A REVOLUTION IN THE EVOLUTION OF AN INDUSTRY
A MODEL OF DISCOVERY In 1995, Exelixis was founded on the belief that the conservation of genes between species, the simple fruit fly, *Drosophila melanogaster*, would be useful in the discovery of new pharmaceutical products. This approach has proven to be extremely productive, and the power and speed of this system have been substantially enhanced by the availability of the *Drosophila* and human genome sequences. Over the course of the last few years, we have added many other genetic systems to our arsenal, including the nematode worm, *Caenorhabditis elegans*; the zebrafish, *Danio rerio*; the mouse, *Mus musculus*; multiple fungal systems; and plant species such as *Chlamydomonas reinhardtii*, *Arabidopsis thaliana*, and a microtome, *Cucurbita maxima*. We believe we are now the leader in model system genetics and comparative genomics.

REVOLUTIONIZING DRUG DISCOVERY EXELIXIS...TRANSLATING THE GENOME INTO HEALTH

The completion of the human genome sequence, together with the sequencing of the genomes of several of our model organisms, has amazed and humbled us all by demonstrating the extraordinary similarities between the genomes of humans and those of simpler organisms. These sequences further validate our approach of characterizing genetic and biochemical processes in simple organisms, where the work can be done quickly and systematically, and then translating that knowledge to humans. We have developed substantial proprietary DNA sequence databases from a variety of organisms, including several insect, fungal, plant, and fish species, and have combined these with the publicly available data from humans, *Drosophila*, *C. elegans*, and other species. The availability of these sequences, together with a complete suite of powerful genetic tools and databases, many of them proprietary to Exelixis, substantially accelerates our already efficient discovery platform. However, we have not stopped there...
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we have the people and the tools to achieve our goals

WE BELIEVE WE CAN FUNDAMENTALLY INCREASE

IN ADDITION TO OUR GENETICS CORE, we have developed extensive capabilities in important bioinformatics, genomics, proteomics, and biochemical technologies, resulting in a powerful, integrated platform that permits us to answer a broad array of disease-based questions in a systematic manner, and to confirm our answers in living organisms. We are able to efficiently translate the functional data from simple organisms to more complex organisms, such as humans. Genomics and informatics play an integral role in this effort, with the primary focus on increasing the speed and efficiency of the overall discovery process. Our informatics capabilities provide a comprehensive set of database analysis tools that allow us to rapidly identify and prioritize the human versions of the genes identified in model systems.

In the last 20 years, the percentage of target identification programs yielding successful drugs has not increased significantly, despite tremendous advances in technology. In fact, some would say that the net result of the application of genomics technology has simply been to maintain and maintain the pipeline at higher cost. We believe that by applying our integrated, biologically-based platform to the discovery process, we can substantially increase the chances of success and shorten the time to market of our discovery projects.

We have stacked the odds of success in our favor by building a comprehensive drug discovery effort that seeks to minimize risk and reduce time at each critical phase of the discovery process. Our projects are based on the targets that emerge from our integrated biological platform. Each of the targets we take forward has good biological data from multiple systems to indicate that its modulation will lead to a desired therapeutic outcome. We believe these targets present a lower risk than targets identified through alternative methodologies. Now we take these targets and format them into high-throughput screening assays with which we find chemicals that are potential drugs. While the industry standard is to format these assays in approximately six months, at Exelixis our average time is two to three months, an example of our aggressive approach to the entire discovery process. We have established a high-throughput screening laboratory that will conduct over 12 screen rounds against millions of compounds in 2001. In addition, we have built extensive capabilities in protein crystallography, cell biology, medicinal chemistry, ADME (absorption, distribution, metabolism, excretion and toxicity), pharmacokinetics, pharmacodynamics, pharmacology, and cheminformatics to support our efforts in drug discovery. We are committed to the continued expansion of our drug discovery capabilities to maintain and increase the quantity and quality of development candidates advancing towards clinical development.
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FROM RESEARCH Using our integrated, genomics-based discovery platform, we have developed proprietary programs in cancer, angiogenesis, and inflammation. Through our unique understanding of the biological basis of disease, we expect to generate a substantial pipeline of products in each of these areas. CANCER is a leading cause of death in developed countries. Our oncology research is focused on several biologic mechanisms: cell cycle checkpoints, DNA damage response and apoptosis, cell proliferation, and cell adhesion. We are developing a number of small molecule drug targets and monoclonal antibody drug targets that selectively kill cancer cells while leaving normal cells unharmed. Drugs against these targets would provide alternatives to current cancer therapies, particularly focused on solid tumors such as breast, prostate, colon, ovarian, and lung cancers. Currently, we have six novel targets in high-throughput screening, and have initiated lead optimization for several exciting leads, with our first development compound expected by the end of 2001.

