- market acceptance of products that we successfully develop and commercially launch; and
- the resources we devote to developing and supporting such products.

Our capital requirements will increase substantially to the extent we advance potential therapeutics into preclinical and clinical development. Our capital requirements will also be affected by any expenditures we make in connection with license agreements and acquisitions of and investments in complementary products and technologies.

We anticipate that our existing capital resources and the revenues we expect to derive from drug discovery alliances, subscriptions to our databases, collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice and technology licenses will enable us to fund our currently planned operations for at least the next two years. However, we may generate less revenues than we expect, and changes may occur that would consume available capital resources more rapidly than we expect. If our capital resources are insufficient to meet future capital requirements, we will have to raise additional funds to continue the development of our technologies and complete the commercialization of products, if any, resulting from our technologies. We cannot be certain that additional financing, whether debt or equity, will be available in amounts or on terms acceptable to us, if at all. We may be unable to raise sufficient additional capital; if so, we will have to curtail or cease operations.

We are an early-stage company, and we may not successfully develop or commercialize any therapeutics or drug targets that we have identified.

Our business strategy of using our technology platform and, specifically, the discovery of the functions of genes using knockout mice to select promising drug targets and developing and commercializing drugs based on our discoveries, in significant part through collaborations and alliances, is unproven. Our success will depend upon our ability to successfully develop potential therapeutics for drug targets we consider to have pharmaceutical value, whether on our own or through collaborations, and to select an appropriate commercialization strategy for each potential therapeutic we choose to pursue.

Biotechnology and pharmaceutical companies have successfully developed and commercialized only a limited number of genomics-derived pharmaceutical products to date. We have not proven our ability to develop or commercialize therapeutics or drug targets that we identify, nor have we advanced any drug candidates to clinical trials. We do not know that any pharmaceutical products based on our drug target discoveries can be successfully commercialized. In addition, we may experience unforeseen technical complications in the processes we use to generate knockout mice, conduct *in vivo* analyses, generate compound libraries, develop screening assays for drug targets or conduct screening of compounds against those drug targets. These complications could materially delay or limit the use of those resources, substantially increase the anticipated cost of generating them or prevent us from implementing our processes at appropriate quality and throughput levels. Finally, the information that we learn from knockout mice may prove not to be useful in identifying pharmaceutically-important drug targets or safe and effective therapies.

We face substantial competition in the discovery of the DNA sequences of genes and their functions and in our drug discovery and product development efforts.

We face significant competition in each of the aspects of our business from companies such as Human Genome Sciences, Inc., Millennium Pharmaceuticals, Inc., Exelixis, Inc. and other similar companies that engage in programs for the discovery and development of drugs utilizing a genetics-based approach to target discovery and validation.

There are a finite number of genes in the human genome, and we believe that the majority of such genes have been identified and that virtually all will be identified within the next few years. We face substantial competition in our efforts to discover and patent the sequence and other information derived from such genes from entities using alternative, and in some cases higher volume and larger scale, approaches for the same purpose. These alternative approaches may ultimately prove superior, in some or all respects, to the use of knockout mice.

We also face competition from other companies in our efforts to discover the functions of genes. The Human Genome Project and a large number of universities and other not-for-profit institutions, many of which are funded by the United States and foreign governments, are also conducting research to discover the functions of genes. Competitors could discover and establish patents on genes or gene products that we identify as promising drug targets, which might hinder or prevent our ability to capitalize on such targets.

We face significant competition from other companies, as well as from universities and other not-for-profit institutions, in our drug discovery and product development efforts. Many of our competitors have substantially greater financial, scientific and human resources than we do. As a result, our competitors may succeed in developing products earlier than we do, obtaining regulatory approvals faster than we do and developing products that are more effective or safer than any that we may develop.

We rely heavily on our collaborators to develop and commercialize pharmaceutical products based on genes that we identify as promising candidates for development as drug targets and our collaborators' efforts may fail to yield pharmaceutical products on a timely basis, if at all.

It is our strategy to develop drug candidates on our own as well as developing drug candidates in collaboration with third parties, particularly when such collaborations enable us to obtain access to technology and expertise that we do not possess internally or is complementary to our own.

Since we do not currently possess the resources necessary to develop, obtain approvals for or commercialize potential pharmaceutical products based on all of the genes that we identify as promising candidates for development as drug targets, we must enter into collaborative arrangements to develop and commercialize some of these products. We have limited or no control over the resources that any collaborator may devote to this effort. Any of our present or future collaborators may not perform their obligations as expected. These collaborators may breach or terminate their agreements with us or otherwise fail to conduct product discovery, development or commercialization activities successfully or in a timely manner. Further, our collaborators may elect not to develop pharmaceutical products arising out of our collaborative arrangements or may not devote sufficient resources to the development, approval, manufacture, marketing or sale of these products. If any of these events occurs, we may not be able to develop or commercialize potential pharmaceutical products.

Some of our existing collaboration agreements contain, and collaborations that we enter into in the future may contain, exclusivity agreements or other limitations on our activities. These agreements may have the effect of limiting our flexibility and may cause us to forego attractive business opportunities.

Cancellations by or conflicts with our collaborators could harm our business.

Our alliance and collaboration agreements may not be renewed and may be terminated in the event either party fails to fulfill its obligations under these agreements. Failures to renew or cancellations by collaborators could mean a significant loss of revenues and could harm our reputation in the business and scientific communities.

In addition, we may pursue opportunities in fields that could conflict with those of our collaborators. Moreover, disagreements could arise with our collaborators over rights to our intellectual property or our rights to share in any of the future revenues of compounds or therapeutic approaches developed by our collaborators. These kinds of disagreements could result in costly and time consuming litigation. Conflicts with our collaborators could reduce our ability to obtain future collaboration agreements and could have a negative impact on our relationship with existing collaborators, materially impairing our business and revenues. Some of our collaborators are also potential competitors or may become competitors in the future. Our collaborators could develop competing products, preclude us from entering into collaborations with their competitors or terminate their agreements with us prematurely. Any of these events could harm our product development efforts.

We may be unsuccessful in developing and commercializing pharmaceutical products on our own.

Our ability to develop and commercialize pharmaceutical products on our own will depend on our ability to internally develop preclinical, clinical, regulatory and sales and marketing capabilities, or enter into arrangements with third parties to provide these functions. It will be expensive and will require significant time for us to develop these capabilities internally. We may not be successful in developing these capabilities or entering into agreements with third parties on favorable terms, or at all. Further, our reliance upon third parties for these capabilities could reduce our control over such activities and could make us dependent upon these parties. Our inability to develop or contract for these capabilities would significantly impair our ability to develop and commercialize pharmaceutical products.

We lack the capability to manufacture compounds for preclinical studies, clinical trials or commercial sales and will rely on third parties to manufacture our potential products, which may harm or delay our product development and commercialization efforts.

We currently do not have the manufacturing capabilities or experience necessary to produce materials for preclinical studies, clinical trials or commercial sales and intend to rely on collaborators and third-party contractors to produce such materials. We will rely on selected manufacturers to deliver materials on a timely basis and to comply with applicable regulatory requirements, including the current Good Manufacturing Practices of the United States Food and Drug Administration, or FDA, which relate to manufacturing and quality control activities. These manufacturers may not be able to produce material on a timely basis or manufacture material at the quality level or in the quantity required to meet our development timelines and applicable regulatory requirements. In addition, there are a limited number of manufacturers that operate under the FDA's current Good Manufacturing Practices and that are capable of producing such materials, and we may experience difficulty finding manufacturers with adequate capacity for our needs. If we are unable to contract for the production of sufficient quantity and quality of materials on acceptable terms, our product development and commercialization efforts may be delayed. Moreover, noncompliance with the FDA's current Good Manufacturing Practices can result in, among other things, fines, injunctions, civil and criminal penalties, product recalls or seizures, suspension of production, failure to obtain marketing approval and withdrawal, suspension or revocation of marketing approvals.

We may engage in future acquisitions, which may be expensive and time consuming and from which we may not realize anticipated benefits.

We may acquire additional businesses, technologies and products if we determine that these businesses, technologies and products complement our existing technology or otherwise serve our strategic goals. We currently have no commitments or agreements with respect to any acquisitions. If we do undertake any transactions of this sort, the process of integrating an acquired business, technology or product may result in operating difficulties and

expenditures and may not be achieved in a timely and non-disruptive manner, if at all, and may absorb significant management attention that would otherwise be available for ongoing development of our business. If we fail to integrate acquired businesses, technologies or products effectively or if key employees of an acquired business leave, the anticipated benefits of the acquisition would be jeopardized. Moreover, we may never realize the anticipated benefits of any acquisition, such as increased revenues and earnings or enhanced business synergies. Future acquisitions could result in potentially dilutive issuances of our equity securities, the incurrence of debt and contingent liabilities and amortization expenses related to intangible assets, which could materially impair our results of operations and financial condition.

If we lose our key personnel or are unable to attract and retain additional personnel, we may be unable to pursue collaborations or develop our own products.

We are highly dependent on Arthur T. Sands, M.D., Ph.D., our president and chief executive officer, as well as other principal members of our management and scientific staff. The loss of any of these personnel could negatively impact our business, financial condition or results of operations and could inhibit our product development and commercialization efforts. Although we have entered into employment agreements with some of our key personnel, including Dr. Sands, these employment agreements are at will. In addition, not all key personnel have employment agreements.

Recruiting and retaining qualified scientific personnel to perform future research and development work will be critical to our success. Competition for experienced scientists is intense. Failure to recruit and retain scientific personnel on acceptable terms could prevent us from achieving our business objectives.

Because all of our target validation operations are located at a single facility, the occurrence of a disaster could significantly disrupt our business.

Our OmniBank mouse clone library and its backup are stored in liquid nitrogen freezers located at our facility in The Woodlands, Texas, and our knockout mouse research operations are carried out entirely at the same facility. While we have developed redundant and emergency backup systems to protect these resources and the facilities in which they are stored, they may be insufficient in the event of a severe fire, flood, hurricane, tornado, mechanical failure or similar disaster. If such a disaster significantly damages or destroys the facility in which these resources are maintained, our business could be disrupted until we could regenerate the affected resources and, as a result, our stock price could decline. Our business interruption insurance may not be sufficient to compensate us in the event of a major interruption due to such a disaster.

Our quarterly operating results have been and likely will continue to fluctuate, and we believe that quarter-to-quarter comparisons of our operating results are not a good indication of our future performance.

Our operating results and, in particular, our ability to generate additional revenues are dependent on many factors, including:

- our ability to establish new research collaborations and technology licenses, and the timing of such arrangements;
- the expiration or other termination of database subscriptions and research collaborations with our collaborators, which may not be renewed or replaced;
- the success rate of our discovery efforts leading to opportunities for new research collaborations and licenses, as well as milestone payments and royalties;
- the timing and willingness of our collaborators to commercialize pharmaceutical products that would result in milestone payments and royalties; and
- general and industry-specific economic conditions, which may affect our and our collaborators' research and development expenditures.

Because of these and other factors, including the risks and uncertainties described in this section, our quarterly operating results have fluctuated in the past and are likely to do so in the future. Due to the likelihood of fluctuations in our revenues and expenses, we believe that quarter-to-quarter comparisons of our operating results are not a good indication of our future performance.

Risks Related to Our Industry

Our ability to patent our inventions is uncertain because patent laws and their interpretation are highly uncertain and subject to change.

The patent positions of biotechnology firms generally are highly uncertain and involve complex legal and factual questions that will determine who has the right to develop or use a particular technology or product. No clear policy has emerged regarding the scope of protection provided in biotechnology patents. The biotechnology patent situation outside the United States is similarly uncertain. Changes in, or different interpretations of, patent laws in the United States or other countries might allow others to use our inventions or to develop and commercialize any technologies or products that we may develop without any compensation to us. We anticipate that these uncertainties will continue for a significant period of time.

Our patent applications may not result in patent rights and, as a result, the protection afforded to our scientific discoveries may be insufficient.

Our disclosures in our patent applications may not be sufficient to meet the statutory requirements for patentability. Our ability to obtain patent protection based on genes or gene sequences will depend, in part, upon identification of a use for the gene or gene sequences sufficient to meet the statutory requirements that an invention have utility and that a patent application enable one to make and use the invention. While the United States Patent and Trademark Office has issued guidelines for the examination of patent applications claiming gene sequences, their therapeutic uses and novel proteins encoded by such genes, the impact of these guidelines is uncertain and may delay or negatively affect our patent position. Furthermore, biologic data in addition to that obtained by our current technologies may be required for issuance of patents covering any potential human therapeutic products that we may develop. If required, obtaining such biologic data could delay, add substantial costs to, or affect our ability to obtain patent protection for such products. There can be no assurance that the disclosures in our current or future patent applications, including those we may file with our collaborators, will be sufficient to meet these requirements. Even if patents are issued, there may be current or future uncertainty as to the scope of the coverage or protection provided by any such patents.

Some court decisions indicate that disclosure of a partial sequence may not be sufficient to support the patentability of a full-length sequence. These decisions have been confirmed by recent pronouncements of the United States Patent and Trademark Office. We believe that these court decisions and the uncertain position of the United States Patent and Trademark Office present a significant risk that the United States Patent and Trademark Office will not issue patents based on patent disclosures limited to partial gene sequences. In addition, we are uncertain about the scope of the coverage, enforceability and commercial protection provided by any patents issued primarily on the basis of gene sequence information.

If other companies and institutions obtain patents relating to our drug target or product candidate discoveries, we may be unable to obtain patents for our inventions based upon those discoveries and may be blocked from using or developing some of our technologies and products.

Many other entities have filed or may file patent applications on genes or gene sequences, uses of those genes or gene sequences, gene products and drug targets, assays for identifying potential therapeutic products, potential therapeutic products and methods of treatment which are identical or similar to some of our filings. Some of these applications attempt to assign biologic function to the genes and proteins based on predictions of function based upon similarity to other genes and proteins or patterns of gene expression. There is the significant possibility that patents claiming the functional uses of such genes and gene products will be issued to our competitors based on such information. If any such patents are issued to other entities, we will be unable to obtain patent protection for the same or similar discoveries that we make. Moreover, we may be blocked from using or developing some of our existing or proposed technologies and products, or may be required to obtain a license that may not be available on reasonable terms, if at all.

Alternatively, the United States Patent and Trademark Office could decide competing patent claims in an interference proceeding. Any such proceeding would be costly, and we may not prevail. In this event, the prevailing party may require us or our collaborators to stop using a particular technology or pursuing a potential product or may require us to negotiate a license arrangement to do so. We may not be able to obtain a license from the prevailing party on acceptable terms, or at all.

The Human Genome Project, as well as many companies and institutions, have identified genes and deposited partial gene sequences in public databases and are continuing to do so. The entire human genome and the entire mouse genome are now publicly known. These public disclosures might limit the scope of our claims or make unpatentable subsequent patent applications on partial or full-length genes or their uses.

Issued or pending patents may not fully protect our discoveries, and our competitors may be able to commercialize technologies or products similar to those covered by our issued or pending patents.

Pending patent applications do not provide protection against competitors because they are not enforceable until they issue as patents. Issued patents may not provide commercially meaningful protection. If anyone infringes upon our or our collaborators' patent rights, enforcing these rights may be difficult, costly and time-consuming and, as a result, it may not be cost-effective or otherwise expedient to pursue litigation to enforce those patent rights. Others may be able to design around these patents or develop unique products providing effects similar to any products that we may develop. Other companies or institutions may challenge our or our collaborators' patents or independently develop similar products that could result in an interference proceeding in the United States Patent and Trademark Office or a legal action.

In addition, others may discover uses for genes, drug targets or therapeutic products other than those covered in our issued or pending patents, and these other uses may be separately patentable. Even if we have a patent claim on a particular gene, drug target or therapeutic product, the holder of a patent covering the use of that gene, drug target or therapeutic product could exclude us from selling a product that is based on the same use of that product.

