

PROSPECTUS

600,600 SHARES

EXELIXIS, INC.

COMMON STOCK

The selling stockholder listed on page 13 is offering up to 600,600 shares of Exelixis, Inc. common stock. We will not receive any proceeds from the sale of the shares by the selling stockholder.

Our common stock trades on the Nasdaq National Market under the symbol EXEL. On October 26, 2001, the last reported sale price of our common stock was \$12.92 per share.

The selling stockholder may sell the shares described in this prospectus in a number of different ways and at varying prices. See "Plan of Distribution" on page 14 for more information about how it may sell its shares. We will not be paying any underwriting discounts or commissions in this offering.

INVESTING IN OUR COMMON STOCK INVOLVES A HIGH DEGREE OF RISK. SEE "RISK FACTORS" BEGINNING ON PAGE 4.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

October 29, 2001

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This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission. You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus. The selling stockholder is offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where such offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock.

Exelixis, Artemis Pharmaceuticals, ACTTAG, the Exelixis, Inc. logos and all other Exelixis product and service names are registered trademarks or trademarks of Exelixis, Inc. in the U.S. and in other selected countries. All other brand names or trademarks appearing in this prospectus are the property of their respective holders.

## EXELIXIS

We believe that we are a leader in the discovery and validation of high-quality novel targets for several major human diseases, and a leader in the discovery of potential new drug therapies, specifically for cancer and other proliferative diseases. Our mission is to develop proprietary products by leveraging our integrated discovery platform to increase the speed, efficiency and quality of pharmaceutical and agricultural product discovery and development.

Through our expertise in biology and drug discovery, built upon a foundation of comparative genomics and model system genetics, we are able to find new drug targets that we believe would be difficult or impossible to uncover using other experimental approaches. Our pharmaceutical research identifies novel genes and proteins expressed by those genes that, when changed, either decrease or increase the activity in a specific disease pathway in a therapeutically relevant manner. These genes and proteins represent either potential product targets or drugs that may treat disease, or prevent disease initiation or progression.

Specifically in cancer, the remarkable evolutionary conservation of the biochemical pathways between humans and "lower" organisms strongly supports the use of simple model systems, such as fruit flies, nematode worms, zebrafish and mice to identify key members of critical cancer pathways that can then be targeted for drug discovery. We expect to develop new cancer drugs by exploiting the underlying "genetic liabilities" of tumor cells to provide specificity in targeting these cells for destruction, while leaving normal cells unharmed. We have discovered and are further developing a number of small molecule drug targets in addition to monoclonal antibody drug targets. Molecules developed against these targets may selectively kill cancer cells while leaving normal cells unharmed, and may provide alternatives to current cancer therapies.

While our proprietary programs focus on drug discovery and development, we believe that our proprietary 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 with double-digit product margins. By partnering with leading companies in multiple industries, we are able to diversify our business risk, while at the same time maximizing our future revenue stream.

We are a Delaware corporation. Our principal executive offices are located at 170 Harbor Way, South San Francisco, California 94080, and our telephone number is (650) 837-7000. In this prospectus, "Exelixis," "we," "us" and "our" refer to Exelixis, Inc., unless the context otherwise requires.

## RISK FACTORS

You should carefully consider the following risk factors, in addition to other information included or incorporated by reference in this prospectus, before making an investment decision. The risks described below are not the only risks we face. Additional risks that we do not yet know of or that we currently think are immaterial may also impair our business operations. If any of the events or circumstances described in the following risks actually occurs, our business may suffer, the trading price of our common stock could decline and you may lose all or part of your investment.

WE HAVE A HISTORY OF NET LOSSES. WE EXPECT TO CONTINUE TO INCUR NET LOSSES, AND WE MAY NOT ACHIEVE OR MAINTAIN PROFITABILITY.

We have incurred net losses each year since our inception, including a net loss of approximately \$36.4 million for the six months ended June 30, 2001. As of that date, we had an accumulated deficit of approximately \$166.5 million. We expect these losses to continue and anticipate negative cash flow for the foreseeable future. The size of these net losses will depend, in part, on the rate of growth, if any, in our license and contract revenues and on the level of our expenses. Our research and development expenditures and general and administrative costs have exceeded our revenues to date, and we expect to spend significant additional amounts to fund research and development in order to enhance our core technologies and undertake product development. As a result, we expect that our operating expenses will increase significantly in the near term and, consequently, we will need to generate significant additional revenues to achieve profitability. Even if we do increase our revenues and achieve profitability, we may not be able to sustain or increase profitability.

WE WILL NEED ADDITIONAL CAPITAL IN THE FUTURE, WHICH MAY NOT BE AVAILABLE TO US.

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

- payments received under collaborative agreements;
- the progress and scope of our collaborative and independent research and development projects;
- our ability to successfully continue development of a recently acquired cancer compound;
- our need to expand our other proprietary product development efforts as well as develop manufacturing and marketing capabilities to commercialize products; and
- the filing, prosecution and enforcement of patent claims.

We anticipate that our current cash and cash equivalents, short-term investments and funding to be received from collaborators will enable us to maintain our currently planned operations for at least the next two years. Changes to our current operating plan may require us to consume available capital resources significantly sooner than we expect. For example, our newly acquired cancer product from our recent relationship with Bristol-Myers Squibb will require significant resources for development that were not in our operational plans prior to acquiring the cancer product. We may be unable to raise sufficient additional capital when we need it, on favorable terms, or at all. If our capital resources are insufficient to meet future capital requirements, we will have to raise additional funds. The sale of equity or convertible debt securities in the future may be dilutive to our stockholders, and debt financing arrangements may require us to pledge certain assets and enter into covenants that would restrict our ability to incur further indebtedness. If we are unable to obtain adequate funds on reasonable terms, we may be required to curtail operations significantly or to obtain funds by entering into financing, supply or collaboration agreements on unattractive terms.