ANGIOGENESIS is the process by which new blood vessels are formed. The ability to block this process is an evolving strategy for cancer therapy, whereby restriction of the tumor blood supply limits its growth. Similarly, anti-angiogenic agents can be used to treat ocular diseases such as diabetic retinopathy and macular degeneration, as well as rheumatoid arthritis and endometriosis. Products that promote angiogenesis could be of therapeutic value in heart disease, infertility, and ulcers. Using fly and zebrafish model systems, we have identified over 150 genes involved in angiogenesis and are actively working to validate and prioritize them as therapeutic targets. INFLAMMATION is a complex process characterized by an abnormal accumulation of specific blood cells and the subsequent release of destructive factors that result in local tissue damage, fibrosis, and pain. Our program is focused on the innate or inborn immune system, which is particularly important in diseases like asthma, inflammatory bowel diseases, and arthritis.
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THE PROCESS OF PROGRESS Cancer is a genetic disease. It is also heterogeneous and progressive, and is characterized by the successive accumulation of mutations, amplifications, and deletions in genes involved in the control of cell growth, survival, and adhesion. Among the most frequently disrupted cancer genes are the tumor suppressors p53, p21/CDP, Rb, and APC, whose function is to maintain cells in a healthy state. These genes and their signaling pathways have been conserved through evolution and serve analogous roles in humans and in model organisms such as the fly and worm.

The Exelixis oncology program leverages our expertise in model organism genetics to perform genome-wide screens in "diseased" animals to identify additional proteins that either restore normal function to the defective pathway or are involved in the selective killing of the diseased cell. These screens are being performed on a scale that allow us to identify the functionally relevant proteins involved in a selected cancer pathway. These "saturation screens" provide us with a comprehensive list of genes from which to select the most attractive targets for developing chemical or antibody-based inhibitors. Once an interesting invertebrate gene is selected, the next step in the drug discovery process is to identify and validate the disease-relevant human counterpart. We do this by using a wide array of comparative genomics, expression arrays, and informatics tools to wade through the billions of units of DNA now available for several species, including humans. In the process of comparing DNA from worms to fly to human, and even human to human, not only do we discover our future drug targets, but we also uncover evolutionary relationships that confirm the remarkably conserved nature of life. Once identified, the human targets are rapidly assessed for disease relevance using focused cellular genetic screens based on their presumed function in a specific pathway (e.g., p53) or by a specific mechanism (e.g., apoptosis).

Validated human proteins are then formatted into biochemical assays suitable for screening against our library of one million compounds in order to identify novel leads for the treatment of cancer. Alternatively, subsets of the validated human proteins may function as targets for the development of antibodies that will become novel cancer therapies, while different subsets will be addressable through alternative therapeutic approaches such as gene therapy. Exelixis is focused internally on the development of small molecule drugs and will develop antibodies and other therapeutic opportunities through partnerships.
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health and well-being

OUR EXPERTISE AND COLLABORATIONS IN MULTIPLE INDUSTRIES

On a global basis, improving the safety of our agricultural practices as well as the cost, access, and quality of food can have just as much impact on the health and well-being of the world's population as the improvement of medical practices. We believe that the application of both our knowledge and technology to these problems is a worthwhile economic and ethical undertaking.

While our proprietary programs focus on drug discovery and development, we believe our core technologies are valuable to all other industries whose products can be enhanced by an understanding of DNA or proteins, including the agrochemical, agricultural, and diagnostic industries. Many of these industries have shorter product development cycles and lower risk than the pharmaceutical industry, while at the same time generating significant sales. By partnering with leading companies in multiple industries, we are able to diversify our business risk, maximize our future revenue stream, and offset some of the cost of our proprietary programs.