We may be involved in patent litigation and other disputes regarding intellectual property rights and may require licenses from third parties for our discovery and development and planned commercialization activities. We may not prevail in any such litigation or other dispute or be able to obtain required licenses.

Our discovery and development efforts as well as our potential products and those of our collaborators may give rise to claims that they infringe the patents of others. This risk will increase as the biotechnology industry expands and as other companies and institutions obtain more patents covering the sequences, functions and uses of genes and the drug targets they encode. We are aware that other companies and institutions have conducted research on many of the same targets that we have identified and have filed patent applications potentially covering many of the genes and encoded drug targets that are the focus of our drug discovery programs. In some cases, patents have issued from these applications. In addition, many companies and institutions have well-established patent portfolios directed to common techniques, methods and means of developing, producing and manufacturing pharmaceutical products. Other companies or institutions could bring legal actions against us or our collaborators for damages or to stop us or our collaborators from engaging in certain discovery or development activities or from manufacturing and marketing any resulting therapeutic products. If any of these actions are successful, in addition to our potential liability for damages, these entities would likely require us or our collaborators to obtain a license in order to continue engaging in the infringing activities or to manufacture or market the resulting therapeutic products or may force us to terminate such activities or manufacturing and marketing efforts.

We may need to pursue litigation against others to enforce our patents and intellectual property rights and may be the subject of litigation brought by third parties to enforce their patent and intellectual property rights. In addition, we may become involved in litigation based on intellectual property indemnification undertakings that we have given to certain of our collaborators. Patent litigation is expensive and requires substantial amounts of management attention. The eventual outcome of any such litigation is uncertain and involves substantial risks.

We believe that there will continue to be significant litigation in our industry regarding patent and other intellectual property rights. We have expended and many of our competitors have expended and are continuing to expend significant amounts of time, money and management resources on intellectual property litigation. If we

become involved in future intellectual property litigation, it could consume a substantial portion of our resources and could negatively affect our results of operations.

Furthermore, in light of recent United States Supreme Court precedent, our ability to enforce our patents against state agencies, including state sponsored universities and research laboratories, is limited by the Eleventh Amendment to the United States Constitution. In addition, opposition by academicians and the government may hamper our ability to enforce our patents against academic or government research laboratories. Finally, enforcement of our patents may cause our reputation in the academic community to be injured.

We use intellectual property that we license from third parties. If we do not comply with these licenses, we could lose our rights under them.

We rely, in part, on licenses to use certain technologies that are important to our business, such as gene targeting and conditional knockout technologies. We do not own the patents that underlie these licenses. Our rights to use these technologies and practice the inventions claimed in the licensed patents are subject to our abiding by the terms of those licenses and the licensors not terminating them. We are currently in compliance with all requirements of these licenses. In many cases, we do not control the filing, prosecution or maintenance of the patent rights to which we hold licenses and rely upon our licensors to prosecute infringement of those rights. The scope of our rights under our licenses may be subject to dispute by our licensors or third parties.

We have not sought patent protection outside of the United States for some of our inventions, and some of our licensed patents only provide coverage in the United States. As a result, our international competitors could be granted foreign patent protection with respect to our discoveries.

We have decided not to pursue patent protection with respect to some of our inventions outside the United States, both because we do not believe it is cost-effective and because of confidentiality concerns. Accordingly, our international competitors could develop, and receive foreign patent protection for, genes or gene sequences, uses of those genes or gene sequences, gene products and drug targets, assays for identifying potential therapeutic products, potential therapeutic products and methods of treatment for which we are seeking United States patent protection. In addition, most of our gene trapping patents and our licensed gene targeting patents cover only the United States and do not apply to discovery activities conducted outside of the United States or, in some circumstances, to importing into the United States products developed using this technology.

We may be unable to protect our trade secrets.

Significant aspects of our intellectual property are not protected by patents. As a result, we seek to protect the proprietary nature of this intellectual property as trade secrets through proprietary information agreements and other measures. While we have entered into proprietary information agreements with all of our employees, consultants, advisers and collaborators, we may not be able to prevent the disclosure of our trade secrets. In addition, other companies or institutions may independently develop substantially equivalent information and techniques.

Our efforts to discover, evaluate and validate potential targets for drug intervention and our drug discovery programs are subject to evolving data and other risks inherent in the drug discovery process.

We are employing our knockout technology and integrated drug discovery platform to systematically discover, evaluate and validate potential targets for drug intervention and to develop drugs to address those targets. The drug discovery and development process involves significant risks of delay or failure due, in part, to evolving data and the uncertainties involved with the applications of new technologies. As we refine and advance our efforts, it is likely that the resulting data will cause us to change our targets from time to time and, therefore, that the targets that we believe at any time to be promising may prove not to be so. These developments can occur at any stage of the drug discovery and development process.

Our industry is subject to extensive and uncertain government regulatory requirements, which could significantly hinder our ability, or the ability of our collaborators, to obtain, in a timely manner or at all, government approval of products based on genes that we identify, or to commercialize such products.

We or our collaborators must obtain approval from the FDA in order to conduct clinical trials and sell our future product candidates in the United States and from foreign regulatory authorities in order to conduct clinical trials and sell our future product candidates in other countries. In order to obtain regulatory approvals for the commercial sale of any products that we may develop, we will be required to complete extensive clinical trials in humans to demonstrate the safety and efficacy of our drug candidates. We or our collaborators may not be able to obtain authority from the FDA or other equivalent foreign regulatory agencies to initiate or complete any clinical trials. In addition, we have limited internal resources for making regulatory filings and dealing with regulatory authorities.

The results from preclinical testing of a drug candidate that is under development may not be predictive of results that will be obtained in human clinical trials. In addition, the results of early human clinical trials may not be predictive of results that will be obtained in larger scale, advanced stage clinical trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials, even after achieving positive results in earlier trials. Negative or inconclusive results from a preclinical study or a clinical trial could cause us, one of our collaborators or the FDA to terminate a preclinical study or clinical trial or require that we repeat it. Furthermore, we, one of our collaborators or a regulatory agency with jurisdiction over the trials may suspend clinical trials at any time if the subjects or patients participating in such trials are being exposed to unacceptable health risks or for other reasons.

Any preclinical or clinical test may fail to produce results satisfactory to the FDA or foreign regulatory authorities. Preclinical and clinical data can be interpreted in different ways, which could delay, limit or prevent regulatory approval. The FDA or institutional review boards at the medical institutions and healthcare facilities where we sponsor clinical trials may suspend any trial indefinitely if they find deficiencies in the conduct of these trials. Clinical trials must be conducted in accordance with the FDA's current Good Clinical Practices. The FDA and these institutional review boards have authority to oversee our clinical trials, and the FDA may require large numbers of test subjects. In addition, we must manufacture, or contract for the manufacture of, the product candidates that we use in our clinical trials under the FDA's current Good Manufacturing Practices.

The rate of completion of clinical trials is dependent, in part, upon the rate of enrollment of patients. Patient accrual is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the study, the nature of the study, the existence of competitive clinical trials and the availability of alternative treatments. Delays in planned patient enrollment may result in increased costs and prolonged clinical development, which in turn could allow our competitors to bring products to market before we do and impair our ability to commercialize our products or potential products.

We or our collaborators may not be able to successfully complete any clinical trial of a potential product within any specified time period. In some cases, we or our collaborators may not be able to complete the trial at all. Moreover, clinical trials may not show our potential products to be both safe and effective. Thus, the FDA and other regulatory authorities may not approve any products that we develop for any indication or may limit the approved indications or impose other conditions.

If our potential products receive regulatory approval, we or our collaborators will remain subject to extensive and rigorous ongoing regulation.

If we or our collaborators obtain initial regulatory approvals from the FDA or foreign regulatory authorities for any products that we may develop, we or our collaborators will be subject to extensive and rigorous ongoing domestic and foreign government regulation of, among other things, the research, development, testing, manufacture, labeling, promotion, advertising, distribution and marketing of our products and product candidates. The failure to comply with these requirements or the identification of safety problems during commercial marketing could lead to the need for product marketing restrictions, product withdrawal or recall or other voluntary or regulatory action, which could delay further marketing until the product is brought into compliance. The failure to comply with these requirements may also subject us or our collaborators to stringent penalties.

Moreover, several of our product development areas involve relatively new technology and have not been the subject of extensive product testing in humans. The regulatory requirements governing these products and related clinical procedures remain uncertain and the products themselves may be subject to substantial review by foreign governmental regulatory authorities that could prevent or delay approval in those countries. Regulatory requirements ultimately imposed on any products that we may develop could limit our ability to test, manufacture and, ultimately, commercialize such products.

The uncertainty of pharmaceutical pricing and reimbursement may decrease the commercial potential of any products that we or our collaborators may develop and affect our ability to raise capital.

Our ability and the ability of our collaborators to successfully commercialize pharmaceutical products will depend, in part, on the extent to which reimbursement for the cost of such products and related treatment will be available from government health administration authorities, private health coverage insurers and other organizations. The pricing, availability of distribution channels and reimbursement status of newly approved pharmaceutical products is highly uncertain. As a result, adequate third-party coverage may not be available for us to maintain price levels sufficient for realization of an appropriate return on our investment in product discovery and development.

In certain foreign markets, pricing or profitability of healthcare products is subject to government control. In the United States, there have been, and we expect that there will continue to be, a number of federal and state proposals to implement similar governmental control. In addition, an increasing emphasis on managed care in the United States has increased and will continue to increase the pressure on pharmaceutical pricing. While we cannot predict the adoption of any such legislative or regulatory proposals or the effect such proposals or managed care efforts may have on our business, the announcement of such proposals or efforts could harm our ability to raise capital, and the adoption of such proposals or efforts could harm our results of operations. Further, to the extent that such proposals or efforts harm other pharmaceutical companies that are our prospective collaborators, our ability to establish corporate collaborations would be impaired. In addition, third-party payers are increasingly challenging the prices charged for medical products and services. We do not know whether consumers, third-party payers and others will consider any products that we or our collaborators develop to be cost-effective or that reimbursement to the consumer will be available or will be sufficient to allow us or our collaborators to sell such products on a profitable basis.

We use hazardous chemicals and radioactive and biological materials in our business; any disputes relating to improper handling, storage or disposal of these materials could be time consuming and costly.

Our research and development processes involve the use of hazardous materials, including chemicals and radioactive and biological materials. Our operations also produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge or any resultant injury from these materials. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of these materials. We could be subject to civil damages in the event of an improper or unauthorized release of, or exposure of individuals to, these hazardous materials. In addition, claimants may sue us for injury or contamination that results from our use or the use by third parties of these materials, and our liability may exceed our total assets. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development or production efforts. We do not currently maintain insurance coverage that would cover these types of environmental liabilities.

We may be sued for product liability.

We or our collaborators may be held liable if any product that we or our collaborators develop, or any product that is made with the use or incorporation of any of our technologies, causes injury or is found otherwise unsuitable during product testing, manufacturing, marketing or sale. Although we currently have and intend to maintain product liability insurance, this insurance may become prohibitively expensive or may not fully cover our potential liabilities. Our inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of products developed by us or our collaborators. If we are sued for any injury caused by our or our collaborators' products, our liability could exceed our total assets.

Public perception of ethical and social issues may limit or discourage the use of our technologies, which could reduce our revenues.

Our success will depend, in part, upon our ability to develop products discovered through our knockout mouse technologies. Governmental authorities could, for ethical, social or other purposes, limit the use of genetic processes or prohibit the practice of our knockout mouse technologies. Claims that genetically engineered products are unsafe for consumption or pose a danger to the environment may influence public perceptions. The subject of genetically modified organisms, like knockout mice, has received negative publicity and aroused public debate in some countries. Ethical and other concerns about our technologies, particularly the use of genes from nature for commercial purposes and the products resulting from this use, could reduce the likelihood of maintaining market acceptance of our technologies.

Item 2. ***Properties***

We currently lease approximately 300,000 square feet of space for our corporate offices and laboratories in buildings located in The Woodlands, Texas, a suburb of Houston, Texas, and approximately 76,000 square feet of space for offices and laboratories near Princeton, New Jersey.

Our facilities in The Woodlands, Texas include two state-of-the art animal facilities totaling approximately 100,000 square feet. These facilities, completed in 1999 and 2002, respectively, were custom designed for the generation and analysis of knockout mice and are accredited by AAALAC International (Association for Assessment and Accreditation of Laboratory Animal Care). These facilities enable us to maintain in-house control over our entire *in vivo* validation process, from the generation of embryonic stem cell clones through the completion of *in vivo* analysis, in a specific pathogen free environment. We believe these facilities, which are among the largest and most sophisticated of their kind in the world, provide us with significant strategic and operational advantages relative to our competitors. Because of the size and sophistication of our facilities, it would require the investment of significant resources over an extended period of time for any competitor to develop facilities with the scale, efficiency and productivity with respect to the analysis of the functionality of genes that our facilities provide.

In October 2000, we entered into a synthetic lease agreement under which the lessor purchased our existing laboratory and office buildings and animal facility in The Woodlands, Texas and agreed to fund the construction of an additional laboratory and office building and a second animal facility. The synthetic lease agreement was subsequently expanded to include funding for the construction of a central plant facility. Including the purchase price for our existing facilities, the synthetic lease, as amended, provides for funding of up to $55.0 million in property and improvements. The term of the agreement is six years, which includes the construction period and a lease period. Lease payments for the new facilities began upon completion of construction, which occurred at the end of the first quarter of 2002. Lease payments are subject to fluctuation based on LIBOR rates. Based on a year-end LIBOR rate of 1.16%, the total lease payments for our facilities would be approximately $0.8 million per year. At the end of the lease term, the lease may be extended for one-year terms, up to seven additional terms, or we may purchase the properties for a price equal to the $54.8 million funded under the synthetic lease for property and improvements plus the amount of any accrued but unpaid lease payments. If we elect not to renew the lease or purchase the properties, we may arrange for the sale of the properties to a third party or surrender the properties to the lessor. If we elect to arrange for the sale of the properties or surrender the properties to the lessor, we have guaranteed approximately 86% of the total original cost as the residual fair value of the properties.

In May 2002, our subsidiary Lexicon Pharmaceuticals (New Jersey), Inc. entered into a lease for a 76,000 square-foot facility in Hopewell, New Jersey. The term of the lease extends until June 30, 2013. The lease provides for an escalating yearly base rent payment of $1.3 million in the first year, $2.1 million in years two and three, $2.2 million in years four to six, $2.3 million in years seven to nine and $2.4 million in years ten and eleven. We are the guarantor of the obligations of our subsidiary under the lease.

We believe that our facilities are well-maintained, in good operating condition and acceptable for our current operations.

Item 3. ***Legal Proceedings***

We are not presently a party to any material legal proceedings.

Item 4. ***Submission of Matters to a Vote of Security Holders***

No matters were submitted during the fourth quarter of the year ended December 31, 2003.

PART II

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

Our common stock has been quoted on The Nasdaq National Market under the symbol "LEXG" since April 7, 2000. Prior to that time, there was no public market for our common stock. The following table sets forth, for the periods indicated, the range of the high and low closing prices per share for our common stock as reported on The Nasdaq National Market.

	High	Low
2002		
First Quarter	$ 12.04	$ 7.98
Second Quarter	$ 9.00	$ 4.12
Third Quarter	$ 6.18	$ 3.51
Fourth Quarter	$ 5.25	$ 3.35
2003		
First Quarter	$ 5.22	$ 3.16
Second Quarter	$ 6.60	$ 4.05
Third Quarter	$ 7.28	$ 4.50
Fourth Quarter	$ 6.14	$ 5.07

As of March 8, 2004, there were approximately 257 holders of record of our common stock.