DIFFICULTIES WE MAY ENCOUNTER MANAGING OUR GROWTH MAY DIVERT RESOURCES AND LIMIT OUR ABILITY TO SUCCESSFULLY EXPAND OUR OPERATIONS.

We have experienced a period of rapid and substantial growth that has placed, and our anticipated growth in the future will continue to place, a strain on our administrative and operational infrastructure. As our operations expand, we expect that we will need to manage multiple locations, including additional locations outside of the United States, and additional relationships with various collaborative partners, suppliers and other third parties. Our ability to manage our operations and growth effectively requires us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to successfully implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls. In addition, acquisitions involve the integration of different financial and management reporting systems. We may not be able to successfully integrate the administrative and operational infrastructure without significant additional

improvements and investments in management systems and procedures.

WE ARE DEPENDENT ON OUR COLLABORATIONS WITH MAJOR COMPANIES. IF WE ARE UNABLE TO ACHIEVE MILESTONES, DEVELOP PRODUCTS OR RENEW OR ENTER INTO NEW COLLABORATIONS, OUR REVENUES MAY DECREASE AND OUR ACTIVITIES MAY FAIL TO LEAD TO COMMERCIALIZED PRODUCTS.

Substantially all of our revenues to date have been derived from collaborative research and development agreements. Revenues from research and development collaborations depend upon continuation of the collaborations, the achievement of milestones and royalties derived from future products developed from our research. If we are unable to successfully achieve milestones or our collaborators fail to develop successful products, we will not earn the revenues contemplated under such collaborative agreements. In addition, some of our collaborations are exclusive and preclude us from entering into additional collaborative arrangements with other parties in the area or field of exclusivity.

We currently have continuing collaborative research agreements with Bayer, Bristol-Myers Squibb (two agreements), Dow AgroSciences, Aventis and Protein Design Labs. Our current collaborative agreement with Bayer is scheduled to expire in 2008, after which it will automatically be extended for one-year terms unless terminated by either party upon 12-month written notice. Our agreement permits Bayer to terminate our collaborative activities prior to 2008 upon the occurrence of specified conditions, such as the failure to agree on key strategic issues after a period of years or the acquisition of Exelixis by certain specified third parties. In addition, our agreements with Bayer are subject to termination at an earlier date if two or more of our Chief Executive Officer, Chief Scientific Officer, Agricultural Biotechnology Program Leader and Chief Informatics Officer cease to have a relationship with us within six months of each other and we are unable to find replacements acceptable to Bayer. The first of our collaborative agreements with Bristol-Myers Squibb expires in September 2002. The funded research term of the second collaborative arrangement, entered into in July 2002, expires in July 2005. Our collaborative agreement with Dow AgroSciences is scheduled to expire in July 2003, after which Dow AgroSciences has the option to renew on an annual basis. Our collaborative research arrangement with Aventis is scheduled to expire in June 2004. Aventis has the right to terminate the research arrangement prior to the expiration date, provided that it pays the annual research funding amount due for the year following termination. Thereafter, the arrangement renews annually unless Aventis terminates automatic renewal prior to the scheduled date of renewal. The Aventis arrangement is conducted through a limited liability company, Agrinomics, which is owned equally by Aventis and Exelixis. Aventis may surrender its interest in Agrinomics and terminate the related research collaboration prior to the scheduled expiration upon the payment of the subsequent year's funding commitment. Bayer and Aventis recently announced an exclusive negotiation period for the purchase of Aventis by Bayer. We have not been advised of the status of those discussions nor are we able to predict the impact of such an acquisition of Aventis, if the acquisition were to occur. Our agreement with Protein Design Labs is scheduled to expire in May 2003. Protein Design Labs has a unilateral right to renew for additional 12 and six month periods thereafter. The five-year term of the convertible promissory note entered into as part of this arrangement is unaffected by whether or not Protein Design Labs renews. If these existing agreements are not renewed or if we are unable to enter into new collaborative agreements on commercially acceptable terms, our revenues and product development efforts may be adversely affected.

We recently announced the reacquisition, effective February 2002, of future rights to research programs in metabolism and Alzheimer's disease previously licensed exclusively to Pharmacia Corporation. The existing agreement with Pharmacia will terminate as of that date. Pharmacia will retain rights to targets under the existing agreement selected prior to the reacquisition date, subject to the payment of milestones for certain of those targets selected and royalties for future development of products against or using those targets but will have no other obligations to make payments to the Company, including approximately \$9.0 million in annual funding that would otherwise be payable for two years if the Company had not elected to reacquire rights to the research at this time. Although we anticipate entering into future collaborations involving either or both of these programs, there can be no assurance that we will be able to enter into new collaborative agreements or that such collaborations will provide revenues equal to or exceeding those otherwise obtainable under the Pharmacia collaboration.

CONFLICTS WITH OUR COLLABORATORS COULD JEOPARDIZE THE OUTCOME OF OUR COLLABORATIVE AGREEMENTS AND OUR ABILITY TO COMMERCIALIZE PRODUCTS.