We have established commercial collaborations with several major pharmaceutical and agricultural companies. Agrinomics LLC, our joint venture with Aventis CropScience S.A., is focused on the development and commercialization of our proprietary Arabidopsis ACITAG™ gene expression technology to "turn on" and "turn off" particular plant genes of interest, which may be used for the development of plants with useful characteristics such as higher drought tolerance or disease resistance. Genoptera LLC, our joint venture with Bayer, is developing novel insecticides and nematicides for crop protection. Together with Pharmacia, we are discovering novel drug targets for the treatment of Alzheimer's disease and type II diabetes and its associated lipid defects. With Bristol-Myers Squibb and Dow AgroSciences, we are applying our proprietary mechanism of action technology to identify the genetic targets of products they provide to us, which are in different stages of development. Our collaborations provide us with substantial funding and in many cases, strategic technology acquisition. Total committed funding, which does not include milestones or royalties, totals over $200 million, one of the highest totals in the industry today.
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PROVIDE STRENGTH FOR THE FOUNDATION OF OUR COMPANY
THE FUTURE There is a shift occurring in genomics — from sequence data to functional knowledge, and from functional knowledge to products. Exelixis was founded on the belief that the genomic sequence would be available, and has built the infrastructure to effectively and efficiently move our biologically validated targets forward in development, both for our partners and for our internal programs. We started as a fruit fly company, and by strategically and aggressively pursuing opportunities, we have built critical mass in multiple disciplines. We committed the resources first to genetics, genomics, and informatics, and now to drug discovery. Our organization is large enough to have critical mass in all of these disciplines, while at the same time small enough to maintain our efficient focus. The results of our diligent efforts on all fronts have created a revolutionary platform on which to discover, develop, and commercialize unique products. It’s a revolution in the evolution of an industry and a company.
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TO OUR STOCKHOLDERS

The year 2000 was filled with significant accomplishments and substantial growth for Exelixis. We completed our successful initial public offering, added to our technology platform, and expanded our relationships with corporate collaborators. Also in the year 2000, the future of medicine was energized by the completion of the sequencing of the human genome. The remarkable similarity of the human genome to the genomes of simpler organisms has validated our approach to the discovery of new pharmaceutical products based on model system genetics and comparative genomics, and gives us even greater confidence as we move forward in our drug discovery programs.

In the year 2000 we saw the results of the efforts that we made over the past five years to build an integrated biological platform. During the course of the year we identified a large number of very high-quality targets for our partnered and proprietary programs. Each of these targets was generated with a substantial amount of biological data to confirm its impact on a disease process. We believe that the quality of these targets can reduce much of the risk inherent in discovery.

This past year also was the year in which our internal drug discovery efforts began to reach critical mass. Over the course of the last two years, we have built a world-class drug discovery organization that we believe paves the way for future commercial success. While we started with a model system genetics core, a key component of our strategy is to develop proprietary cancer products by leveraging our integrated discovery platform to increase the speed, efficiency, and quality of pharmaceutical product discovery and development.

Additionally, we believe our proprietary technologies are valuable to other industries whose products can be enhanced by an understanding of DNA or proteins, including the agrochemical, agricultural, and diagnostic industries. We are committed to increasing stockholder value through our efforts to improve all aspects of the drug discovery process. We believe that by understanding the biological basis of disease we can find better drug targets and, by optimizing chemistry, high-throughput screening, and other aspects of the process, we can use those targets to identify better drugs quickly and efficiently. We have gathered the intellectual property, secured the financial resources, assembled a diverse and talented group of scientists led by an experienced management team, and are on our way to achieving our vision—to discover and develop innovative products for the treatment of cancer and to work with our partners for the development of products with commercial utility in a variety of industries.

We have identified many cancer-related targets and have potent lead compounds that are in preclinical testing for activity and safety.
HIGHLIGHTS OF 2000:

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<th>JANUARY</th>
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<td>Bayer and Exelixis form Genoptera LLC, for the development of novel, broad-spectrum insecticides and nematicides.</td>
<td>Exelixis publishes Drosophila p53 existence and function in <em>Cell</em>.</td>
<td>Exelixis completes initial public offering resulting in net proceeds of $124.7 million.</td>
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PROGRESS IN INTERNAL PROGRAMS

We are committed to our focus on oncology and I am proud of the advancements we have made in this regard through hiring, partnerships, and internal expansion. We filled several key drug discovery positions, including Vice President of Drug Discovery and senior positions in new lead discovery, molecular pharmacology, and structural biology, as well as many positions in medicinal chemistry and pharmacology. We have identified many cancer-related targets, have brought 12 of them into high-throughput screening, and have identified potent lead compounds that are in preclinical testing for activity and safety. Our discovery compound library now contains more than one million highly diverse small molecule, drug-like compounds, and we have a current high-throughput screening capacity of 100,000 compounds per day.