We have never paid cash dividends on our common stock. We anticipate that we will retain all of our future earnings, if any, for use in the expansion and operation of our business and do not anticipate paying cash dividends in the foreseeable future.

Item 6. ***Selected Financial Data***

The statement of operations data for the years ended December 31, 2003, 2002 and 2001and the balance sheet data as of December 31, 2003 and 2002 have been derived from our audited financial statements included elsewhere in this annual report on Form 10-K. The statements of operations data for the years ended December 31, 2000 and 1999, and the balance sheet data as of December 31, 2001, 2000 and 1999 have been derived from our audited financial statements not included in this annual report on Form 10-K. Our historical results are not necessarily indicative of results to be expected for any future period. The data presented below has been derived from financial statements that have been prepared in accordance with accounting principles generally accepted in the United States and should be read with our financial statements, including the notes, and with "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this annual report on Form 10-K.

	Year Ended December 31,				
	2003	2002	2001	2000	1999
Statements of Operations Data:	(in thousands, except per share data)				
Revenues	$ 42,838	$ 35,200	$ 30,577	$ 14,459	$ 4,738
Operating expenses:					
Research and development, including stock-based compensation of $5,048 in 2003, $5,155 in 2002, $5,539 in 2001 and $10,883 in 2000	82,198	74,859	53,355	31,647	14,646
General and administrative, including stock-based compensation of $5,067 in 2003, $5,113 in 2002, $5,231 in 2001 and $9,958 in 2000	23,233	23,234	20,861	18,289	2,913
Total operating expenses	105,431	98,093	74,216	49,936	17,559
Loss from operations	(62,593)	(62,893)	(43,639)	(35,477)	(12,821)
Interest and other income, net	1,471	3,223	8,467	9,483	346
Net loss before cumulative effect of a change in accounting principle	(61,122)	(59,670)	(35,172)	(25,994)	(12,475)
Cumulative effect of a change in accounting principle	(3,076)	—	—	—	—
Net loss	(64,198)	(59,670)	(35,172)	(25,994)	(12,475)
Accretion on redeemable convertible preferred stock	—	—	—	(134)	(536)
Net loss attributable to common stockholders	$ (64,198)	$ (59,670)	$ (35,172)	$ (26,128)	$ (13,011)
Net loss per common share basic and diluted:					
Net loss before cumulative effect of a change in accounting principle	$ (1.08)	$ (1.14)	$ (0.70)	$ (0.63)	$ (0.53)
Cumulative effect of a change in accounting principle	(0.05)	—	—	—	—
Net loss per common share, basic and diluted	$ (1.13)	$ (1.14)	$ (0.70)	$ (0.63)	$ (0.53)
Shares used in computing net loss per common share, basic and diluted	56,820	52,263	50,213	41,618	24,530

	As of December 31,				
	2003	2002	2001	2000	1999
Balance Sheet Data:	(in thousands)				
Cash, cash equivalents and investments, including restricted cash and investments of $57,514 in 2003, $57,710 in 2002, $43,338 in 2001 and $13,879 in 2000	$ 161,001	$ 123,096	$ 166,840	$ 202,680	$ 9,156
Working capital	139,739	111,833	147,663	194,801	2,021
Total assets	284,199	201,772	239,990	220,693	22,295
Long-term debt, net of current portion	56,344	4,000	—	1,834	3,577
Redeemable convertible preferred stock	—	—	—	—	30,050
Accumulated deficit	(213,943)	(149,745)	(90,075)	(54,903)	(28,909)
Stockholders' equity (deficit)	166,216	169,902	218,372	207,628	(21,937)

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

The following discussion and analysis should be read with "Selected Financial Data" and our financial statements and notes included elsewhere in this annual report on Form 10-K.

Overview

We are a biopharmaceutical company focused on the discovery of breakthrough treatments for human disease. We are using gene knockout technology to systematically discover the physiological functions of genes in living mammals, or *in vivo*. We generate our gene function discoveries using knockout mice – mice whose DNA has been altered to disrupt, or "knock out," the function of the altered gene. Our patented gene trapping and gene targeting technologies enable us to rapidly generate these knockout mice by altering the DNA of genes in a special variety of mouse cells, called embryonic stem cells, which can be cloned and used to generate mice with the altered gene. We employ an integrated platform of advanced medical technologies to systematically discover and validate which genes, when knocked out, result in a favorable medical profile with pharmaceutical utility. We then pursue those genes and the proteins they encode as potential targets for therapeutic intervention in our drug discovery programs.

We employ internal resources and drug discovery alliances to discover potential small molecule drugs, therapeutic antibodies and therapeutic proteins for *in vivo*-validated drug targets that we consider to have high pharmaceutical value. We use our own sophisticated libraries of drug-like chemical compounds and an industrialized medicinal chemistry platform to identify small molecule drug candidates for our *in vivo*-validated drug targets. We have established alliances with Bristol-Myers Squibb Company to discover and develop novel small molecule drugs in the neuroscience field; Genentech, Inc. for the discovery of therapeutic proteins and antibody targets; with Abgenix, Inc. for the discovery and development of therapeutic antibodies based on our drug target discoveries; and with Incyte Corporation for the discovery and development of therapeutic proteins. In addition, we have established collaborations and license agreements with many other leading pharmaceutical and biotechnology companies under which we receive fees and, in many cases, are eligible to receive milestone and royalty payments, for access to some of our technologies and discoveries for use in their own drug discovery efforts.

We derive substantially all of our revenues from drug discovery alliances, subscriptions to our databases, target validation collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice, technology licenses and compound library sales. To date, we have generated a substantial portion of our revenues from a limited number of sources.

Our operating results and, in particular, our ability to generate additional revenues are dependent on many factors, including our success in establishing research collaborations and technology licenses, expirations of our research collaborations and database subscriptions, the success rate of our discovery efforts leading to opportunities for new research collaborations and licenses, as well as milestone payments and royalties, the timing and willingness of collaborators to commercialize products which may result in royalties, and general and industry-specific economic conditions which may affect research and development expenditures. Our future revenues from collaborations, alliances and database subscriptions are uncertain because our existing agreements have fixed terms or relate to specific projects of limited duration. Our future revenues from technology licenses are uncertain because they depend, in large part, on securing new agreements. Subject to limited exceptions, we do not intend to offer subscriptions to our databases or continue to make our compound libraries available for purchase in the future. Our ability to secure future revenue-generating agreements will depend upon our ability to address the needs of our potential future collaborators and licensees, and to negotiate agreements that we believe are in our long-term best interests. We may determine that our interests are better served by retaining rights to our discoveries and advancing our therapeutic programs to a later stage, which could limit our near-term revenues. Because of these and other factors, our quarterly operating results have fluctuated in the past and are likely to do so in the future, and we do not believe that quarter-to-quarter comparisons of our operating results are a good indication of our future performance.

Since our inception, we have incurred significant losses and, as of December 31, 2003, we had an accumulated deficit of $213.9 million. Our losses have resulted principally from costs incurred in research and development, general and administrative costs associated with our operations, and non-cash stock-based compensation expenses associated with stock options granted to employees and consultants prior to our April 2000 initial public offering. Research and development expenses consist primarily of salaries and related personnel costs,

material costs, facility costs, depreciation on property and equipment, legal expenses resulting from intellectual property prosecution and other expenses related to our drug discovery and LexVision programs, the development and analysis of knockout mice and our other target validation research efforts, and the development of compound libraries. General and administrative expenses consist primarily of salaries and related expenses for executive, finance and other administrative personnel, professional fees and other corporate expenses including business development and general legal activities, as well as expenses related to our patent infringement litigation against Deltagen, Inc., which was settled in September 2001. In connection with the expansion of our drug discovery programs and our target validation research efforts, we expect to incur increasing research and development and general and administrative costs. As a result, we will need to generate significantly higher revenues to achieve profitability.

As of December 31, 2003 we had net operating loss carryforwards of approximately $131.8 million. We also had research and development tax credit carryforwards of approximately $8.1 million. The net operating loss and credit carryforwards will expire at various dates beginning in 2011, if not utilized. Utilization of the net operating losses and credits may be significantly limited due to a change in ownership as defined by provisions of the Internal Revenue Code of 1986 and similar state provisions. The annual limitation may result in the expiration of net operating losses and credits before utilization.

Critical Accounting Policies

Revenue Recognition

We recognize revenues when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed and determinable, and collectibility is reasonably assured. Payments received in advance under these arrangements are recorded as deferred revenue until earned.

Fees for access to our databases and other target validation resources are recognized ratably over the subscription or access period. Payments received under target validation collaborations are recognized as revenue as we perform our obligations related to such research to the extent such fees are non-refundable. Non-refundable upfront fees and annual research funding under our drug discovery alliances are recognized as revenue on a straight-line basis over the estimated period of service, generally the contractual research term. Milestone-based fees are recognized upon completion of specified milestones according to contract terms. Non-refundable technology license fees are recognized as revenue upon the grant of the license when performance is complete and there is no continuing involvement.

Revenues recognized from multiple element contracts are allocated to each element of the arrangement based on the relative fair value of the elements. The determination of fair value of each element is based on objective evidence. When revenues for an element are specifically tied to a separate earnings process, revenue is recognized when the specific performance obligation associated with the element is completed. When revenues for an element are not specifically tied to a separate earnings process, they are recognized ratably over the term of the agreement.

A change in our revenue recognition policy or changes in the terms of contracts under which we recognize revenues could have an impact on the amount and timing of our recognition of revenues.

Research and Development Expenses

Research and development expenses consist of costs incurred for company-sponsored as well as collaborative research and development activities. These costs include direct and research-related overhead expenses and are expensed as incurred. Patent costs and technology license fees for technologies that are utilized in research and development and have no alternative future use are expensed when incurred.

Prior to preclinical development work, we are unable to segregate the costs related to research performed on drug candidates because the drug candidate is often not specifically identified until the later stages of our research. When we begin the formal preclinical process in preparation for filing an IND, we intend to account on a program by program basis for the costs related to the development of the identified candidate. To date, we have not advanced any drug products into formal preclinical development.

Goodwill Impairment

Goodwill is not amortized, but is tested at least annually for impairment at the reporting unit level. We have determined that the reporting unit is the single operating segment disclosed in our current financial statements. Impairment is the condition that exists when the carrying amount of goodwill exceeds its implied fair value. The first step in the impairment process is to determine the fair value of the reporting unit and then compare it to the carrying value, including goodwill. We determined that the market capitalization approach is the most appropriate method of measuring fair value of the reporting unit. Under this approach, fair value is calculated as the average closing price of our common stock for the 30 days preceding the date that the annual impairment test is performed, multiplied by the number of outstanding shares on that date. A control premium, which is representative of premiums paid in the marketplace to acquire a controlling interest in a company, is then added to the market capitalization to determine the fair value of the reporting unit. If the fair value exceeds the carrying value, no further action is required and no impairment loss is recognized. Additional impairment assessments may be performed on an interim basis if we encounter events or changes in circumstances that would indicate that, more likely than not, the carrying value of goodwill has been impaired. There was no impairment of goodwill in 2003.

Recent Accounting Pronouncements

In November 2002, the Emerging Issues Task Force, or EITF, reached a consensus on EITF Issue No. 00-21, "Accounting for Revenue Arrangements with Multiple Deliverables." This consensus requires that revenue arrangements with multiple deliverables be divided into separate units of accounting if the delivered items have value to the customer on a standalone basis, there is objective and reliable evidence of fair value of the undelivered items and, if the arrangement includes a general right of return, performance of the undelivered item is considered probable and substantially in our control. The final consensus is applicable to agreements entered into in fiscal periods beginning after June 15, 2003. The adoption of EITF 00-21 did not have a material impact on our financial statements.

In December 2002, the FASB issued Statement of Financial Accounting Standards, or SFAS, No. 148, "Accounting for Stock-Based Compensation – Transition and Disclosure." 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 No. 123 to require prominent disclosures in both annual and interim financial statements about the method of accounting for stock-based accounting for employee compensation and the effect of the method used on reported results. We have elected to continue to follow the intrinsic value method of accounting as prescribed by Accounting Principles Board Opinion No. 25 (or APB 25), "Accounting for Stock Issued to Employees," to account for employee stock options.

In January 2003, the FASB issued Interpretation No. 46, or FIN 46, "Consolidation of Variable Interest Entities – an Interpretation of ARB No. 51." FIN 46 was revised in December 2003. It requires that unconsolidated variable interest entities be consolidated by their primary beneficiaries. A primary beneficiary is the party that absorbs a majority of the entity's expected losses or residual benefits. FIN 46 applied immediately to variable interest entities created after January 31, 2003, but was effective for the period ending December 31, 2003 for variable interest entities created before February 1, 2003. We adopted FIN 46 on December 31, 2003 and determined that the lessor under the synthetic lease is a variable interest entity as defined by FIN 46, and that we absorb a majority of the variable interest entity's expected losses. Accordingly, we consolidated the assets of the variable interest entity, which were comprised of property and improvements funded under the synthetic lease. These assets had a carrying value of $54.8 million, net of accumulated depreciation of $3.1 million on December 31, 2003. We also consolidated the variable interest entity's debt of $52.3 million and non-controlling interests of $2.5 million. Additionally, we recorded a cumulative effect of a change in accounting principle equal to the accumulated depreciation of $3.1 million for the period from the date the buildings were placed in service under the synthetic lease through December 31, 2003. These improvements will be depreciated over their useful lives. Due to our residual value guarantee on the property, the non-recourse feature of the underlying debt, and certain other provisions of the lease arrangement, we do not allocate any of the variable interest entity's depreciation or interest expenses to the non-controlling interest. As permitted by applicable accounting standards, we had previously accounted for our involvement with the variable interest entity as an operating lease.

Results of Operations

Years Ended December 31, 2003 and 2002

Revenues. Total revenues and dollar and percentage changes as compared to the prior year are as follows (dollar amounts are presented in millions):

	Year Ended December 31,	
	2003	2002
Total revenues	$ 42.8	$ 35.2
Dollar increase	$ 7.6	
Percentage increase	22%	

- *Subscription and license fees* – Revenue from subscriptions and license fees increased 21% to $21.6 million due to additional technology licenses granted to pharmaceutical and biotechnology companies in 2003.

- *Collaborative research* – Revenue from collaborative research increased 24% to $21.2 million primarily due to increased revenue under our drug discovery alliances with Genentech, Inc. and Bristol-Myers Squibb Company, offset in part by a decrease in revenues from target validation collaborations due to the scheduled conclusion of many of these arrangements.

- *Compound libraries and other* – Revenue from compound library sales and other decreased 81% to $46,000 due to the fact that we are not making our compound libraries available for purchase, subject to limited exceptions. We may, however, provide additional quantities of selected compounds or optimization services under existing compound sales agreements.

In 2003, Incyte Corporation, Amgen, Inc., Bristol-Myers Squibb and Genentech represented 23%, 15%, 14% and 14% of revenues, respectively. In 2002, Incyte, Bristol-Myers Squibb and Millennium Pharmaceuticals, Inc. represented 28%, 14% and 11% of revenues, respectively.

Research and Development Expenses. Research and development expenses and dollar and percentage changes as compared to the prior year are as follows (dollar amounts are presented in millions):

	Year Ended December 31,	
	2003	2002
Total research and development expense	$ 82.2	$ 74.9
Dollar increase	$ 7.3	
Percentage increase	10%	

Research and development expenses consist primarily of salaries and other personnel-related expenses, stock-based compensation expenses, laboratory supplies, facility and equipment costs, consulting and other services. The change in 2003 as compared to 2002 resulted primarily from the following costs:

- *Personnel* – Personnel costs increased 14% to $35.0 million primarily due to increased personnel to support the expansion of our drug discovery programs, merit pay increases for employees and increasing employee benefit costs. Salaries, bonuses, employee benefits, payroll taxes, recruiting and relocation costs are included in personnel costs.