We intend to conduct proprietary research programs in specific disease and agricultural product areas that are not covered by our collaborative agreements. Our pursuit of opportunities in agricultural and pharmaceutical markets could, however, result in conflicts with our collaborators in the event that any of our collaborators takes the position that our internal activities overlap with those

areas that are exclusive to our collaborative agreements, and we should be precluded from such internal activities. Moreover, disagreements with our collaborators could develop over rights to our intellectual property. In addition, our collaborative agreements may have provisions that give rise to disputes regarding the rights and obligations of the parties. Any conflict with our collaborators could lead to the termination of our collaborative agreements, delay collaborative activities, reduce our ability to renew agreements or obtain future collaboration agreements or result in litigation or arbitration and would negatively impact our relationship with existing collaborators.

We have limited or no control over the resources that our collaborators may choose to devote to our joint efforts. Our collaborators may breach or terminate their agreements with us or fail to perform their obligations thereunder. Further, our collaborators may elect not to develop products arising out of our collaborative arrangements or may fail to devote sufficient resources to the development, manufacture, market or sale of such products. Certain of our collaborators could also become our competitors in the future. If our collaborators develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain necessary regulatory approvals, terminate their agreements with us prematurely or fail to devote sufficient resources to the development and commercialization of our products, our product development efforts could be delayed and may fail to lead to commercialized products.

WE ARE DEPLOYING UNPROVEN TECHNOLOGIES, AND WE MAY NOT BE ABLE TO DEVELOP COMMERCIALY SUCCESSFUL PRODUCTS.

You must evaluate us in light of the uncertainties and complexities affecting a biotechnology company. Our technologies are still in the early stages of development. Our research and operations thus far have allowed us to identify a number of product targets for use by our collaborators and our own internal development programs. We are not certain, however, of the commercial value of any of our current or future targets, and we may not be successful in expanding the scope of our research into new fields of pharmaceutical or pesticide research, or other agricultural applications such as enhancing plant traits to produce superior crop yields, disease resistance or increased nutritional content. Significant research and development, financial resources and personnel will be required to capitalize on our technology, develop commercially viable products and obtain regulatory approval for such products.

WE HAVE NO EXPERIENCE IN DEVELOPING, MANUFACTURING AND MARKETING PRODUCTS AND MAY BE UNABLE TO COMMERCIALIZE PROPRIETARY PRODUCTS.

We recently acquired a development compound, an analog to rebeccamycin ("Rebeccamycin"), directed against cancer under our recent collaborative arrangement with Bristol-Myers Squibb. Clinical development of Rebeccamycin to date has been conducted by the National Cancer Institute, or the NCI, and manufacturing of this product has been the responsibility of Bristol-Myers Squibb. Rebeccamycin has recently completed Phase I clinical studies and is in Phase I and early Phase II clinical trials being conducted by the NCI. We are currently in negotiations with the NCI to use the results of the clinical studies they have conducted and are conducting in order to determine what additional studies, if any, will be conducted by the NCI or us. There can be no assurance that we will successfully agree upon further development plans, the respective rights and obligations of the parties to conduct additional clinical studies or the timing of such studies. In addition, there can be no assurance that the clinical studies conducted to date will support further clinical development or be accepted by the Food and Drug Administration, or FDA, in conjunction with any application for product approval submitted to the FDA for Rebeccamycin. Moreover, although Bristol-Myers Squibb has provided the NCI with sufficient quantities of Rebeccamycin to complete the existing Phase I and II clinical studies, development necessary for further clinical studies and product approval will require us to either develop internal manufacturing capabilities or retain a third party to manufacture the product. In addition, we have recently hired a new Senior Vice President responsible for clinical development of this product, as well as any new potential products that we may develop. As a result, we have limited experience in clinical development and no experience in manufacturing potential drug products. Accordingly, the development of Rebeccamycin is subject to significant risk and uncertainty, particularly with respect to our ability to successfully develop, manufacture and market Rebeccamycin as a product.

With respect to products developed against our proprietary drug targets, we will rely on our collaborators to develop and commercialize products based on our research and development efforts. We have limited or no experience in using the targets that we identify to develop our own proprietary products. Our recent success in applying our drug development capabilities to our proprietary targets in cancer are subject to significant risk and uncertainty, particularly with respect to our ability to meet currently estimated timelines and goals for completing preclinical development efforts and filing an Investigational New Drug Application, or IND, for compounds developed. In order for us to

commercialize products, we would need to significantly enhance our capabilities with respect to product development, and establish manufacturing and marketing capabilities, either directly or through outsourcing or licensing arrangements. We may not be able to enter into such outsourcing or licensing agreements on commercially reasonable terms, or at all.

SINCE OUR TECHNOLOGIES HAVE MANY POTENTIAL APPLICATIONS AND WE HAVE LIMITED RESOURCES, OUR FOCUS ON A PARTICULAR AREA MAY RESULT IN OUR FAILURE TO CAPITALIZE ON MORE PROFITABLE AREAS.

We have limited financial and managerial resources. This requires us to focus on product candidates in specific industries and forego opportunities with regard to other products and industries. For example, depending on our ability to allocate resources, a decision to concentrate on a particular agricultural program may mean that we will not have resources available to apply the same technology to a pharmaceutical project. While our technologies may permit us to work in both areas, resource commitments may require trade-offs resulting in delays in the development of certain programs or research areas, which may place us at a competitive disadvantage. Our decisions impacting resource allocation may not lead to the development of viable commercial products and may divert resources from more profitable market opportunities. Moreover, our recent acquisition of Rebeccamycin will require that resources and management time be directed to clinical development and manufacturing of this potential product. There can be no assurance that allocating resources and time to these efforts will allow us to remain competitive in existing programs and potential areas of future research. The resources dedicated to the development of Rebeccamycin may limit or hinder our ability to meet currently estimated timelines and goals for completing preclinical development efforts and filing an IND for our proprietary compounds.

OUR COMPETITORS MAY DEVELOP PRODUCTS AND TECHNOLOGIES THAT MAKE OURS OBSOLETE.