Early in the year we announced the publication of our discovery of a Drosophila gene functionally related to the human tumor suppressor gene p53. These data have significance in the study of cancer and cancer treatments, and what is most rewarding to us is that while the human p53 gene was discovered more than a decade ago, the function of the gene was identified by Exelixis scientists using the model system Drosophila. Our data demonstrate that, as in human tumors, the loss of p53 function in Drosophila renders cells resistant to radiation-induced apoptosis (programmed cell death).

We entered into a Cooperative Research and Development Agreement with the National Institutes of Health, National Cancer Institute (NCI), to rapidly identify the mechanism of action for NCI compounds, all of which have demonstrated anti-cancer activity. This program allows us to identify the molecular target and biochemical pathways modulated by a specific compound, and then develop a drug lead with an improved therapeutic profile.

On the agricultural front, we completed the genomic sequencing of *Ustilago maydis*, commonly known as corn smut, an important model system for plant fungal diseases. This step marked the first major milestone in the expansion of our agricultural biotechnology program beyond chemical insecticides and nematicides. Through our acquisition of Agritepe, we have gained a very powerful combination of expertise, technologies, and intellectual property in plant genetics, which coupled with our internal programs and genomic and bioinformatic expertise, gives us one of the leading plant biotechnology programs in the industry.

PROGRESS THROUGH STRATEGIC COLLABORATIONS AND ACQUISITIONS

As a revolutionary biotechnology company, we are focused on the improvement of human health through better pharmaceutical and agricultural products. By partnering with leading companies in multiple industries, we are able to diversify our business risk, while at the same time maximize our potential future revenues. We have commercial collaborations with Aventis CropScience S.A., Bayer Corporation, Bristol-Myers Squibb Company, Dow AgroSciences LLC, and Pharmacia Corporation, which provide us with substantial funding, including licensing fees, research funding, milestone payments when specific objectives are met, and royalties if our partners successfully develop and commercialize products. In addition, many of these collaborations have included the acquisition of strategic
technologies. Committed funding from these collaborations, not including milestone payments or royalties, totals over $200 million.

During 2000, we established new collaborations and continued to build on those already in place. For our existing partnerships, we exceeded the expectations for delivery of targets to those partners across the board. Our Bristol-Myers Squibb (BMS) collaboration was substantially expanded based on the initial success in our three-year agreement signed in 1999. BMS has committed to this enhanced level of research funding for the remainder of the agreement, in which Exelixis is identifying the mechanism of action for pharmaceutical compounds received from BMS.

The new partnerships initiated in 2000 include our relationship with Dow AgroSciences to identify the mechanism of action for novel fungicides and herbicides for crop protection. An added feature of this collaboration is our access to proprietary compounds from Dow AgroSciences that may be useful in our internal drug discovery programs.

Another collaboration formed in 2000 was the three-way collaboration among Sangamo BioSciences, Inc., Artemis Pharmaceuticals GmbH, and Exelixis to develop a novel approach to produce knock-out mice for functional gene validation. Artemis is a company co-founded by Exelixis and headquartered in Cologne, Germany, with whom we have a very close research and strategic relationship. The combination of the three companies' technologies gives us an extremely powerful suite of methodologies that will allow us to answer questions that are otherwise difficult to address, and to shorten the time currently required to generate knock-out mice.

In early 2000, we established a joint venture with Bayer to discover new generations of insecticides and nematicides. These products will be based on novel targets identified by Exelixis using our proprietary model system genetics technologies, and formatted into high-throughput screening assays at Exelixis. The joint venture, called Genoptera LLC, was an outgrowth from and expansion of an Exelixis-Bayer collaboration established in 1998.

In addition to commercial collaborations, we continuously strive to enhance our powerful array of integrated genetics and genomics technologies through technology collaborations or licensing arrangements with commercial and academic institutions. These relationships include a supply agreement with Agilent Technologies, Inc., which provides us with customizable DNA microarrays. We use the Agilent flexible microarray platform for expression profiling in a variety of ways, to study toxicological profiles of drugs in our Mechanism of Action program for example, or as a step in validating our proprietary targets in oncology. We have a similar relationship with Affymetrix, Inc., for the use of their gene chips. Through our collaborative agreement with Orchid BioSciences, Inc., we are using Orchid's custom SNPcode™ product to customize and analyze more than 100 different

Committed funding from our collaborations, not including milestone payments or royalties, totals over $200 million.
SNPs simultaneously, greater than a ten-fold increase over current technology. This allows us to move from a functional phenotype to a cloned gene several times faster than previously possible, without sacrificing accuracy.