- *Stock-based compensation* – Stock based compensation expense, primarily relating to option grants made prior to our April 2000 initial public offering, decreased 2% to $5.0 million.

- *Laboratory supplies* – Laboratory supplies expense increased 5% to $11.1 million due primarily to an increase in drug discovery activities such as high throughput screening.

- *Facilities and equipment* – Facility and equipment costs increased 13% to $19.8 million primarily due to increased rent resulting from the May 2002 lease of our facility in Hopewell, New Jersey and increased property taxes on our facilities in The Woodlands, Texas. Additionally, depreciation expense increased as a result of purchases of capital equipment and leasehold improvements.

- *Consulting and other services* – Consulting and other services decreased by 1% to $7.7 million. Consulting and other services include subscriptions to third-party databases, technology licenses and legal and patent fees.

- *Other* – Other costs increased by 17% to $3.6 million.

General and Administrative Expenses. General and administrative expenses and dollar and percentage changes as compared to the prior year are as follows (dollar amounts are presented in millions):

	Year Ended December 31,	
	2003	2002
Total general and administrative expense	$ 23.2	$ 23.2
Dollar increase	$ —	
Percentage increase	—	

General and administrative expenses consist primarily of personnel costs to support our research activities, stock-based compensation expense, facility and equipment costs and professional fees, such as legal fees. The change in 2003 as compared to 2002 resulted primarily from the following costs:

- *Personnel* – Personnel costs decreased 4% to $10.6 million primarily due to decreased staffing in overhead departments. Salaries, bonuses, employee benefits, payroll taxes, recruiting and relocation costs are included in personnel costs.

- *Stock-based compensation* – Stock based compensation expense, primarily relating to option grants made prior to our April 2000 initial public offering, decreased 1% to $5.1 million.

- *Facilities and equipment* – Facility and equipment costs increased 12% to $3.6 million primarily due to increased rent resulting from the May 2002 lease of our facility in Hopewell, New Jersey and increased property taxes on our facilities in The Woodlands, Texas.

- *Professional fees* – Professional fees increased 43% to $1.6 million primarily due to increased legal fees.

- *Other* – Other costs increased 13% to $2.3 million.

Interest and Other Income. Interest and other income decreased 44% to $1.8 million in 2003 from $3.2 million in 2002. This decrease resulted primarily from lower average cash and investment balances and lower average interest rates on our investments.

Net Loss and Net Loss Per Common Share Before Cumulative Effect of a Change in Accounting Principle. Net loss before a change in accounting principle increased to $61.1 million in 2003 from $59.7 million in 2002. Net loss per common share before a change in accounting principle decreased to $1.08 in 2003 from $1.14 in 2002. Net loss before a change in accounting principle includes stock-based compensation expense of $10.1 million and $10.3 million in 2003 and 2002, respectively.

Change In Accounting Principle. As discussed in "Recent Accounting Pronouncements" above, we adopted FIN 46 on December 31, 2003 and determined that the lessor under the synthetic lease is a variable interest entity as defined by FIN 46, and that we absorb a majority of the variable interest entity's expected losses. Accordingly, we recorded a cumulative effect of a change in accounting principle equal to the accumulated depreciation of

$3.1 million for the period from the date the buildings were placed in service under the synthetic lease through December 31, 2003.

Net Loss and Net Loss Per Common Share. Net loss increased to $64.2 million in 2003 from $59.7 million in 2002. Net loss per common share decreased to $1.13 in 2003 from $1.14 in 2002.

Years Ended December 31, 2002 and 2001

Revenues. Total revenues and dollar and percentage changes as compared to the prior year are as follows (dollar amounts are presented in millions):

	Year Ended December 31,	
	2002	2001
Total revenues	$ 35.2	$ 30.6
Dollar increase	$ 4.6	
Percentage increase	15%	

- *Subscription and license fees* – Revenue from subscriptions and license fees increased 21% to $17.9 million due to subscriptions to our LexVision database.

- *Collaborative research* – Revenue from collaborative research increased 52% to $17.1 million primarily due to increased revenue from target validation collaborations and our drug discovery alliance with Incyte.

- *Compound libraries and other* – Revenue from compound library sales and other decreased 95% to $0.2 million due to the fact that we did not make our compound libraries available for purchase in 2002 and, subject to limited exceptions, do not intend to make our compound libraries available for purchase in the future. We may, however, provide additional quantities of selected compounds or optimization services under existing compound sales agreements.

In 2002, Incyte, Bristol-Myers Squibb and Millennium Pharmaceuticals represented 28%, 14% and 11% of revenues, respectively. In 2001, Incyte, Bristol-Myers Squibb and Merck & Co., Inc. represented 16%, 13% and 12% of revenues, respectively.

Research and Development Expenses. Research and development expenses and dollar and percentage changes as compared to the prior year are as follows (dollar amounts are presented in millions):

	Year Ended December 31,	
	2002	2001
Total research and development expense	$ 74.9	$ 53.4
Dollar increase	$ 21.5	
Percentage increase	40%	

Research and development expenses consist primarily of salaries and other personnel-related expenses, stock-based compensation expenses, laboratory supplies, facility and equipment costs, consulting and other services. The change in 2002 as compared to 2001 resulted primarily from the following costs:

- *Personnel* – Personnel costs increased 35% to $30.8 million primarily due to increased personnel to support the expansion of our drug discovery programs, a full year of medicinal chemistry operations and merit pay increases for employees. Salaries, bonuses, employee benefits, payroll taxes, recruiting and relocation costs are included in personnel costs.

- *Stock-based compensation* – Stock based compensation expense, primarily relating to option grants made prior to our April 2000 initial public offering, decreased 7% to $5.2 million.

- *Laboratory supplies* – Laboratory supplies expense increased 28% to $10.6 million due primarily to an increase in drug discovery activities and a full year of medicinal chemistry operations.

- *Facilities and equipment* – Facility and equipment costs increased 98% to $17.5 million due to increased rent, maintenance costs and property taxes resulting from our expansion in 2002 into additional facilities in The Woodlands, Texas and a full year of medicinal chemistry operations. Additionally, depreciation expense increased as a result of purchases of capital equipment and leasehold improvements.

- *Consulting and other services* – Consulting and other services increased by 83% to $7.7 million, primarily due to increased fees related to third party database subscriptions. Consulting and other services include subscriptions to third-party databases, technology licenses and legal and patent fees.

- *Other* – Other costs decreased 17% to $3.1 million.

General and Administrative Expenses. General and administrative expenses and dollar and percentage changes as compared to the prior year are as follows (dollar amounts are presented in millions):

	Year Ended December 31,	
	2002	2001
Total general and administrative expense	$ 23.2	$ 20.9
Dollar increase	$ 2.3	
Percentage increase	11%	

General and administrative expenses consist primarily of personnel costs to support our research activities, stock-based compensation expense, facility and equipment costs and professional fees, such as legal fees. The change in 2002 as compared to 2001 resulted primarily from the following costs:

- *Personnel* – Personnel costs increased 59% to $11.1 million primarily due to increased personnel to support our research activities and merit pay increases for employees. Salaries, bonuses, employee benefits, payroll taxes, recruiting and relocation costs are included in personnel costs.

- *Stock-based compensation* – Stock based compensation expense, primarily relating to option grants made prior to our April 2000 initial public offering, decreased 2% to $5.1 million

- *Facilities and equipment* – Facility and equipment costs increased 81% to $3.2 million primarily due to increased rent and property taxes resulting from the expansion in 2002 into additional facilities in The Woodlands, Texas.

- *Professional fees* – Professional fees decreased 73% to $1.1 million primarily due to a reduction in legal costs as a result of the September 2001 settlement of our patent infringement litigation against Deltagen, Inc.

- *Other* – Other costs increased 1% to $2.7 million.

Interest and Other Income. Interest and other income decreased 63% to $3.2 million in 2002 from $8.8 million in 2001. This decrease resulted from lower cash and investment balances and lower average interest rates during 2002.

Net Loss and Net Loss Per Common Share. Net loss increased to $59.7 million in 2002 from $35.2 million in 2001. Net loss per common share increased to $1.14 in 2002 from $0.70 in 2001. Net loss includes stock-based compensation expense of $10.3 million and $10.8 million in 2002 and 2001, respectively.

Liquidity and Capital Resources

We have financed our operations from inception primarily through sales of common and preferred stock, contract and milestone payments to us under our database subscription, collaboration and license agreements, equipment financing arrangements and leasing arrangements. From our inception through December 31, 2003, we had received net proceeds of $293.1 million from issuances of common and preferred stock, including $203.2 million of net proceeds from the initial public offering of our common stock in April 2000 and $50.1 million from our July 2003 common stock offering. In addition, from our inception through December 31, 2003, we received $172.2 million in cash payments from database subscription and technology license fees, drug discovery alliances, target validation collaborations, sales of compound libraries and reagents and government grants, of which $131.3 million had been recognized as revenues through December 31, 2003.

As of December 31, 2003, we had $161.0 million in cash, cash equivalents and short-term investments (including $57.5 million of restricted cash and investments), as compared to $123.1 million (including $57.7 million of restricted cash and investments) as of December 31, 2002. We used cash of $7.7 million in operations in 2003. This consisted primarily of the net loss for the year of $64.2 million offset by non-cash charges of $10.1 million related to stock-based compensation expense, $10.2 million related to depreciation expense, $3.1 million related to the cumulative effect of a change in accounting principle and $1.2 million related to amortization of intangible assets other than goodwill; a $29.0 million increase in deferred revenue; and changes in other operating assets and liabilities of $2.8 million. Financing activities provided cash of $50.4 million, consisting primarily of the $50.1 million in net proceeds from our July 2003 common stock offering.

In October 2000, we entered into a synthetic lease agreement under which the lessor purchased our existing laboratory and office buildings and animal facility in The Woodlands, Texas and agreed to fund the construction of an additional laboratory and office building and a second animal facility. The synthetic lease agreement was subsequently expanded to include funding for the construction of a central plant facility for the distribution of utilities and related services among our facilities. Including the purchase price for our existing facilities, the synthetic lease, as amended, provided for funding of up to $55.0 million in property and improvements. The term of the agreement is six years, which includes the construction period and a lease period. Lease payments for the new facilities began upon completion of construction, which occurred at the end of the first quarter of 2002. Lease payments are subject to fluctuation based on LIBOR rates. Based on a year-end LIBOR rate of 1.16%, our total lease payments would be approximately $0.8 million per year. At the end of the lease term, the lease may be extended for one-year terms, up to seven additional terms, or we may purchase the properties for a price equal to the $54.8 million funded under the synthetic lease for property and improvements plus the amount of any accrued but unpaid lease payments. If we elect not to renew the lease or purchase the properties, we may arrange for the sale of the properties to a third party or surrender the properties to the lessor. If we elect to arrange for the sale of the properties or surrender the properties to the lessor, we have guaranteed approximately 86% of the total original cost as the residual fair value of the properties. We are required to maintain restricted cash or investments to collateralize borrowings made under the synthetic lease agreement. In addition, we have agreed to maintain cash and investments of at least $12.0 million in excess of our restricted cash and investments. If our cash and investments fall below that level, we may be required to seek a waiver of that agreement or to purchase the properties or arrange for their sale to a third party. Because our cost to purchase the properties would not materially exceed the $54.8 million funded under the synthetic lease for property and improvements and would likely be less than the amount of restricted cash and investments we are required to maintain under the synthetic lease, we believe that any requirement that we do so would not have a material adverse effect on our financial condition. As of December 31, 2003 and 2002, we maintained restricted cash and investments of $57.0 million and $57.2 million, respectively, to collateralize funding for property and improvements under the synthetic lease of $54.8 million and $55.0 million.

We are considering replacing our synthetic lease agreement covering all of our facilities in The Woodlands, Texas, and we are currently engaged in discussions to do so. We expect that any such new arrangement would require us to maintain substantially lower amounts of restricted cash and investments while increasing our lease payments with respect to these facilities, as compared to our synthetic lease agreement.

In May 2002, our subsidiary Lexicon Pharmaceuticals (New Jersey), Inc. entered into a lease for a 76,000 square-foot facility in Hopewell, New Jersey. The term of the lease extends until June 30, 2013. The lease provides for an escalating yearly base rent payment of $1.3 million in the first year, $2.1 million in years two and three,

$2.2 million in years four to six, $2.3 million in years seven to nine and $2.4 million in years ten and eleven. We are the guarantor of the obligations of our subsidiary under the lease.

In December 2002, we borrowed $4.0 million under a note agreement with Genentech. The proceeds of the loan are to be used to fund research efforts under our alliance with Genentech for the discovery of therapeutic proteins and antibody targets. The note matures on or before December 31, 2005, but we may prepay it at any time. We may repay the note, at our option, in cash, in shares of our common stock valued at the then-current market value, or in a combination of cash and shares, subject to certain limitations. The note accrues interest at an annual rate of 8%, compounded quarterly.

Including the lease and debt obligations described above, we had incurred the following contractual obligations as of December 31, 2003:

	Payments due by period (in millions)				
Contractual Obligations	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Long-term debt	$ 56.3	$ —	$ 56.3	$ —	$ —
Other long-term liabilities	2.5	—	2.5	—	—
Interest payment obligations	2.6	0.8	1.8	—	—
Operating leases	22.0	2.2	4.4	4.6	10.8
Obligations under purchase orders	1.9	1.9	—	—	—
Total	$ 85.3	$ 4.9	$ 65.0	$ 4.6	$ 10.8

Our future capital requirements will be substantial and will depend on many factors, including our ability to obtain alliance, collaboration and technology license agreements, the amount and timing of payments under such agreements, the level and timing of our research and development expenditures, market acceptance of our products, the resources we devote to developing and supporting our products and other factors. Our capital requirements will also be affected by any expenditures we make in connection with license agreements and acquisitions of and investments in complementary technologies and businesses. We expect to devote substantial capital resources to continue our research and development efforts, to expand our support and product development activities, and for other general corporate activities. We believe that our current unrestricted cash and investment balances and revenues we expect to derive from subscriptions to our databases, target validation collaborations, technology licenses and drug discovery alliances will be sufficient to fund our operations at least through the next two years. During or after this period, if cash generated by operations is insufficient to satisfy our liquidity requirements, we will need to sell additional equity or debt securities, restructure or replace our synthetic lease to reduce the required amount of restricted cash and investments, or obtain additional credit arrangements. Additional financing may not be available on terms acceptable to us or at all. The sale of additional equity or convertible debt securities may result in additional dilution to our stockholders.

Disclosure about Market Risk

We are exposed to limited market and credit risk on our cash equivalents which have maturities of three months or less. We maintain a short-term investment portfolio which consists of U.S. government agency debt obligations, investment grade commercial paper, corporate debt securities and certificates of deposit that mature three to twelve months from the time of purchase, which we believe are subject to limited market and credit risk. We currently do not hedge interest rate exposure or hold any derivative financial instruments in our investment portfolio.

We are exposed to interest rate risk because our synthetic lease payments fluctuate based upon LIBOR rates. A hypothetical 1% increase in LIBOR rates would result in $0.5 million of additional interest expense under the lease.

We have operated primarily in the United States and substantially all sales to date have been made in U.S. dollars. Accordingly, we have not had any material exposure to foreign currency rate fluctuations.

Item 7A. ***Quantitative and Qualitative Disclosures About Market Risk***

See "Disclosure about Market Risk" under "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" for quantitative and qualitative disclosures about market risk.

Item 8. ***Financial Statements and Supplementary Data***

The financial statements required by this Item are incorporated under Item 15 in Part IV of this report.

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

On March 26, 2002, the Board of Directors and its audit committee dismissed Arthur Andersen LLP as our independent public accountants and engaged Ernst & Young LLP to serve as our independent auditors for the fiscal year ending December 31, 2002, subject to stockholder ratification.