The biotechnology industry is highly fragmented and is characterized by rapid technological change. In particular, the area of gene research is a rapidly evolving field. We face, and will continue to face, intense competition from large biotechnology and pharmaceutical companies, as well as academic research institutions, clinical reference laboratories and government agencies that are pursuing research activities similar to ours. Some of our competitors have entered into collaborations with leading companies within our target markets, including some of our existing collaborators. Our future success will depend on our ability to maintain a competitive position with respect to technological advances.

Any products that are developed through our technologies will compete in highly competitive markets. Further, our competitors may be more effective at using their technologies to develop commercial products. Many of the organizations competing with us have greater capital resources, larger research and development staffs and facilities, more experience in obtaining regulatory approvals and more extensive product manufacturing and marketing capabilities. As a result, our competitors may be able to more easily develop technologies and products that would render our technologies and products, and those of our collaborators, obsolete and noncompetitive.

IF WE ARE UNABLE TO ADEQUATELY PROTECT OUR INTELLECTUAL PROPERTY, THIRD PARTIES MAY BE ABLE TO USE OUR TECHNOLOGY, WHICH COULD ADVERSELY AFFECT OUR ABILITY TO COMPETE IN THE MARKET.

Our success will depend in part on our ability to obtain patents and maintain adequate protection of the intellectual property related to our technologies and products. The patent positions of biotechnology companies, including our patent position, are generally uncertain and involve complex legal and factual questions. We will be able to protect our intellectual property rights from unauthorized use by third parties only to the extent that our technologies are covered by valid and enforceable patents or are effectively maintained as trade secrets. The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the U.S., and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. We will continue to apply for patents covering our technologies and products as and when we deem appropriate. However, these applications may be challenged or may fail to result in issued patents. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. Furthermore, others may independently develop similar or alternative technologies or design around our patents. In addition, our patents may be challenged, invalidated or fail to provide us with any competitive advantages.

We rely on trade secret protection for our confidential and proprietary information. We have taken security measures to protect our proprietary information and trade secrets, but these measures may not provide adequate protection. While we seek to protect our proprietary information by entering

into confidentiality agreements with employees, collaborators and consultants, we cannot assure you that our proprietary information will not be disclosed, or that we can meaningfully protect our trade secrets. In addition, our competitors may independently develop substantially equivalent proprietary information or may otherwise gain access to our trade secrets.

LITIGATION OR THIRD PARTY CLAIMS OF INTELLECTUAL PROPERTY INFRINGEMENT COULD REQUIRE US TO SPEND SUBSTANTIAL TIME AND MONEY AND ADVERSELY AFFECT OUR ABILITY TO DEVELOP AND COMMERCIALIZE PRODUCTS.

Our commercial success depends in part on our ability to avoid infringing patents and proprietary rights of third parties, and not breaching any licenses that we have entered into with regard to our technologies. Other parties have filed, and in the future are likely to file, patent applications covering genes and gene fragments, techniques and methodologies relating to model systems, and products and technologies that we have developed or intend to develop. If patents covering technologies required by our operations are issued to others, we may have to rely on licenses from third parties, which may not be available on commercially reasonable terms, or at all.

Third parties may accuse us of employing their proprietary technology without authorization. In addition, third parties may obtain patents that relate to our technologies and claim that use of such technologies infringes these patents. Regardless of their merit, such claims could require us to incur substantial costs, including the diversion of management and technical personnel, in defending ourselves against any such claims or enforcing our patents. In the event that a successful claim of infringement is brought against us, we may be required to pay damages and obtain one or more licenses from third parties. We may not be able to obtain these licenses at a reasonable cost, or at all. Defense of any lawsuit or failure to obtain any of these licenses could adversely affect our ability to develop and commercialize products.

THE LOSS OF KEY PERSONNEL OR THE INABILITY TO ATTRACT AND RETAIN ADDITIONAL PERSONNEL COULD IMPAIR OUR ABILITY TO EXPAND OUR OPERATIONS.

We are highly dependent on the principal members of our management and scientific staff, the loss of whose services might adversely impact the achievement of our objectives and the continuation of existing collaborations. In addition, recruiting and retaining qualified scientific personnel to perform future research and development work will be critical to our success. We do not currently have sufficient executive management and technical personnel to fully execute our business plan. There is currently a shortage of skilled executives and employees with technical expertise, and this shortage is likely to continue. As a result, competition for skilled personnel is intense and turnover rates are high. Although we believe we will be successful in attracting and retaining qualified personnel, competition for experienced scientists from numerous companies, academic and other research institutions may limit our ability to do so.

Our business operations will require additional expertise in specific industries and areas applicable to products identified and developed through our technologies. These activities will require the addition of new personnel, including management and technical personnel and the development of additional expertise by existing employees. The inability to attract such personnel or to develop this expertise could prevent us from expanding our operations in a timely manner, or at all.

OUR COLLABORATIONS WITH OUTSIDE SCIENTISTS MAY BE SUBJECT TO RESTRICTION AND CHANGE.

We work with scientific advisors and collaborators at academic and other institutions that assist us in our research and development efforts. These scientists are not our employees and may have other commitments that would limit their availability to us. Although our scientific advisors and collaborators generally agree not to do competing work, if a conflict of interest between their work for us and their work for another entity arises, we may lose their services. In addition, although our scientific advisors and collaborators sign agreements not to disclose our confidential information, it is possible that valuable proprietary knowledge may become publicly known through them.