In July, we announced our licensing of “forward genetic” mouse technology from the Wisconsin Alumni Research Foundation. This technology, which represents a powerful approach for elucidating gene function, complements our existing technology in vertebrate systems with forward mouse genetics.

Of particular note, our acquisition of Agritope, Inc., which we renamed Exelixis Plant Sciences, was completed at the end of 2000. This acquisition builds on our diverse platform technology to round out our agricultural capabilities. With the technology and intellectual property base of Exelixis Plant Sciences, we believe we will be able to generate additional income through nearer-term agricultural programs. This in turn will allow us to continue to focus our internal research on our oncology development program.

The licenses and acquisitions described here serve as examples of our continuous pursuit of new technologies and novel products which will further enhance our own proprietary platform and allow us to speed the discovery and development of new pharmaceutical products.

EXPANSION OF ORGANIZATIONAL RESOURCES

In 2000, the essential groundwork was laid for still greater accomplishments in the future.

We completed our IPO in April, raising $124.7 million in a less than optimal market. We filled key management and drug discovery positions to move our programs forward thoughtfully and efficiently. We ended the year in a strong financial position, with cash, cash equivalents, and short-term investments of approximately $112.5 million. We have the people, the financing, and the infrastructure in place today to support our partnered programs and significantly expand our internal programs.

LOOKING AHEAD

Exelixis has repeatedly demonstrated the ability to execute on our business strategy, and has built a solid scientific, financial, and business base. We have moved forward aggressively and expect to continue to do so. We look forward to keeping you apprised of our progress, our accomplishments, and our growth, as we continue our pursuit of leadership in drug discovery. In the years ahead, we expect to advance proprietary cancer products into the clinic while at the same time continuing to build our integrated discovery platform.

I would like to thank our stockholders, our partners, and our talented and dedicated employees for their continued support and commitment. I am confident that Exelixis is poised for commercial success in the years to come, that we will discover, develop, and deliver innovative pharmaceutical and agricultural products to people around the globe.

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President and Chief Executive Officer
March 15, 2001
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D. Ry Wagner, Ph.D.
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San Jose, California

ANNUAL MEETING
The annual meeting of stockholders will be held at 8:00 a.m. on Tuesday, May 22, 2001
at the company's corporate headquarters at 170 Harbor Way, South San Francisco,
California.

SEC FORM 10-K
A copy of the Exelixis annual report on
Form 10-K filed with the Securities and Exchange Commission is available free of charge from the company's Investor Relations Department at Exelixis by calling
650-837-7000 or via e-mail: info@exelixis.com

STOCK INFORMATION
The common stock of the company is traded on the Nasdaq National Market System under the symbol EXEL. No dividends have been paid on the common stock since the company's inception.

Quarter Ending High Low
June 30, 2000 $33.94 $14.60
September 30, 2000 49.25 31.38
December 31, 2000 32.94 11.56
MANAGEMENT

George A. Scangos, Ph.D.
President and Chief Executive Officer

Geoffrey Dykx, M.D., Ph.D.
Executive Vice President

Glen Y. Sato
Chief Financial Officer

Lloyd M. Kurimoto
Senior Vice President, Corporate Development

Christian Burk, Ph.D.
Vice President and Chief Information Officer

Michael M. Morrissey, Ph.D.
Vice President, Discovery Research

Gregory D. Plowman, M.D., Ph.D.
Vice President, Pharmaceutical Research

Pamela A. Zimnon, J.D., L.L.M.
Vice President, Corporate Technology Development

Matthew G. Kramet
General Manager and Vice President, Agricultural Trait Development, Exelixis Plant Sciences

D. Ray Wanger, Ph.D.
Vice President, Research, Exelixis Plant Sciences

CORPORATE HEADQUARTERS

Exelixis, Inc.
170 Harbor Way
PO. Box 511
South San Francisco, CA 94083-0511
Phone: 650-837-7000
Fax: 650-837-8300
Email: info@exelixis.com
http://www.exelixis.com

CORPORATE COUNSEL

Cooley Godward LLP
Palo Alto, California

TRANSFER AGENT

Mellon Investor Services
85 Challenger Road
Overpeck Center
Ridgefield Park, NJ 07660
800-356-2017
201-296-4000
http://www.melloninvestor.com

INDEPENDENT ACCOUNTANTS

PricewaterhouseCoopers LLP
San Jose, California

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Quarter Ending High Low
June 30, 2000 $33.94 $14.50
September 30, 2000 49.25 31.38
December 31, 2000 32.94 11.56
A REVOLUTION IN THE EVOLUTION OF AN INDUSTRY