Arthur Andersen's report on our consolidated financial statements for the fiscal year ended December 31, 2001 did not contain an adverse opinion or disclaimer of opinion, nor was it qualified or modified as to uncertainty, audit scope or accounting principles.

During the fiscal year ended December 31, 2001 and through the date of the Board of Directors' decision, there were no disagreements with Arthur Andersen on any matter of accounting principle or practice, financial statement disclosure, or auditing scope or procedure which, if not resolved to Arthur Andersen's satisfaction, would have caused them to make reference to the subject matter in connection with their report on our consolidated financial statements for such year; and there were no reportable events as defined in Item 304(a)(1)(v) of Regulation S-K.

During the fiscal year ended December 31, 2001 and through the date of the Board of Directors' decision, we did not consult Ernst & Young LLP with respect to the application of accounting principles to a specified transaction, either completed or proposed, or the type of audit opinion that might be rendered on our consolidated financial statements, or any other matters or reportable events as set forth in Items 304(a)(2)(i) and (ii) of Regulation S-K.

Item 9A. ***Controls and Procedures***

Our chief executive officer and chief financial officer have concluded that our disclosure controls and procedures (as defined in rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934) are sufficiently effective to ensure that the information required to be disclosed by us in the reports we file under the Securities Exchange Act is gathered, analyzed and disclosed with adequate timeliness, accuracy and completeness, based on an evaluation of such controls and procedures conducted within 90 days prior to the date hereof.

Subsequent to our evaluation, there were no significant changes in internal controls or other factors that could significantly affect internal controls, including any corrective actions with regard to significant deficiencies and material weaknesses.

PART III

Item 10. ***Directors and Executive Officers of the Registrant***

The information required by this Item as to our directors and executive officers is hereby incorporated by reference from the information appearing under the captions "Election of Directors," "Executive Officers" and "Code of Ethics" in our definitive proxy statement which involves the election of directors and is to be filed with the Securities and Exchange Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2003.

Item 11. ***Executive Compensation***

The information required by this Item as to our management is hereby incorporated by reference from the information appearing under the captions "Executive Compensation" and "Election of Director – Director Compensation" in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2003. Notwithstanding the foregoing, in accordance with the instructions to Item 402 of Regulation S-K, the information contained in our proxy statement under the sub-heading "Report of the Compensation Committee of the Board of Directors" and "Performance Graph" shall not be deemed to be filed as part of or incorporated by reference into this annual report on Form 10-K.

Item 12. ***Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters***

The information required by this Item as to the ownership by management and others of our securities is hereby incorporated by reference from the information appearing under the caption "Stock Ownership of Certain Beneficial Owners and Management" in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2003.

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

The information required by this Item as to certain business relationships and transactions with our management and other related parties is hereby incorporated by reference to such information appearing under the captions "Certain Transactions" and "Compensation Committee Interlocks and Insider Participation" in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2003.

Item 14. ***Principal Accounting Fees and Services***

The information required by this Item as to the fees we pay our principal accountant is hereby incorporated by reference from the information appearing under the caption "Compensation of Independent Auditors" in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2003.

PART IV

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

(a) Documents filed as a part of this report:

1. Consolidated Financial Statements

All other financial statement schedules are omitted because they are not applicable or not required, or because the required information is included in the financial statements or notes thereto.

2. Exhibits

Exhibit No.		Description
3.1	—	Restated Certificate of Incorporation (filed as Exhibit 3.1 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
3.2	—	Restated Bylaws (filed as Exhibit 3.2 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.1	—	Employment Agreement with Arthur T. Sands, M.D., Ph.D. (filed as Exhibit 10.1 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.2	—	Employment Agreement with James R. Piggott, Ph.D. (filed as Exhibit 10.2 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.3	—	Employment Agreement with Jeffrey L. Wade, J.D. (filed as Exhibit 10.3 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.4	—	Employment Agreement with Brian P. Zambrowicz, Ph.D. (filed as Exhibit 10.4 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.5	—	Employment Agreement with Julia P. Gregory (filed as Exhibit 10.5 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.6	—	Employment Agreement with Alan Main, Ph.D. (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2001 and incorporated by reference herein).
10.7	—	Form of Indemnification Agreement with Officers and Directors (filed as Exhibit 10.7 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).

Exhibit No.		Description
10.8	—	2000 Equity Incentive Plan (filed as Exhibit 10.8 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.9	—	2000 Non-Employee Directors' Stock Option Plan (filed as Exhibit 10.9 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.10	—	Coelacanth Corporation 1999 Stock Option Plan (filed as Exhibit 99.1 to the Company's Registration Statement on Form S-8 (Registration No. 333-66380) and incorporated by reference herein).
†10.11	—	LexVision Database and Collaboration Agreement, dated September 26, 2000, with Bristol-Myers Squibb Company (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated September 26, 2000 and incorporated by reference herein).
†10.12	—	LexVision Database and Collaboration Agreement, dated June 27, 2001, with Incyte Genomics, Inc. (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2001 and incorporated by reference herein).
†10.13	—	Therapeutic Protein Alliance Agreement, dated June 27, 2001, with Incyte Genomics, Inc. (filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2001 and incorporated by reference herein).
*†10.14	—	Amended and Restated Collaboration and License Agreement, dated November 19, 2003, with Genentech, Inc.
*†10.15	—	Collaboration and License Agreement, dated December 17, 2003, with Bristol-Myers Squibb Company
10.16	—	Synthetic Lease Financing Facility with First Security Bank, National Association, the Lenders and Holders named therein, and Bank of America, N.A. (filed as Exhibit 10.12 to the Company's Annual Report on Form 10-K for the year ended December 31, 2000 and incorporated by reference herein).
10.17	—	Lease Agreement, dated October 21, 1998, between Coelacanth Chemical Corporation and ARE-279 Princeton Road, LLC. (filed as Exhibit 10.18 to the Company's Annual Report on Form 10-K for the year ended December 31, 2001 and incorporated by reference herein).
10.18	—	Lease Agreement, dated May 23, 2002, between Lexicon Pharmaceuticals (New Jersey), Inc. and Townsend Property Trust Limited Partnership (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2002 and incorporated by reference herein).
21.1	—	Subsidiaries (filed as Exhibit 21.1 to the Company's Annual Report on Form 10-K for the year ended December 31, 2001 and incorporated by reference herein).
*23.1	—	Consent of Ernst & Young LLP
*23.2	—	Information regarding consent of Arthur Andersen LLP
*24.1	—	Power of Attorney (contained in signature page)
*31.1	—	Certification of CEO Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
*31.2	—	Certification of CFO Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
*32.1	—	Certification of CEO and CFO Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

Exhibit No.		Description
99.1	—	Letter to the Securities and Exchange Commission regarding Audit Assurances (filed as Exhibit 99.1 to the Company's Annual Report on Form 10-K for the year ended December 31, 2001 and incorporated by reference herein).

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* Filed herewith.

† Confidential treatment has been requested for a portion of this exhibit. The confidential portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission.

(b) Reports on Form 8-K:

On October 30, 2003, we filed a Current Report on Form 8-K dated October 30, 2003 relating to our issuance of a press release reporting our financial results for the quarter ended September 30, 2003, which press release included our consolidated balance sheet data and consolidated statements of operations data for the period.

Signatures

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

Lexicon Genetics Incorporated

Date: March 12, 2004

By: /s/ ARTHUR T. SANDS
Arthur T. Sands, M.D., Ph.D.
President and Chief Executive Officer

Date: March 12, 2004

By: /s/ JULIA P. GREGORY
Julia P. Gregory
Executive Vice President, Corporate Development and Chief Financial Officer

Power of Attorney

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Julia P. Gregory and Jeffrey L. Wade, or either of them, each with the power of substitution, his or her attorney-in-fact, to sign any amendments to this Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, here ratifying and confirming all that each of said attorneys-in-fact, or his or her substitute or substitutes, may do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ ARTHUR T. SANDS Arthur T. Sands, M.D., Ph.D.	President and Chief Executive Officer (Principal Executive Officer)	March 12, 2004
/s/ JULIA P. GREGORY Julia P. Gregory	Executive Vice President, Corporate Development and Chief Financial Officer (Principal Financial and Accounting Officer)	March 12, 2004
/s/ C. THOMAS CASKEY C. Thomas Caskey, M.D.	Chairman of the Board of Directors	March 12, 2004
/s/ SAM L. BARKER Sam L. Barker, Ph.D.	Director	March 12, 2004
/s/ PATRICIA M. CLOHERTY Patricia M. Cloherty	Director	March 12, 2004
/s/ ROBERT J. LEFKOWITZ Robert J. Lefkowitz, M.D.	Director	March 12, 2004
/s/ ALAN S. NIES Alan S. Nies. M.D.	Director	March 12, 2004

Report of Independent Auditors

To the Board of Directors and Stockholders
of Lexicon Genetics Incorporated:

We have audited the accompanying consolidated balance sheets of Lexicon Genetics Incorporated and subsidiary (the Company) as of December 31, 2003 and 2002, and the related consolidated statements of operations, stockholders' equity and cash flows for the years then ended. 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. The financial statements of the Company for the year ended December 31, 2001 was audited by other auditors who have ceased operations and whose report dated February 22, 2002 expressed an unqualified opinion on those statements before the reclassification adjustment described in Note 4.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards 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. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Lexicon Genetics Incorporated as of December 31, 2003 and 2002, and the consolidated results of its operations and its cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States.

As discussed in Note 3 to the consolidated financial statements, during 2003 the Company adopted relevant portions of Financial Accounting Standards Board Interpretation No. 46, "Consolidation of Variable Interest Entities – An Interpretation of ARB No. 51."

As discussed above, the financial statements of the Company for the year ended December 31, 2001 were audited by other auditors who have ceased operations. As described in Note 4, these financial statements have been revised. We audited the reclassification adjustment described in Note 4 that was applied to revise the 2001 financial statements. In our opinion, such reclassification adjustment is appropriate and has been properly applied. However, we were not engaged to audit, review or apply any procedures to the 2001 financial statements of the Company other than with respect to such reclassification adjustment and, accordingly, we do not express an opinion or any other form of assurance on the 2001 financial statements taken as a whole.

/s/ ERNST & YOUNG LLP

Houston, Texas
February 12, 2004

Report of Independent Public Accountants

To the Board of Directors and Stockholders
of Lexicon Genetics Incorporated:

We have audited the accompanying consolidated balance sheets of Lexicon Genetics Incorporated (a Delaware corporation) and subsidiary as of December 31, 2001 and 2000, and the related consolidated statements of operations, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2001. These financial statements are the responsibility of Lexicon Genetics Incorporated's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards 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. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Lexicon Genetics Incorporated and subsidiary as of December 31, 2001 and 2000, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2001, in conformity with accounting principles generally accepted in the United States.

ARTHUR ANDERSEN LLP

Houston, Texas
February 22, 2002

This is a copy of the report issued by Arthur Andersen LLP, Lexicon's former independent public accountants, in connection with the Company's annual report on Form 10-K for the year ended December 31, 2001. This report has not been reissued by Arthur Andersen LLP in connection with Lexicon's annual report on Form 10-K for the year ended December 31, 2003. See Exhibit 23.2 for further information.

Lexicon Genetics Incorporated

Consolidated Balance Sheets
(In thousands, except par value)

	As of December 31, 2003	As of December 31, 2002
Assets		
Current assets:		
Cash and cash equivalents	$ 81,915	$ 39,362
Restricted cash	56,963	29,487
Short-term investments, including restricted investments of $551 and $28,223, respectively	22,123	54,247
Accounts receivable, net of allowances of $109 for 2003 and 2002	6,571	5,143
Prepaid expenses and other current assets	3,933	4,893
Total current assets	171,505	133,132
Property and equipment, net of accumulated depreciation of $31,941 and $19,768, respectively	83,676	37,362
Goodwill	25,798	25,798
Intangible assets, net of amortization of $2,960 and $1,760, respectively	3,040	4,240
Other assets	180	1,240
Total assets	$ 284,199	$ 201,772
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 5,884	$ 4,378
Accrued liabilities	4,757	4,161
Current portion of deferred revenue	21,125	12,760
Total current liabilities	31,766	21,299
Deferred revenue, net of current portion	26,567	5,887
Long-term debt	56,344	4,000
Other long-term liabilities	3,306	684
Total liabilities	117,983	31,870
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $.01 par value; 5,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $.001 par value; 120,000 shares authorized; 62,827 and 52,367 shares issued and outstanding, respectively	63	52
Additional paid-in capital	380,995	330,701
Deferred stock compensation	(899)	(11,106)
Accumulated deficit	(213,943)	(149,745)
Total stockholders' equity	166,216	169,902
Total liabilities and stockholders' equity	$ 284,199	$ 201,772

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

Lexicon Genetics Incorporated

Consolidated Statements of Operations
(In thousands, except per share amounts)

	Year Ended December 31,		
	2003	2002	2001
Revenues:			
Subscription and license fees	$ 21,550	$ 17,871	$ 14,744
Collaborative research	21,242	17,088	11,220
Compound libraries and other	46	241	4,613
Total revenues	42,838	35,200	30,577
Operating expenses:			
Research and development, including stock-based compensation of $5,048, $5,155, and $5,539, respectively	82,198	74,859	53,355
General and administrative, including stock-based compensation of $5,067, $5,113, and $5,231, respectively	23,233	23,234	20,861
Total operating expenses	105,431	98,093	74,216
Loss from operations	(62,593)	(62,893)	(43,639)
Interest and other income	1,796	3,230	8,781
Interest expense	(325)	(7)	(314)
Net loss before cumulative effect of a change in accounting principle	(61,122)	(59,670)	(35,172)
Cumulative effect of a change in accounting principle	(3,076)	—	—
Net loss	$ (64,198)	$ (59,670)	$ (35,172)
Net loss per common share basic and diluted:			
Net loss before cumulative effect of a change in accounting principle	$ (1.08)	$ (1.14)	$ (0.70)
Cumulative effect of a change in accounting principle	(0.05)	—	—
Net loss per common share, basic and diluted	$ (1.13)	$ (1.14)	$ (0.70)
Shares used in computing net loss per common share, basic and diluted	56,820	52,263	50,213

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

Lexicon Genetics Incorporated

Consolidated Statements of Stockholders' Equity

(In thousands)

	Common Stock		Additional Paid-In	Deferred Stock		Accumulated Other	Total Stockholders'
	Shares	Par Value	Capital	Compensation	Accumulated Deficit	Comprehensive Loss	Equity
Balance at December 31, 2000	48,272	$ 48	$ 296,120	$ (33,637)	$ (54,903)	$ —	$ 207,628
Deferred stock compensation, net of reversals	—	—	(958)	958	—	—	—
Deferred stock compensation of options assumed in acquisition	—	—	—	(351)	—	—	(351)
Amortization of deferred stock compensation	—	—	—	10,770	—	—	10,770
Common stock issued in connection with acquisition	2,919	3	35,213	—	—	—	35,216
Exercise of common stock options	419	1	717	—	—	—	718
Exercise of common stock warrants	412	—	—	—	—	—	—
Net loss	—	—	—	—	(35,172)	—	(35,172)
Unrealized loss on long-term investments	—	—	—	—	—	(437)	(437)
Comprehensive loss	—	—	—	—	—	—	(35,609)
Balance at December 31, 2001	52,022	52	331,092	(22,260)	(90,075)	(437)	218,372
Deferred stock compensation, net of reversals	—	—	(985)	985	—	—	—
Issuance of restricted stock	18	—	99	(99)	—	—	—
Amortization of deferred stock compensation	—	—	—	10,268	—	—	10,268
Cancellation of equity securities in connection with acquisition	(7)	—	(79)	—	—	—	(79)
Exercise of common stock options	330	—	574	—	—	—	574
Exercise of common stock warrants	4	—	—	—	—	—	—
Net loss	—	—	—	—	(59,670)	—	(59,670)
Reversal of unrealized loss on sale of long-term investments	—	—	—	—	—	437	437
Comprehensive loss	—	—	—	—	—	—	(59,233)
Balance at December 31, 2002	52,367	52	330,701	(11,106)	(149,745)	—	169,902
Deferred stock compensation, net of reversals	—	—	(92)	92	—	—	—
Amortization of deferred stock compensation	—	—	—	10,115	—	—	10,115
Public offering of common stock, net of offering costs	10,240	10	50,147	—	—	—	50,157
Exercise of common stock options	102	1	239	—	—	—	240
Exercise of common stock warrants	118	—	—	—	—	—	—
Net and comprehensive loss	—	—	—	—	(64,198)	—	(64,198)
Balance at December 31, 2003	62,827	$ 63	$ 380,995	$ (899)	$ (213,943)	$ —	$ 166,216