OUR POTENTIAL THERAPEUTIC PRODUCTS ARE SUBJECT TO A LENGTHY AND UNCERTAIN REGULATORY PROCESS THAT MAY NOT RESULT IN THE NECESSARY REGULATORY APPROVALS, WHICH COULD ADVERSELY AFFECT OUR ABILITY TO COMMERCIALIZE PRODUCTS.

The FDA must approve any drug or biologic product before it can be marketed in the U.S. Any products resulting from our research and development efforts must also be approved by the regulatory agencies of foreign governments before the product can be sold outside the U.S. Before a new drug application or biologics license application can be filed with the FDA, the product candidate must undergo extensive clinical trials, which can take many years and may require substantial expenditures. The regulatory process also requires

preclinical testing. Data obtained from preclinical and clinical activities are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. In addition, delays or rejections may be encountered based upon changes in regulatory policy for product approval during the period of product development and regulatory agency review. The clinical development and regulatory approval process is expensive and time consuming. Any failure to obtain regulatory approval could delay or prevent us from commercializing products.

Our efforts to date have been primarily limited to identifying targets. Significant research and development efforts will be necessary before any products resulting from such targets can be commercialized. If regulatory approval is granted to any of our products, this approval may impose limitations on the uses for which a product may be marketed. Further, once regulatory approval is obtained, a marketed product and its manufacturer are subject to continual review, and discovery of previously unknown problems with a product or manufacturer may result in restrictions and sanctions with respect to the product, manufacturer and relevant manufacturing facility, including withdrawal of the product from the market.

SOCIAL ISSUES MAY LIMIT THE PUBLIC ACCEPTANCE OF GENETICALLY ENGINEERED PRODUCTS, WHICH COULD REDUCE DEMAND FOR OUR PRODUCTS.

Although our technology is not dependent on genetic engineering, genetic engineering plays a prominent role in our approach to product development. For example, research efforts focusing on plant traits may involve either selective breeding or modification of existing genes in the plant under study. Public attitudes may be influenced by claims that genetically engineered products are unsafe for consumption or pose a danger to the environment. Such claims may prevent our genetically engineered products from gaining public acceptance. The commercial success of our future products will depend, in part, on public acceptance of the use of genetically engineered products including drugs and plant and animal products.

The subject of genetically modified organisms has received negative publicity, which has aroused public debate. For example, certain countries in Europe are considering regulations that may ban products or require express labeling of products that contain genetic modifications or are "genetically modified." Adverse publicity has resulted in greater regulation internationally and trade restrictions on imports of genetically altered products. If similar action is taken in the U.S., genetic research and genetically engineered products could be subject to greater domestic regulation, including stricter labeling requirements. To date, our business has not been hampered by these activities. However, such publicity in the future may prevent any products resulting from our research from gaining market acceptance and reduce demand for our products.

LAWS AND REGULATIONS MAY REDUCE OUR ABILITY TO SELL GENETICALLY ENGINEERED PRODUCTS THAT OUR COLLABORATORS OR WE DEVELOP IN THE FUTURE.

Our collaborators or we may develop genetically engineered agricultural and animal products. The field-testing, production and marketing of genetically engineered products are subject to regulation by federal, state, local and foreign governments. Regulatory agencies administering existing or future regulations or legislation may prevent us from producing and marketing genetically engineered products in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays or other impediments to our product development programs and the commercialization of products.

The FDA has released a policy statement stating that it will apply the same regulatory standards to foods developed through genetic engineering as it applies to foods developed through traditional plant breeding. Genetically engineered food products will be subject to premarket review, however, if these products raise safety questions or are deemed to be food additives. Our products may be subject to lengthy FDA reviews and unfavorable FDA determinations if they raise questions regarding safety or our products are deemed to be food additives.

The FDA has also announced that it will not require genetically engineered agricultural products to be labeled as such, provided that these products are as safe and have the same nutritional characteristics as conventionally developed products. The FDA may reconsider or change its policies, and local or state authorities may enact labeling requirements, either of which could have a material adverse effect on our ability or the ability of our collaborators to develop and market products resulting from our efforts.

WE USE HAZARDOUS CHEMICALS AND RADIOACTIVE AND BIOLOGICAL MATERIALS IN OUR BUSINESS. ANY CLAIMS RELATING TO IMPROPER HANDLING, STORAGE OR DISPOSAL OF THESE MATERIALS COULD BE TIME CONSUMING AND COSTLY.



Our research and development processes involve the controlled use of hazardous materials, including chemicals, radioactive and biological materials. Our operations produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from these materials. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. We may be sued for any injury or contamination that results from our use or the use by third parties of these materials, and our liability may exceed our insurance coverage and our total assets. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development and production efforts.

In addition, our collaborators may use hazardous materials in connection with our collaborative efforts. To our knowledge, their work is performed in accordance with applicable biosafety regulations. In the event of a lawsuit or investigation, however, we could be held responsible for any injury caused to persons or property by exposure to, or release of, these hazardous materials use by these parties. Further, we may be required to indemnify our collaborators against all damages and other liabilities arising out of our development activities or products produced in connection with these collaborations.

WE EXPECT THAT OUR QUARTERLY RESULTS OF OPERATIONS WILL FLUCTUATE, AND THIS FLUCTUATION COULD CAUSE OUR STOCK PRICE TO DECLINE, CAUSING INVESTOR LOSSES.

Our quarterly operating results have fluctuated in the past and are likely to fluctuate in the future. A number of factors, many of which we cannot control, could subject our operating results and stock price to volatility, including:

- recognition of license, milestone or other fees;
- payments of licensing fees to third parties;
- acceptance of our technologies and platforms;
- the success rate of our discovery efforts leading to milestones and royalties;
- the introduction of new technologies or products by our competitors;
- the timing and willingness of collaborators to commercialize our products;
- our ability to enter into new collaborative relationships;
- the termination or non-renewal of existing collaborations;
- general and industry-specific economic conditions that may affect our collaborators' research and development expenditures; and
- exposure to fluctuations in foreign currency.

A large portion of our expenses, including expenses for facilities, equipment and personnel, are relatively fixed in the short term. In addition, we expect operating expenses to increase significantly during the next year. Accordingly, if our revenues decline or do not grow as anticipated due to the expiration of existing contracts or our failure to obtain new contracts, our inability to meet milestones or other factors, we may not be able to correspondingly reduce our operating expenses. Failure to achieve anticipated levels of revenues could therefore significantly harm our operating results for a particular fiscal period.

Due to the possibility 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. As a result, in some future quarters, our operating results may not meet the expectations of stock market analysts and investors, which could result in a decline in the price of our stock.

OUR STOCK PRICE MAY BE EXTREMELY VOLATILE.

We believe the trading price of our common stock will remain highly volatile and may fluctuate substantially due to factors such as the following:

- the announcement of new products or services by us or our competitors;
- quarterly variations in our or our competitors' results of operations;
- failure to achieve operating results projected by securities analysts;
- changes in earnings estimates or recommendations by securities analysts;
- developments in the biotechnology industry;
- acquisitions of other companies or technologies; and
- general market conditions and other factors, including factors unrelated to our operating performance or the operating performance of our competitors.

These factors and fluctuations, as well as general economic, political and market conditions, may materially adversely affect the market price of our common stock.

In the past, following periods of volatility in the market price of a company's securities, securities class action litigation has often been instituted. A securities class action suit against us could result in substantial costs and divert management's attention and resources, which could have a material and adverse effect on our business.

WE ARE EXPOSED TO RISKS ASSOCIATED WITH ACQUISITIONS.

We have made, and may in the future make, acquisitions of, or significant investments in, businesses with complementary products, services and/or technologies. Acquisitions involve numerous risks, including, but not limited to:

- difficulties and increased costs in connection with integration of the personnel, operations, technologies and products of acquired companies;
- diversion of management's attention from other operational matters;
- the potential loss of key employees of acquired companies;
- the potential loss of key collaborators of the acquired companies;
- lack of synergy, or the inability to realize expected synergies, resulting from the acquisition;
- exposure to fluctuations in foreign currency;
- differences in foreign laws, business practices, statutes, regulations and tax provisions; and
- acquired intangible assets becoming impaired as a result of technological advancements or worse-than-expected performance of the acquired company.

Mergers and acquisitions are inherently risky, and the inability to effectively manage these risks could materially and adversely affect our business, financial condition and results of operations.

IF PRODUCT LIABILITY LAWSUITS ARE SUCCESSFULLY BROUGHT AGAINST US, WE COULD FACE SUBSTANTIAL LIABILITIES THAT EXCEED OUR RESOURCES.

We may be held liable if any product our collaborators or we develop causes injury or is found otherwise unsuitable during product testing, manufacturing, marketing or sale. Although we intend to obtain general liability and product liability insurance, this insurance may be prohibitively expensive, or may not fully cover our potential liabilities. Inability to obtain sufficient insurance coverage at an acceptable cost or to otherwise protect ourselves against potential product liability claims could prevent or inhibit the commercialization of products developed by our collaborators or us.

OUR FACILITIES ARE LOCATED NEAR KNOWN EARTHQUAKE FAULT ZONES, AND THE OCCURRENCE OF AN EARTHQUAKE OR OTHER CATASTROPHIC DISASTER COULD CAUSE DAMAGE TO OUR FACILITIES AND EQUIPMENT, WHICH COULD REQUIRE US TO CEASE OR CURTAIL OPERATIONS.

Given our location, our facilities are vulnerable to damage from earthquakes. We are also vulnerable to damage from other types of disasters, including fire, floods, power loss, communications failures and similar events. If any disaster were to occur, our ability to operate our business at our facilities would be seriously, or potentially completely, impaired. In addition, the unique nature of our research activities could cause significant delays in our programs and make it difficult for us to recover from a disaster. The insurance we maintain may not be adequate to cover our losses resulting from disasters or other business interruptions. Accordingly, an earthquake or other disaster could materially and adversely harm our ability to conduct business.

FUTURE SALES OF OUR COMMON STOCK MAY DEPRESS OUR STOCK PRICE.

If our stockholders sell substantial amounts of our common stock (including shares issued upon the exercise of outstanding options and warrants) in the public market, the market price of our common stock could fall. These sales also might make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deemed appropriate. In October 2000, a significant number of shares of our common stock held by existing stockholders became freely tradable, subject in some instances to the volume and other limitations of Rule 144. Sales of these shares and other shares of common stock held by existing stockholders could cause the market price of our common stock to decline.

SOME OF OUR EXISTING STOCKHOLDERS CAN EXERT CONTROL OVER US, AND MAY NOT MAKE DECISIONS THAT ARE IN THE BEST INTERESTS OF ALL STOCKHOLDERS.