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

Lexicon Genetics Incorporated

Consolidated Statements of Cash Flows

(In thousands)

	Year Ended December 31,		
	2003	2002	2001
Cash flows from operating activities:			
Net loss	$ (64,198)	$ (59,670)	$ (35,172)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	10,215	9,111	5,220
Amortization of intangible assets, other than goodwill	1,200	1,200	560
Amortization of deferred stock compensation	10,115	10,268	10,770
Loss on sale of long-term investments	—	197	—
Gain on disposal of property and equipment	(18)	—	—
Cumulative effect of a change in accounting principle	3,076	—	—
Changes in operating assets and liabilities:			
Increase in accounts receivable	(1,428)	(599)	(1,409)
(Increase) decrease in prepaid expenses and other current assets	960	484	(2,531)
(Increase) decrease in other assets	1,060	3,965	(4,919)
Increase in accounts payable and other liabilities	2,257	700	1,089
Increase in deferred revenue	29,045	5,552	8,402
Net cash used in operating activities	(7,716)	(28,792)	(17,990)
Cash flows from investing activities:			
Purchases of property and equipment	(4,824)	(19,766)	(13,471)
Proceeds from disposal of property and equipment	48	—	—
(Increase) decrease in restricted cash	(27,476)	(22,794)	7,186
Purchase of short-term investments	(33,313)	(91,962)	(355,869)
Maturities of short-term investments	65,437	171,109	387,345
Purchase of long-term investments	—	—	(10,835)
Sale of long-term investments	—	10,638	—
Payment of transaction costs, net of cash acquired	—	—	(752)
Net cash provided by (used in) investing activities	(128)	47,225	13,604
Cash flows from financing activities:			
Proceeds from issuance of common stock	50,397	574	718
Proceeds from debt borrowings	—	4,000	—
Repayment of debt borrowings	—	—	(3,909)
Net cash provided by (used in) financing activities	50,397	4,574	(3,191)
Net increase (decrease) in cash and cash equivalents	42,553	23,007	(7,577)
Cash and cash equivalents at beginning of year	39,362	16,355	23,932
Cash and cash equivalents at end of year	$ 81,915	$ 39,362	$ 16,355
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 4	$ 7	$ 330
Supplemental disclosure of noncash investing and financing activities:			
Unrealized (loss) and reversal of unrealized loss on long-term investments	$ —	$ 437	$ (437)
Issuance (cancellation) of equity securities in connection with acquisition	$ —	$ (79)	$ 35,216
Deferred stock compensation, net of reversals	$ 92	$ 886	$ 958
Retirement of property and equipment	$ 1,148	$ 90	$ 181
Property and equipment recorded in connection with consolidation of variable interest entity	$ 54,811	$ —	$ —
Long-term debt recorded in connection with consolidation of variable interest entity	$ (52,344)	$ —	$ —
Other long-term liabilities recorded in connection with consolidation of variable interest entity	$ (2,467)	$ —	$ —

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

Lexicon Genetics Incorporated

Notes to Consolidated Financial Statements

December 31, 2003

1. Organization and Operations

Lexicon Genetics Incorporated (Lexicon or the Company) is a Delaware corporation incorporated on July 7, 1995. Lexicon was organized to discover the functions and pharmaceutical utility of genes and use those gene function discoveries in the discovery and development of pharmaceutical products for the treatment of human disease.

Lexicon has financed its operations from inception primarily through sales of common and preferred stock, contract and milestone payments received under database subscription and collaboration agreements, technology licenses, equipment financing arrangements and leasing arrangements. The Company's future success is dependent upon many factors, including, but not limited to, its ability to discover promising candidates for drug target or therapeutic protein development using its gene knockout technology, establish additional research contracts and agreements for access to its technology, achieve milestones under such contracts and agreements, obtain and enforce patents and other proprietary rights in its discoveries, comply with federal and state regulations, and maintain sufficient capital to fund its activities. As a result of the aforementioned factors and the related uncertainties, there can be no assurance of the Company's future success.

2. Summary of Significant Accounting Policies

Basis of Presentation: The accompanying consolidated financial statements include the accounts of Lexicon and its subsidiary. Intercompany transactions and balances are eliminated in consolidation.

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

Cash, Cash Equivalents and Short-term Investments: Lexicon considers all highly-liquid investments with original maturities or auction-based interest rate reset dates of three months or less to be cash equivalents. Management determines the appropriate classification of its cash equivalents and short-term investments at the time of purchase. Short-term investments consist of U.S. government agency debt obligations, investment grade commercial paper, corporate debt securities and certificates of deposit that have maturities of three to twelve months from the date of purchase. Short-term investments are classified as held-to-maturity securities in the accompanying financial statements. Held-to-maturity securities are carried at amortized cost.

Restricted Cash and Investments: Lexicon is required to maintain restricted cash or investments to collateralize borrowings made under the synthetic lease agreement under which it leases its office and laboratory facilities in The Woodlands, Texas (see Note 9) as well as to collateralize standby letters of credit for the leases on its office and laboratory facilities in East Windsor and Hopewell, New Jersey (see Note 10). As of December 31, 2003 and 2002, the Company maintained restricted cash and investments of $57.5 million and $57.7 million, respectively, under these agreements.

Concentration of Credit Risk: Lexicon's cash equivalents, short-term investments and trade receivables represent potential concentrations of credit risk. The Company minimizes potential concentrations of risk in cash equivalents and short-term investments by placing investments in high-quality financial instruments. The Company's accounts receivable are unsecured and are concentrated in pharmaceutical and biotechnology companies located in the United States and Europe. The Company has not experienced any significant credit losses to date and, at December 31, 2003, management believes that the Company has no significant concentrations of credit risk.

Segment Information and Significant Customers: Lexicon operates in one business segment, which primarily focuses on the discovery of the functions and pharmaceutical utility of genes and the use of those gene function discoveries in the discovery and development of pharmaceutical products for the treatment of human disease. Substantially all of the Company's revenues have been derived from subscriptions to its databases, drug discovery alliances, target validation collaborations for the development and, in some cases, analysis of the physiological

effects of genes altered in knockout mice, technology licenses and compound library sales. In 2003, Incyte Corporation, Amgen Inc., Bristol-Myers Squibb Company and Genentech, Inc. represented 23%, 15%, 14% and 14% of revenues, respectively. In 2002, Incyte, Bristol-Myers Squibb and Millennium Pharmaceuticals, Inc. represented 28%, 14% and 11% of revenues, respectively. In 2001, Incyte, Bristol-Myers Squibb and Merck & Co., Inc. represented 16%, 13% and 12% of revenues, respectively.

Property and Equipment: Property and equipment are carried at cost and depreciated using the straight-line method over the estimated useful life of the assets which ranges from three to 40 years. Maintenance, repairs and minor replacements are charged to expense as incurred. Significant renewals and betterments are capitalized.

Impairment of Long-Lived Assets: Under Statement of Financial Accounting Standards (SFAS) No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets," long-lived assets and certain identifiable intangible assets to be held and used are reviewed for impairment when events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Determination of recoverability is based on an estimate of undiscounted future cash flows resulting from the use of the asset and its eventual disposition. In the event that such cash flows are not expected to be sufficient to recover the carrying amount of the assets, the assets are written down to their estimated fair values.

Goodwill Impairment: Under SFAS No. 142, "Goodwill and Other Intangible Assets," goodwill is not amortized, but is tested at least annually for impairment at the reporting unit level. Impairment is the condition that exists when the carrying amount of goodwill exceeds its implied fair value. The first step in the impairment process is to determine the fair value of the reporting unit and then compare it to the carrying value, including goodwill. If the fair value exceeds the carrying value, no further action is required and no impairment loss is recognized. Additional impairment assessments may be performed on an interim basis if the Company encounters events or changes in circumstances that would indicate that, more likely than not, the carrying value of goodwill has been impaired. There was no impairment of goodwill in 2003.

Revenue Recognition: Revenues are recognized when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed and determinable and collectibility is reasonably assured. Payments received in advance under these arrangements are recorded as deferred revenue until earned. Revenues are earned from database subscriptions, drug discovery alliances, target validation collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice, technology licenses and compound library sales.

Fees for access to databases and other target validation resources are recognized ratably over the subscription or access period. Payments received under target validation collaborations are recognized as revenue as Lexicon performs its obligations related to such research to the extent such fees are non-refundable. Non-refundable upfront fees and annual research funding under our drug discovery alliances are recognized as revenue on a straight line basis over the estimated period of service, generally the contractual research term. Milestone-based fees are recognized upon completion of specified milestones according to contract terms. Non-refundable technology license fees are recognized as revenue upon the grant of the license when performance is complete and there is no continuing involvement. Compound library sales are recognized as revenue upon shipment.

Revenues recognized from multiple element contracts are allocated to each element of the arrangement based on the relative fair values of the elements. The determination of fair value of each element is based on objective evidence. In accordance with Staff Accounting Bulletin (SAB) No. 104, "Revenue Recognition," when revenues for an element are specifically tied to a separate earnings process, revenue is recognized when the specific performance obligation associated with the element is completed. When revenues for an element are not specifically tied to a separate earnings process, they are recognized ratably over the term of the agreement.

Research and Development Expenses: Research and development expenses consist of costs incurred for company-sponsored as well as collaborative research and development activities. These costs include direct and research-related overhead expenses and are expensed as incurred. Patent costs and technology license fees for technologies that are utilized in research and development and have no alternative future use are expensed when incurred.

Stock-Based Compensation: As further discussed in Note 12, Lexicon has three stock-based compensation plans, which are accounted for under the recognition and measurement provisions of Accounting Principles Board (APB) Opinion No. 25, "Accounting for Stock Issued to Employees, and Related Interpretations." Under the intrinsic value

method described in APB Opinion No. 25, no compensation expense is recognized if the exercise price of the employee stock option equals the market price of the underlying stock on the date of grant. Lexicon recognized $10.1 million, $10.3 million and $10.8 million of stock-based compensation during 2003, 2002 and 2001, respectively, which was primarily related to option grants made prior to Lexicon's April 2000 initial public offering. The following table illustrates the effect on net loss and net loss per share if the fair value recognition provisions of SFAS No. 123, "Accounting for Stock Based Compensation," had been applied to all outstanding and unvested awards in each period:

	Year Ended December 31,		
	2003	2002	2001
		(in thousands)	
Net loss, as reported	$ (64,198)	$ (59,670)	$ (35,172)
Add: Stock-based employee compensation expense included in reported net loss	10,115	10,268	10,770
Deduct: Total stock-based employee compensation expense determined under fair value based method for all awards	(26,344)	(25,913)	(20,616)
Pro forma net loss	$ (80,427)	$ (75,315)	$ (45,018)
Net loss per common share, basic and diluted			
As reported	$ (1.13)	$ (1.14)	$ (0.70)
Pro forma	$ (1.42)	$ (1.44)	$ (0.90)

Net Loss Per Common Share: Net loss per common share is computed using the weighted average number of shares of common stock outstanding. Shares associated with stock options and warrants are not included because they are antidilutive.

Comprehensive Loss: Comprehensive loss is comprised of net loss and unrealized gains and losses on long-term investments, which are considered available-for-sale securities. Comprehensive loss is reflected in the consolidated statements of stockholders' equity. During 2002, Lexicon sold its available-for-sale security for $10.6 million, resulting in a realized loss of $197,000 reflected in its net loss for the year. As a result, there is no accumulated other comprehensive loss as of December 31, 2003 or 2002.

3. Recent Accounting Pronouncements

In November 2002, the Emerging Issues Task Force, or EITF, reached a consensus on EITF Issue No. 00-21, "Accounting for Revenue Arrangements with Multiple Deliverables." This consensus requires that revenue arrangements with multiple deliverables be divided into separate units of accounting if the delivered items have value to the customer on a standalone basis, there is objective and reliable evidence of fair value of the undelivered items and, if the arrangement includes a general right of return, performance of the undelivered item is considered probable and substantially in our control. The final consensus is applicable to agreements entered into in fiscal periods beginning after June 15, 2003. The adoption of EITF 00-21 did not have a material impact on the Company's financial statements.

In December 2002, the Financial Accounting Standards Board (FASB) issued SFAS No. 148, "Accounting for Stock-Based Compensation – Transition and Disclosure." 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 No. 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. The Company has elected to continue to follow the intrinsic value method of accounting as prescribed by APB Opinion No. 25, "Accounting for Stock Issued to Employees," to account for employee stock options. The additional disclosures required under SFAS No. 148 are effective for fiscal years ending after December 15, 2002, and have been provided in Note 2.

In January 2003, the FASB issued Interpretation No. 46, or FIN 46, "Consolidation of Variable Interest Entities – An Interpretation of ARB No. 51." FIN 46 was revised in December 2003. It requires that unconsolidated variable interest entities be consolidated by their primary beneficiaries. A primary beneficiary is the party that absorbs a majority of the entity's expected losses or residual benefits. FIN 46 applied immediately to variable interest entities created after January 31, 2003, but was effective for the period ending December 31, 2003 for variable interest

entities created before February 1, 2003. The Company adopted FIN 46 on December 31, 2003 and determined that the lessor under the synthetic lease, as discussed in Note 9, is a variable interest entity as defined by FIN 46, and that the Company absorbs a majority of the variable interest entity's expected losses. Accordingly, the Company consolidated the assets of the variable interest entity, which were comprised of property and improvements funded under the synthetic lease. These assets had a carrying value of $54.8 million, net of accumulated depreciation of $3.1 million on December 31, 2003. Such amounts are included in property and equipment in the accompanying consolidated balance sheet as of December 31, 2003. The Company also consolidated the variable interest entity's debt of $52.3 million and non-controlling interests of $2.5 million, which amounts are included in long-term debt and other long-term liabilities, respectively, in the accompanying consolidated balance sheet as of December 31, 2003. Additionally, the Company recorded a cumulative effect of a change in accounting principle equal to the accumulated depreciation of $3.1 million for the period from the date the buildings were placed in service under the synthetic lease through December 31, 2003. These improvements will be depreciated over their useful lives. Due to the Company's residual value guarantee on the property, the non-recourse feature of the underlying debt, and certain other provisions of the lease arrangement, the Company did not allocate any of the variable interest entity's depreciation or interest expenses to the non-controlling interest. The Company had previously accounted for its involvement with the variable interest entity as an operating lease.

4. Reclassification

In the accompanying statement of cash flows for the year ended December 31, 2001, Lexicon has reclassified the amount of restricted cash from cash and cash equivalents into a separate line item.