Due to their combined stock holdings, our officers, directors and principal stockholders (stockholders holding more than 5% of our common stock) acting together, may be able to exert significant influence over all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. In addition, this concentration of ownership may delay or prevent a change in control of our company, even when a change may be in the best interests of our stockholders. In addition, the interests of these stockholders may not always coincide with our interests as a company or the interests of other stockholders. Accordingly, these stockholders could cause us to enter into transactions or agreements that you would not approve.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some of the statements in this prospectus and the documents incorporated by reference are forward-looking statements. These statements are based on our current expectations, assumptions, estimates and projections about our business and our industry, and involve known and unknown risks, uncertainties and other factors that may cause our or our industry's results, levels of activity, performance or achievement to be materially different from any future results, levels of activity, performance or achievements expressed or implied in or contemplated by the forward-looking statements. Words such as "believe," "anticipate," "expect," "intend," "plan," "will," "may," "should," "estimate," "predict," "potential," "continue" or the negative of such terms or other similar expressions, identify forward-looking statements. In addition, any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements. Our actual results could differ materially from those anticipated in such forward-looking statements as a result of several factors more fully described under the caption "Risk Factors" and in the documents incorporated by reference. The forward-looking statements made in this prospectus relate only to events as of the date on which the statements are made.

USE OF PROCEEDS

The proceeds from the sale of the common stock offered pursuant to this prospectus are solely for the account of the selling stockholder. We will not receive any proceeds from the sale of these shares of common stock.

SELLING STOCKHOLDER

We are registering the shares covered by this prospectus on behalf of the selling stockholder named in the table below. We issued all of the shares to the selling stockholder in a private placement transaction. We have registered the shares to permit the selling stockholder and its pledgees, donees, transferees or other successors-in-interest that receive their shares from the selling stockholder as a gift, partnership distribution or other non-sale related transfer after the date of this prospectus to resell the shares. The selling stockholder has agreed not to offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise dispose of the shares covered by this prospectus without our consent until July 17, 2002.

The following table sets forth the name of the selling stockholder, the number of shares owned by it, the number of shares that may be offered under this prospectus, the number of shares of our common stock owned by the selling stockholder as of September 30, 2001, and the number of shares of our common stock owned by the selling stockholder after this offering is completed. On July 17, 2001, in connection with the issuance of the shares covered by this prospectus, the selling stockholder entered into a cancer research collaboration and license agreement with us, and thus is one of our corporate partners. The number of shares in the column "Number of Shares Being Offered" represents all of the shares that the selling stockholder may offer under this prospectus. The selling stockholder may sell some, all or none of the shares registered hereunder. Except for the lock-up described above, we do not know how long the selling stockholder will hold the shares before selling them. The shares offered by this prospectus may be offered from time to time by the selling stockholder.

Beneficial ownership is determined in accordance with Rule 13d-3(d) promulgated by the SEC under the Securities Exchange Act of 1934. Unless otherwise noted, none of the share amounts set forth below represent more than 1% of our outstanding stock as of September 30, 2001, adjusted as required by rules promulgated by the SEC. The percentages of shares owned prior to the offering are based on 49,235,515 shares of our common stock outstanding on September 30, 2001, giving effect to the sale of 600,600 shares to the selling stockholder in the private placement.

NAME	SHARES BENEFICIALLY OWNED PRIOR TO THE OFFERING		NUMBER OF SHARES BEING OFFERED	SHARES BENEFICIALLY OWNED AFTER THE OFFERING (1)	
	NUMBER	PERCENT		NUMBER	PERCENT
Bristol-Myers Squibb Company . . . . .	600,600	1.22%	600,600	0	*

(1) Does not constitute a commitment to sell any or all of the stated number of

shares of common stock. The number of shares offered shall be determined from time to time by the selling stockholder at its sole discretion. The number of shares to be owned by the selling stockholder after the offering, assuming the sale of all of the stated number of shares of common stock, will be less than one percent of its outstanding shares after the offering.

#### PLAN OF DISTRIBUTION

The selling stockholder may sell the shares from time to time. The selling stockholder will act independently of us in making decisions regarding the timing, manner and size of each sale. The sales may be made on one or more exchanges or in the over-the-counter market or otherwise, at prices and at terms then prevailing or at prices related to the then current market price, or in privately negotiated transactions. The selling stockholder may effect these transactions by selling the shares to or through broker-dealers. The selling stockholder may sell its shares in one or more of, or a combination of:

- a block trade in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by a broker-dealer for its account under this prospectus;
- an exchange distribution in accordance with the rules of an exchange; - ordinary brokerage transactions and transactions in which the broker solicits purchasers; and
- privately negotiated transactions.

To the extent required, this prospectus may be amended or supplemented from time to time to describe a specific plan of distribution. If the plan of distribution involves an arrangement with a broker-dealer for the sale of shares through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker or dealer, the amendment or supplement will disclose:

- the name of the selling stockholder and of the participating broker-dealer(s);
- the number of shares involved;
- the price at which the shares were sold;
- the commissions paid or discounts or concessions allowed to the broker-dealer(s), where applicable;
- that a broker-dealer(s) did not conduct any investigation to verify the information set out or incorporated by reference in this prospectus; and
- other facts material to the transaction.

The selling stockholder has agreed not to offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise dispose of the shares covered by this prospectus without our consent until July 17, 2002. From time to time, the selling stockholder may transfer, pledge, donate or assign its shares of common stock to lenders or others and each of such persons will be deemed to be a "selling stockholder" for purposes of this prospectus. The number of shares of common stock beneficially owned by the selling stockholder will decrease as and when it takes such actions. The plan of distribution for the selling stockholder's shares of common stock sold under this prospectus will otherwise remain unchanged, except that the transferees, pledgees, donees or other successors will be selling stockholders hereunder. Upon being notified by a selling stockholder that a donee or pledgee intends to sell more than 500 shares, we will file a supplement to this prospectus.