5. Investments

Investments at December 31, 2003 and 2002 were as follows:

	As of December 31, 2003			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
		(In thousands)		
Held-to-maturity:				
Certificates of deposit	$ 561	$ —	$ —	$ 561
U.S. government agencies	3,500	2	—	3,502
Corporate debt securities	16,572	—	(13)	16,559
Commercial paper	1,490	—	(2)	1,488
Total held-to-maturity investments	$ 22,123	$ 2	$ (15)	$ 22,110

	As of December 31, 2002			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
		(In thousands)		
Held-to-maturity:				
Certificates of deposit	$ 6,091	$ —	$ —	$ 6,091
U.S. government agencies	7,036	5	—	7,041
Corporate debt securities	13,719	8	(3)	13,724
Commercial paper	26,127	—	—	26,127
Other debt securities	1,274	7	—	1,281
Total held-to-maturity investments	$ 54,247	$ 20	$ (3)	$ 54,264

6. Property and Equipment

Property and equipment at December 31, 2003 and 2002 are as follows:

	Estimated Useful Lives In Years	As of December 31, 2003	2002
		(In thousands)	
Computers and software	3-5	$ 11,519	$ 10,996
Furniture and fixtures	5-7	7,676	8,595
Laboratory equipment	3-7	29,847	27,282
Leasehold improvements	3-10	11,765	10,257
Buildings	15-40	51,246	—
Land	—	3,564	—
Total property and equipment		115,617	57,130
Less: Accumulated depreciation		(31,941)	(19,768)
Net property and equipment		$ 83,676	$ 37,362

7. Income Taxes

Lexicon recognizes deferred tax liabilities and assets for the expected future tax consequences of events that have been recognized differently in the financial statements and tax returns. Under this method, deferred tax liabilities and assets are determined based on the difference between the financial statement carrying amounts and tax bases of liabilities and assets using enacted tax rates and laws in effect in the years in which the differences are expected to reverse. Deferred tax assets are evaluated for realization based on a more-likely-than-not criteria in determining if a valuation allowance should be provided.

The components of Lexicon's deferred tax assets (liabilities) at December 31, 2003 and 2002 are as follows:

	As of December 31, 2003	2002
	(In thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 46,130	$ 39,887
Research and development tax credits	8,105	7,113
Stock-based compensation	7,468	5,828
Deferred revenue	16,685	4,686
Other	1,628	1,230
Total deferred tax assets	80,016	58,744
Deferred tax liabilities:		
Property and equipment	(1,643)	(990)
Other	(59)	(138)
Total deferred tax liabilities	(1,702)	(1,128)
Less: Valuation allowance	(78,314)	(57,616)
Net deferred tax assets	$ —	$ —

At December 31, 2003, Lexicon had net operating loss carryforwards of approximately $131.8 million and research and development tax credit carryforwards of approximately $8.1 million available to reduce future income taxes. These carryforwards will begin to expire in 2011. A change in ownership, as defined by federal income tax regulations, could significantly limit the Company's ability to utilize its carryforwards. Based on the federal tax law limits and the Company's cumulative loss position, Lexicon concluded it was appropriate to establish a full valuation allowance for its net deferred tax assets until an appropriate level of profitability is sustained. During 2003, the valuation allowance increased $20.7 million primarily due to the Company's current year net loss, and the current year research tax credits.

8. Goodwill and Other Intangible Assets

On July 12, 2001, Lexicon completed the acquisition of Coelacanth Corporation in a merger. Coelacanth, now Lexicon Pharmaceuticals (New Jersey), Inc., forms the core of Lexicon Pharmaceuticals, the division of the

Company responsible for small molecule compound discovery. The results of Lexicon Pharmaceuticals (New Jersey), Inc. are included in the Company's results of operations for the period subsequent to the acquisition.

Goodwill, associated with the acquisition, of $25.8 million, which represents the excess of the $36.0 million purchase price over the fair value of the underlying net identifiable assets, was assigned to the consolidated entity, Lexicon. There was no change in the carrying amount of goodwill for the year ended December 31, 2003. In accordance with SFAS No. 142, the goodwill balance is not subject to amortization, but is tested at least annually for impairment at the reporting unit level, which is the Company's single operating segment. The Company performed an impairment test of goodwill on its annual impairment assessment date. This test did not result in an impairment of goodwill.

Other intangible assets represent Coelacanth's technology platform, which consists of its proprietary ClickChem™ reactions, novel building blocks and compound sets, automated production systems, high throughput ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) capabilities and its know-how and trade secrets. The Company expects to amortize the value assigned to other intangible assets on a straight-line basis over an estimated life of five years.

The amortization expense for the year ended December 31, 2003 was $1.2 million. The estimated amortization expense for the next five years is as follows:

	For the Year Ending December 31 (In thousands)
2004	$ 1,200
2005	1,200
2006	640
2007	—
2008	—

9. Debt Obligations

Genentech Loan: On December 31, 2002, Lexicon borrowed $4.0 million under a note agreement with Genentech, Inc. The proceeds of the loan are to be used to fund research efforts under the alliance agreement with Genentech discussed in Note 14. The note matures on December 31, 2005, but the Company may prepay it at any time. The Company may repay the note, at its option, in cash, in shares of common stock valued at the then-current market price, or in a combination of cash and shares, subject to certain limitations. The note accrues interest at an annual rate of 8%, compounded quarterly. The note is subordinated in right of payment to borrowings made under Lexicon's synthetic lease, which is discussed below.

Synthetic Lease Obligation: In October 2000, Lexicon entered into a synthetic lease agreement under which the lessor purchased the Company's existing laboratory and office buildings and animal facility in The Woodlands, Texas and agreed to fund the construction of an additional laboratory and office building and a second animal facility. The synthetic lease agreement was subsequently expanded to include funding for the construction of a central plant facility. Including the purchase price for the Company's existing facilities, the synthetic lease, as amended, provides for funding of up to $55.0 million in property and improvements. The term of the agreement is six years, which includes the construction period and a lease period. Lease payments for the new facilities began upon completion of construction, which occurred at the end of the first quarter of 2002. Lease payments are subject to fluctuation based on LIBOR rates. Based on a year-end LIBOR rate of 1.16%, the Company's total lease payments would be approximately $0.8 million per year. At the end of the lease term, the lease may be extended for one-year terms, up to seven additional terms, or the Company may purchase the properties for a price equal to the $54.8 million funded under the synthetic lease for property and improvements plus the amount of any accrued but unpaid lease payments. If the Company elects not to renew the lease or purchase the properties, it may arrange for the sale of the properties to a third party or surrender the properties to the lessor. If the Company elects to arrange for the sale of the properties or surrender the properties to the lessor, it has guaranteed approximately 86% of the total original cost as the residual fair value of the properties. The Company is required to maintain restricted cash or investments to collateralize borrowings made under the synthetic lease agreement. In addition, Lexicon has agreed to maintain cash and investments of at least $12.0 million in excess of the Company's restricted cash and investments. If the Company's cash and investments fall below that level, the Company may be required to seek a waiver of that agreement or to purchase the properties or arrange for their sale to a third party. Because the Company's cost to purchase the properties would not materially exceed the $54.8 million funded under the synthetic

lease for property and improvements and would likely be less than the amount of restricted cash and investments it is required to maintain under the synthetic lease, the Company believes that any requirement that it do so would not have a material adverse effect on its financial condition. As of December 31, 2003 and 2002, the Company maintained restricted cash and investments of $57.0 million and $57.2 million, respectively, to collateralize funding for property and improvements under the synthetic lease of $54.8 million and $55.0 million. Lexicon consolidated the lessor under its synthetic lease upon adoption of FIN 46. See Note 3, "Recent Accounting Pronouncements," for information on the financial statement impact.

10. Commitments and Contingencies

Operating Lease Obligation: Lexicon's subsidiary leases laboratory and office space in East Windsor and Hopewell, New Jersey under agreements which expire in January 2004 and June 2013, respectively. Lexicon is the guarantor of the obligations of its subsidiary under the Hopewell lease. The Company is required to maintain restricted investments to collateralize the East Windsor and Hopewell leases. As of December 31, 2003 and 2002, the Company had $0.5 million in restricted investments to collateralize standby letters of credit for these leases. Additionally, Lexicon leases certain equipment under operating leases.

Rent expense for all operating leases was approximately $3.7 million, $2.8 million, and $0.9 million for the years ended December 31, 2003, 2002 and 2001, respectively. These amounts included rent expense related to the synthetic lease. Lexicon consolidated the lessor under its synthetic lease upon adoption of FIN 46 on December 31, 2003. Future payments under the synthetic lease agreement will be included in interest expense rather than rent expense. The table below includes non-cancelable future lease payments for the facilities in New Jersey:

	For the Year Ending December 31 (In thousands)
2004	$ 2,196
2005	2,191
2006	2,248
2007	2,248
2008	2,309
Thereafter	10,921
Total	$ 22,113

Employment Agreements: Lexicon has entered into employment agreements with certain of its corporate officers. Under the agreements, each officer receives a base salary, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The employment agreements are at-will and contain non-competition agreements. The agreements also provide for a termination clause, which requires either a six or 12-month payment based on the officer's salary, in the event of termination or change in corporate control.

11. Capital Stock

Common Stock: In July 2003, Lexicon completed the public offering and sale of 10.0 million shares of its common stock at a price of $5.25 per share. In August 2003, the underwriters partially exercised their over-allotment option, purchasing an additional 240,000 shares. The total net proceeds from the offering was $50.1 million, after deducting underwriting discounts of $3.2 million and offering expenses of $0.4 million.

12. Stock Options and Warrants

Stock Options

2000 Equity Incentive Plan: In September 1995, Lexicon adopted the 1995 Stock Option Plan, which was subsequently amended and restated in February 2000 as the 2000 Equity Incentive Plan (the "Equity Incentive Plan"). The Equity Incentive Plan will terminate in 2010 unless the Board of Directors terminates it sooner. The Equity Incentive Plan provides that it will be administered by the Board of Directors, or a committee appointed by the Board of Directors, which determines recipients and types of options to be granted, including number of shares under the option and the exercisability of the shares. The Equity Incentive Plan is presently administered by the Compensation Committee of the Board of Directors.

The Equity Incentive Plan provides for the grant of incentive stock options to employees and nonstatutory stock options to employees, directors and consultants of the Company. The plan also permits the grant of stock bonuses and restricted stock purchase awards. Incentive stock options have an exercise price of 100% or more of the fair market value of our common stock on the date of grant. Nonstatutory stock options may have an exercise price as low as 85% of fair market value on the date of grant. The purchase price of other stock awards may not be less than 85% of fair market value. However, the plan administrator may award bonuses in consideration of past services without a purchase payment. Shares may be subject to a repurchase option in the discretion of the plan administrator.

The Board of Directors initially authorized and reserved an aggregate of 11,250,000 shares of common stock for issuance under the Equity Incentive Plan. On January 1 of each year for ten years, beginning in 2001, the number of shares reserved for issuance under the Equity Incentive Plan automatically will be increased by the greater of:

- 5% of Lexicon's outstanding shares on a fully-diluted basis; or
- that number of shares that could be issued under awards granted under the Equity Incentive Plan during the prior 12-month period;

provided that the Board of Directors may provide for a lesser increase in the number of shares reserved under the Equity Incentive Plan for any year. The total number of shares reserved in the aggregate may not exceed 60,000,000 shares over the ten-year period.

As of December 31, 2003, an aggregate of 15,000,000 shares of common stock had been reserved for issuance, options to purchase 12,669,159 shares were outstanding and 1,795,078 shares had been issued upon the exercise of stock options issued under the Equity Incentive Plan.

2000 Non-Employee Directors' Stock Option Plan: In February 2000, Lexicon adopted the 2000 Non-Employee Directors' Stock Option Plan (the "Directors' Plan") to provide for the automatic grant of options to purchase shares of common stock to non-employee directors of the Company. Under the Directors' Plan, non-employee directors first elected after the closing of the Company's initial public offering receive an initial option to purchase 30,000 shares of common stock. In addition, on the day following each of the Company's annual meetings of stockholders, beginning with the annual meeting in 2001, each non-employee director who has been a director for at least six months is automatically granted an option to purchase 6,000 shares of common stock. Initial option grants become vested and exercisable over a period of five years and annual option grants become vested over a period of 12 months from the date of grant. Options granted under the Directors' Plan have an exercise price equal to the fair market value of the Company's common stock on the date of grant and term of ten years from the date of grant.

The Board of Directors initially authorized and reserved a total of 600,000 shares of its common stock for issuance under the Directors' Plan. On the day following each annual meeting of Lexicon's stockholders, for 10 years, starting in 2001, the share reserve will automatically be increased by a number of shares equal to the greater of:

- 0.3% of the Company's outstanding shares on a fully-diluted basis; or
- that number of shares that could be issued under options granted under the Directors' Plan during the prior 12-month period;

provided that the Board of Directors may provide for a lesser increase in the number of shares reserved under the Directors' Plan for any year.

As of December 31, 2003, an aggregate of 600,000 shares of common stock had been reserved for issuance, options to purchase 131,000 shares were outstanding and no options had been exercised under the Directors' Plan.

Coelacanth Corporation 1999 Stock Option Plan: Lexicon assumed the Coelacanth Corporation 1999 Stock Option Plan (the "Coelacanth Plan") and the outstanding stock options under the plan in connection with our July 2001 acquisition of Coelacanth Corporation. The Company will not grant any further options under the plan. As outstanding options under the plan expire or terminate, the number of shares authorized for issuance under the plan will be correspondingly reduced.

The purpose of the plan was to provide an opportunity for employees, directors and consultants of Coelacanth to acquire a proprietary interest, or otherwise increase their proprietary interest, in Coelacanth as an incentive to continue their employment or service. Both incentive and nonstatutory options are outstanding under the plan.

Most outstanding options vest over time and expire ten years from the date of grant. The exercise price of options awarded under the plan was determined by the plan administrator at the time of grant. In general, incentive stock options have an exercise price of 100% or more of the fair market value of Coelacanth common stock on the date of grant and nonstatutory stock options have an exercise price as low as 85% of fair market value on the date of grant.

As of December 31, 2003, an aggregate of 122,649 shares of common stock had been reserved for issuance, options to purchase 89,012 shares of common stock were outstanding, options to purchase 10,689 shares of common stock had been cancelled and 22,948 shares of common stock had been issued upon the exercise of stock options issued under the Coelacanth Plan.

Stock-Based Compensation: SFAS No. 123, "Accounting for Stock-Based Compensation," allows companies to adopt one of two methods for accounting for stock options. Lexicon has elected the method that requires disclosure only of stock-based compensation. Because of this election, the Company is required to account for its employee stock-based compensation plans under APB Opinion No. 25 and its related interpretations. Accordingly, deferred compensation is recorded for stock-based compensation grants based on the excess of the estimated fair value of the common stock on the measurement date over the exercise price. The deferred compensation is amortized over the vesting period of each unit of stock-based compensation grant, generally four years. If the exercise price of the stock-based compensation grants is equal to the estimated fair value of the Company's stock on the date of grant, no compensation expense is recorded.

During the year ended December 31, 2000, Lexicon recorded $54.1 million in aggregate deferred compensation relating to options issued to employees and non-employee directors prior to our initial public offering. During the years ended December 31, 2003, 2002 and 2001, the Company recognized $10.1 million, $10.3 million and $10.7 million, respectively, in compensation expense relating to these options. Additionally, during the years ended December 31, 2003 and 2002, the Company reversed approximately $79,000 and $612,000, respectively, of deferred compensation and additional paid-in capital for unamortized deferred compensation related to the forfeiture of nonvested options by terminated employees. Total amortization expense was revised to the extent amortization had previously been recorded for nonvested options.

The pro forma information regarding net loss required by SFAS No. 123 has been included in Note 2. The information has been determined as if Lexicon had accounted for its employee stock options under the fair-value method as defined by SFAS No. 123. For purposes of pro forma disclosures, the estimated fair value of the options is amortized to expense over the vesting period of the options using the straight-line method. The fair value of these options was estimated at the date of grant using the Black-Scholes method and the following weighted-average assumptions for 2003, 2002 and 2001:

- volatility factors of 92%, 100% and 109%, respectively;
- risk-free interest rates of 3.40%, 4.64%, and 5.03%, respectively;
- expected option lives of seven years;
- three percent expected turnover; and
- no dividends.