The selling stockholder may enter into hedging transactions with broker-dealers in connection with distributions of the shares or otherwise. In these transactions, broker-dealers may engage in short sales of the shares in the course of hedging the positions they assume with the selling stockholder. The selling stockholder also may sell shares short and redeliver the shares to close out short positions. The selling stockholder may enter into option or other transactions with broker-dealers that require the delivery to the broker-dealer of the shares. The broker-dealer may then resell or otherwise transfer the shares under this prospectus. The selling stockholder also may loan or pledge the shares to a broker-dealer. The broker-dealer may sell the loaned shares, or upon a default the broker-dealer may sell the pledged shares under this prospectus.

In effecting sales, broker-dealers engaged by the selling stockholder may arrange for other broker-dealers to participate in the resales. Broker-dealers or agents may receive compensation in the form of commissions, discounts or concessions from the selling stockholder. Broker-dealers or agents may also receive compensation from the purchasers of the shares for whom they act as agents or to whom they sell as principals, or both. Compensation as to a particular broker-dealer might be in excess of customary commissions and will be in amounts to be negotiated in connection with the sale. A broker-dealer or agent and any other participating broker-dealer or the selling stockholder may be deemed to be an "underwriter" within the meaning of Section 2(11) of the Securities Act in connection with sales of the shares. Accordingly, any

commission, discount or concession received by them and any profit on the resale of the shares purchased by them may be deemed to be underwriting discounts or commissions under the Securities Act. Because the selling stockholder may be deemed to be an "underwriter" within the meaning of Section 2(11) of the Securities Act, the selling stockholder will be subject to the prospectus delivery requirements of the Securities Act. In addition, any securities covered by this prospectus that qualify for sale under Rule 144 promulgated under the Securities Act may be sold under Rule 144 rather than under this prospectus. The selling stockholder has advised that it has not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of the shares. There is no underwriter or coordinating broker acting in connection with the proposed sale of shares by the selling stockholder.

The shares will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in some states the shares may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the shares may not simultaneously engage in market making activities with respect to our common stock for a period of two business days prior to the commencement of the distribution. In addition, the selling stockholder will be subject to applicable provisions of the Exchange Act and the associated rules and regulations under the Exchange Act, including Regulation M, which provisions may limit the timing of purchases and sales of shares of our common stock by the selling stockholder. We will make copies of this prospectus available to the selling stockholder and have informed the selling stockholder of the need to deliver copies of this prospectus to purchasers at or prior to the time of any sale of the shares.

We will bear all costs, expenses and fees in connection with the registration of the shares. The selling stockholder will pay all commissions and discounts, if any, attributable to the sales of the shares. The selling stockholder may agree to indemnify any broker-dealer or agent that participates in transactions involving sales of the shares against specific liabilities, including liabilities arising under the Securities Act. We have agreed to indemnify the selling stockholder against specific liabilities in connection with the offering of the shares, including liabilities arising under the Securities Act.

We have agreed to maintain the effectiveness of this registration statement until the earlier of such time as all the shares have been sold by the selling stockholder or such time as all of the shares may be sold pursuant to Rule 144(k) under the Securities Act. The selling stockholder may sell all, some or none of the shares offered by this prospectus.

## LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon by Cooley Godward LLP, Palo Alto, California.

### EXPERTS

The consolidated financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2000, have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, independent accountants, given on the authority of said firm as experts in auditing and accounting.

### WHERE YOU CAN FIND MORE INFORMATION ABOUT EXELIXIS

You should rely only on the information provided or incorporated by reference in this prospectus. We have authorized no one to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front of the document.

We have filed with the SEC a resale registration statement on Form S-3 to register the common stock offered by this prospectus. However, this prospectus does not contain all of the information contained in the registration statement and the exhibits and schedules to the registration statement. We strongly encourage you to carefully read the registration statement and the exhibits and schedules to the registration statement.

We file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's Public Reference Room at 450 Fifth Street, N.W., Washington, DC 20549 or at the SEC's other public reference rooms located in New York, New York and Chicago, Illinois. You can request copies of these documents by contacting the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms. Our SEC filings are also available to the public from the SEC's website at [www.sec.gov](http://www.sec.gov).

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The SEC allows us to "incorporate by reference" the information contained in documents that we file with them, which means that we can disclose important information to you by referring to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings we will make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934.

The following documents filed with the SEC are incorporated by reference in this prospectus:

1. Our Annual Report on Form 10-K for the year ended December 31, 2000;
2. Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2001;
3. Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2001;
4. Our Current Reports on Form 8-K, filed on May 15, 2001 pursuant to Item 2 of such report, and filed on July 18, 2001 and July 26, 2001 pursuant to Item 5 of such report; and
5. The description of our common stock set forth in our registration statement on Form 8-A, filed with the SEC on April 6, 2000.

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. You should direct any requests for documents to Exelixis, Inc., Attention: Investor Relations, 170 Harbor Way, P.O. Box 511, South San Francisco, California 94083, telephone: (650) 837-7000.

WE HAVE NOT AUTHORIZED ANY DEALER, SALESPERSON OR OTHER PERSON TO GIVE ANY INFORMATION OR REPRESENT ANYTHING NOT CONTAINED IN THIS PROSPECTUS. YOU SHOULD RELY ONLY ON THE INFORMATION PROVIDED OR INCORPORATED BY REFERENCE IN THIS PROSPECTUS. YOU SHOULD NOT RELY ON ANY UNAUTHORIZED INFORMATION. THIS PROSPECTUS DOES NOT OFFER TO SELL OR BUY ANY SHARES IN ANY JURISDICTION IN WHICH IT IS UNLAWFUL. THE INFORMATION IN THIS PROSPECTUS IS CURRENT AS OF THE DATE ON THE COVER.

600,600 SHARES  
EXELIXIS, INC.  
COMMON STOCK

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PROSPECTUS

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OCTOBER 29, 2001