Lexicon records the fair value of options issued to non-employee consultants, including Scientific Advisory Panel members, at the fair value of the options issued. The fair values of the issuances were estimated using the Black-Scholes pricing model with the assumptions noted in the preceding paragraph. Any expense is recognized over the service period or at the date of issuance if the options are fully vested and no performance obligation exists. The Company reversed expense of $6,000 for the year ended December 31, 2003 for the decline in fair value of options issued to non-employee consultants and recognized expense of $79,000 and $109,000 in the years ended December 31, 2002 and 2001, respectively.

If vesting continues in accordance with the outstanding individual stock options, Lexicon expects to record amortization expense for deferred stock compensation of $0.9 million in 2004.

Stock Option Activity: The following is a summary of option activity under Lexicon's stock option plans:

	Options Outstanding	Weighted Average Exercise Price
	(In thousands)	
Balance at December 31, 2000	8,253	$ 4.33
Granted	2,493	11.31
Exercised	(419)	1.71
Canceled	(224)	9.17
Balance at December 31, 2001	10,103	6.04
Granted	2,200	8.68
Exercised	(330)	1.74
Canceled	(601)	9.70
Balance at December 31, 2002	11,372	6.47
Granted	1,897	4.24
Exercised	(102)	2.34
Canceled	(278)	8.92
Balance at December 31, 2003	12,889	6.12
Exercisable at December 31, 2003	9,345	$ 5.73

The weighted average fair values of options granted during the years ended December 31, 2003, 2002 and 2001 were $3.52, $7.32 and $10.31, respectively. As of December 31, 2003, 1,004,763 shares of common stock were available for grant under Lexicon's stock option plans.

Stock Options Outstanding: The following table summarizes information about stock options outstanding at December 31, 2003:

Options Outstanding				Options Exercisable	
Range of Exercise Price	Outstanding as of December 31, 2003	Weighted Average Remaining Contractual Life (In Years)	Weighted Average Exercise Price	Exercisable as of December 31, 2003	Weighted Average Exercise Price
	(In thousands)			(In thousands)	
$0.0003 - $0.22	886	1.9	$ 0.05	886	$ 0.05
1.67 – 2.50	5,509	5.3	2.41	5,419	2.41
3.16 – 4.70	1,534	9.1	3.92	44	4.18
4.76 – 7.00	633	9.1	5.62	145	5.75
7.20 – 10.55	1,994	8.0	9.34	1,035	9.33
10.87 – 16.00	1,715	7.3	12.60	1,268	12.55
16.63 – 22.06	401	6.3	19.51	362	19.51
25.25 – 31.63	35	6.8	27.00	28	27.12
38.00 – 38.50	182	6.7	38.49	158	38.49
	12,889		$ 6.12	9,345	$ 5.73

Warrants

On May 7, 1998, Lexicon issued to the placement agent for the Series A Preferred Stock private placement a warrant to purchase 605,001 shares of common stock at an exercise price of $2.50 per share. The warrant provided that the exercise price could be paid in cash or by way of a "cashless" exercise based upon the difference between fair market value and exercise price. The value of the warrant, along with the offering costs associated with the private placement, were accreted back to the Series A Preferred Stock through the conversion date of the Series A Preferred Stock. This warrant was exercised in 2001 by way of a cashless exercise, resulting in the issuance of a total of 412,648 shares of common stock.

In July 1998, Lexicon issued a warrant to purchase 249,999 shares of common stock at an exercise price of $2.50 per share, in connection with the grant to the Company of an option to lease additional real property. Amortization of the remaining balance of $155,000 on the lease option was expensed in 2000 upon the Company's completion of a synthetic lease agreement under which the lessor purchased the optioned real property under an arrangement providing for its lease to the Company (see Note 9). The warrant was exercised in 2003 by way of a cashless exercise, resulting in the issuance of a total of 117,784 shares of common stock.

In connection with the acquisition of Coelacanth in July 2001, Lexicon assumed Coelacanth's outstanding warrants to purchase 25,169 shares of common stock. The warrants expire on March 31, 2009. The fair value of the warrants was included in the total purchase price for the acquisition. As of December 31, 2003, warrants to purchase 16,483 shares of common stock, with an exercise price of $11.93 per share, remained outstanding.

Aggregate Shares Reserved for Issuance

As of December 31, 2003 an aggregate of 12,905,654 shares of common stock were reserved for issuance upon exercise of outstanding stock options and warrants and 1,004,763 additional shares were available for future grants under Lexicon's stock option plans.

13. Benefit Plans

Lexicon has established an Annual Profit Sharing Incentive Plan (the Profit Sharing Plan). The purpose of the Profit Sharing Plan is to provide for the payment of incentive compensation out of the profits of the Company to certain of its employees. Participants in the Profit Sharing Plan are entitled to an annual cash bonus equal to their proportionate share (based on salary) of 15 percent of the Company's annual pretax income, if any.

Lexicon maintains a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code. The plan covers substantially all full-time employees. Participating employees may defer a portion of their pretax earnings, up to the Internal Revenue Service annual contribution limit. Beginning in 2000, the Company was required to match employee contributions according to a specified formula. The matching contributions totaled approximately $637,000, $645,000, and $332,000 in 2003, 2002 and 2001, respectively. Company contributions are vested based on the employee's years of service, with full vesting after four years of service.

14. Collaboration and License Agreements

Lexicon derives substantially all of its revenues from drug discovery alliances, target validation collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice, technology licenses, subscriptions to its databases and compound library sales.

Drug Discovery Alliances

Lexicon has entered into the following alliances for the discovery and development of therapeutics based on its *in vivo* drug target discovery efforts:

Abgenix, Inc. Lexicon established a drug discovery alliance with Abgenix in July 2000 to discover novel therapeutic antibodies using the Company's target validation technologies and Abgenix's technology for generating fully human monoclonal antibodies. Lexicon and Abgenix expanded and extended the alliance in January 2002, with the intent of accelerating the selection of *in vivo*-validated antigens for antibody discovery and the development and commercialization of therapeutic antibodies based on those targets. Under the alliance agreement, the Company and Abgenix will each have the right to obtain exclusive commercialization rights, including sublicensing rights, for an equal number of qualifying therapeutic antibodies, and will each receive milestone payments and royalties on sales of therapeutic antibodies from the alliance that are commercialized by the other party or a third party sublicensee. Each party will bear its own expenses under the alliance. The expanded alliance also provides us with access to Abgenix's XenoMouse® technology for use in some of our own drug discovery programs. The agreement, as extended, has a term of four years ending July 2004, subject to the right of the parties to extend the term for up to three additional one-year periods.

Bristol-Myers Squibb Company: Lexicon established an alliance with Bristol-Myers Squibb in December 2003 to discover, develop and commercialize small molecule drugs in the neuroscience field. Lexicon is contributing a number of drug discovery programs at various stages of development. Lexicon will continue to use its gene knockout technology to identify additional drug targets with promise in the neuroscience field. For those targets that are selected for the alliance, Lexicon and Bristol-Myers Squibb will work together, on an exclusive basis, to identify, characterize and carry out the preclinical development of small molecule drugs, and will share equally both in the costs and in the work attributable to those efforts. As drugs resulting from the collaboration enter clinical trials, Bristol-Myers Squibb will have the first option to assume full responsibility for clinical development and commercialization. Lexicon received an upfront payment of $36.0 million and is entitled to receive research funding of $30.0 million in the initial three years of the agreement. Bristol-Myers Squibb has the option to extend the discovery portion of the alliance for an additional two years in exchange for further committed research funding

of up to $50.0 million. Lexicon may receive additional cash payments for exceeding specified research productivity levels. Lexicon will also receive clinical and regulatory milestone payments for each drug target for which Bristol-Myers Squibb develops a drug under the alliance. Lexicon will earn royalties on sales of drugs commercialized by Bristol-Myers Squibb. The party with responsibility for the clinical development and commercialization of drugs resulting from the alliance will bear the costs of those efforts. Revenue recognized under this agreement was $0.8 million for the year ended December 31, 2003.

Genentech, Inc. Lexicon established a drug discovery alliance with Genentech in December 2002 to discover novel therapeutic proteins and antibody targets. Under the alliance agreement, Lexicon will use its target validation technologies to discover the functions of secreted proteins and potential antibody targets identified through Genentech's internal drug discovery research. Genentech will have exclusive rights in the discoveries resulting from the collaboration for the research, development and commercialization of therapeutic proteins and antibodies. Lexicon will retain certain other rights in those discoveries, including rights for the development of small molecule drugs. Lexicon received an upfront payment of $9.0 million and funding under a $4.0 million loan in 2002. The terms of the loan are discussed in Note 9. In addition, Lexicon can receive up to $24.0 million in performance payments for its work in the collaboration as it is completed, of which $3.0 million has been received as of December 31, 2003. Total revenue recognized under this agreement was $6.0 million and $0.1 million for the years ended December 31, 2003 and 2002, respectively. Lexicon will also receive milestone payments and royalties on sales of therapeutic proteins and antibodies for which Genentech obtains exclusive rights. The agreement has an expected collaboration term of three years.

Incyte Corporation. Lexicon established a drug discovery alliance with Incyte in June 2001 to discover novel therapeutic proteins using the Company's target validation technologies in the discovery of the functions of secreted proteins from Incyte's LifeSeq® Gold database. Lexicon receives research funding under the agreement, $15.0 million of which has been received as of December 31, 2003. Revenue recognized under this agreement was $5.0 million, $5.0 million and $2.5 million for the years ended December 31, 2003, 2002 and 2001, respectively. Under the alliance agreement, the Company and Incyte will each have the right to obtain exclusive commercialization rights, including sublicensing rights, for an equal number of qualifying therapeutic proteins, and will each receive milestone payments and royalties on sales of therapeutic proteins from the alliance that are commercialized by the other party or a third party sublicensee. The agreement will terminate in June 2004.

Revenues from drug discovery alliances are included in collaborative research revenue in the accompanying consolidated statements of operations.

LexVision Collaborations

Lexicon has entered into the following collaborations for access to the Company's LexVision database of *in vivo*-validated drug targets:

Bristol-Myers Squibb Company. Lexicon established a LexVision collaboration with Bristol-Myers Squibb in September 2000, under which Bristol-Myers Squibb has non-exclusive access to the Company's LexVision database and OmniBank library for the discovery of small molecule drugs. The Company receives annual access fees under this agreement, and is entitled to receive milestone payments and royalties on products Bristol-Myers Squibb develops using the Company's technology. Revenue recognized under this agreement was $5.0 million, $5.0 million and $4.0 million for the years ended December 31, 2003, 2002 and 2001, respectively. The agreement, as amended, has a term of five years, although either party may terminate the agreement after four years.

Incyte Corporation. Lexicon established a LexVision collaboration with Incyte in June 2001, under which Incyte has non-exclusive access to the Company's LexVision database and OmniBank library for the discovery of small molecule drugs. The Company receives annual access fees under this agreement, and is entitled to receive milestone payments and royalties on products Incyte develops using the Company's technology. Revenue recognized under this agreement was $5.0 million, $5.0 million and $2.5 million for the years ended December 31, 2003, 2002 and 2001, respectively. The agreement will terminate in June 2004.

15. Selected Quarterly Financial Data

The table below sets forth certain unaudited statements of operations data, and net loss per common share data, for each quarter of 2003 and 2002.

(In thousands, except per share data)

	Quarter Ended			
	March 31	June 30	September 30	December 31
	(Unaudited)			
2003				
Revenues	$ 8,106	$ 8,921	$ 12,111	$ 13,700
Loss from operations	$ (17,532)	$ (17,852)	$ (14,868)	$ (12,341)
Net loss before cumulative effect of a change in accounting principle	$ (17,145)	$ (17,619)	$ (14,558)	$ (11,800)
Cumulative effect of a change in accounting principle	—	—	—	(3,076)
Net loss	$ (17,145)	$ (17,619)	$ (14,558)	$ (14,876)
Net loss per common share before cumulative effect of a change in accounting principle	$ (0.33)	$ (0.34)	$ (0.24)	$ (0.19)
Cumulative effect of a change in accounting principle	—	—	—	(0.05)
Net loss per common share, basic and diluted	$ (0.33)	$ (0.34)	$ (0.24)	$ (0.24)
Shares used in computing net loss per common share	$ 52,371	$ 52,496	$ 59,475	$ 62,794
2002				
Revenues	$ 7,656	$ 9,411	$ 8,013	$ 10,120
Loss from operations	$ (15,177)	$ (15,640)	$ (17,491)	$ (14,585)
Net loss	$ (14,059)	$ (14,940)	$ (16,809)	$ (13,862)
Net loss per common share, basic and diluted	$ (0.27)	$ (0.29)	$ (0.32)	$ (0.26)
Shares used in computing net loss per common share	52,126	52,250	52,314	52,357

EXECUTIVE OFFICERS

Arthur T. Sands, M.D., Ph.D.
President and Chief Executive Officer

Julia P. Gregory
Executive Vice President, Corporate Development
and Chief Financial Officer

Jeffrey L. Wade, J.D.
Executive Vice President and General Counsel

Brian P. Zambrowicz, Ph.D.
Executive Vice President, Research

Walter F. Colbert
Senior Vice President, Human Resources
and Corporate Services

Lance K. Ishimoto, J.D., Ph.D.
Senior Vice President, Intellectual Property

Alan J. Main, Ph.D.
Senior Vice President, Lexicon Pharmaceuticals

James R. Piggott, Ph.D.
Senior Vice President, Pharmaceutical Biology

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Sam L. Barker, Ph.D.
Principal, Clearview Projects
Former Executive Vice President,
Bristol-Myers Squibb Company

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Chairman, U.S. Russia Investment Fund
Former Co-Chairman, Patricof & Co. Ventures, Inc.

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Alan S. Nies, M.D.
Chairman, Lexicon Genetics Medical Advisory Board
Former Senior Vice President, Merck & Co., Inc.

Arthur T. Sands, M.D., Ph.D.
President and Chief Executive Officer,
Lexicon Genetics Incorporated

CORPORATE INFORMATION

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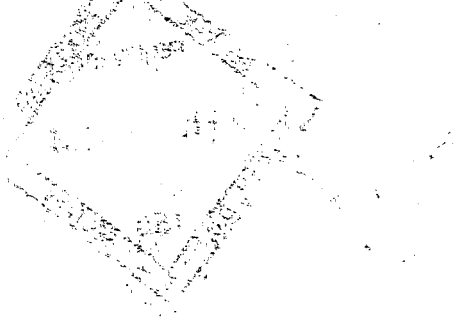
www.mellon-investor.com

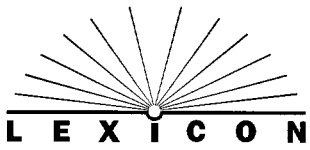
Our 2003 annual report on Form 10-K is available, without charge, upon request by contacting our Corporate Communications Department at 281-863-3000.

Our annual meeting of shareholders will be held at 1:30 p.m. CDT on May 19, 2004 at the Marriott Woodlands Waterway Hotel and Convention Center, 1601 Lake Robbins Drive, The Woodlands, Texas 77380.

Visit our corporate website at http://www.lexicon-genetics.com.

This annual report to shareholders contains forward-looking statements. These statements involve risks, uncertainties and other important factors that may cause the actual results of Lexicon to be materially different from any future results expressed or implied by such forward-looking statements. Information identifying such risks, uncertainties and other important factors is contained in the sections entitled "Factors Affecting Forward-Looking Statements" and "Business – Risk Factors" in our annual report on Form 10-K for the year ended December 31, 2003, as filed with the Securities and Exchange Commission and included as part of this annual report to shareholders.





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