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Check th if no long subject to Section 1 Form 4 c Form 5 obligatio	rsuant to S	F CHANGES IN BENEFICIAL OWNERSHIP OF SECURITIES Section 16(a) of the Securities Exchange Act of 1934, Public Utility Holding Company Act of 1935 or Sectior					Expires: January 31 2005 Estimated average burden hours per response 0.5			
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(Print or Type]	Responses)									
	Address of Reporting	g Person <u>*</u>	Symbol	r Name and RSON PIL			-	5. Relationship of Issuer		
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	(Street)			ndment, Da nth/Day/Year)	-	1		6. Individual or Jo Applicable Line) _X_ Form filed by C	One Reporting Pe	rson
COLUMBI	A, SC 29223							Form filed by M Person	lore than One Re	porting
(City)	(State)	(Zip)	Tabl	e I - Non-D	erivative	Secur	ities Acq	uired, Disposed of	, or Beneficial	ly Owned
1.Title of Security (Instr. 3)	2. Transaction Dat (Month/Day/Year)		n Date, if	3. Transactic Code (Instr. 8)	4. Securi on(A) or Di (Instr. 3,	4 and (A)	d of (D)	5. Amount of Securities Beneficially Owned Following Reported Transaction(s)	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	
G				Code V	Amount	or (D)	Price	(Instr. 3 and 4)		
Common Stock	02/21/2006			S	5,000	D	\$ 60	23,982	D	
Common Stock	02/27/2006			S	1,000	D	\$ 61.13	22,982	D	
Common Stock	02/28/2006			S	1,000	D	\$ 60 54	21,982	D	

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Persons who respond to the collection of SE information contained in this form are not required to respond unless the form displays a currently valid OMB control number.

SEC 1474 (9-02)

 Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned

 (e.g., puts, calls, warrants, options, convertible securities)

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	4. Transact Code (Instr. 8)	5. orNumber of Derivativ Securities Acquired (A) or Disposed of (D) (Instr. 3, 4, and 5)		ate	Amou Unde Secur	le and unt of rlying rities : 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Nu Deriv Secur Bene Owne Follo Repo Trans (Instr
			Code V	(A) (D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		

Reporting Owners

Reporting Owner Name / Address	Relationships					
	Director	10% Owner	Officer	Other		
RUSSELL DONALD S JR ONE TIFTGREEN CIRCLE COLUMBIA, SC 29223	Х					
Signatures						
Robert A. Reed, Attorney in Fact	0	2/28/2006				
<u>**</u> Signature of Reporting Person		Date				
Explanation of Re	spon	ses:				

* If the form is filed by more than one reporting person, see Instruction 4(b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations. See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, *see* Instruction 6 for procedure. Potential persons who are to respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB number. d about factors you should consider before buying shares of our common stock.

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.

Prospectus dated August 7, 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 we have provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with additional or different information. We are not making an offer of these shares of common stock in any jurisdiction where the offer is not permitted. You should assume that the information contained in this prospectus or any prospectus supplement is accurate only as of the date on the front of document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference.

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.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission utilizing a "shelf" registration process. Under this shelf process, we may offer from time to time the shares of our common stock described in this prospectus in one or more offerings for up to a total amount of \$150,000,000. This prospectus provides you with a general description of our common stock that we may offer. Each time we use this prospectus to offer shares of our common stock, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplements may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with additional information described below under the heading "Where You Can Find More Information About Exelixis."

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 then 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.

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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.

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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 \$12.7 million for the three months ended March 31, 2001. As of that date, we had an accumulated deficit of approximately \$142.8 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 operation 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 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.

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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 locations outside 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 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 Office, 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 second arrangement, entered into 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 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 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 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. 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 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 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 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 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 commercially 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

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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 product (Rebeccamycin) directed against cancer under our recent collaborative agreement 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 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 to date and 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 FDA in conjunction with any application for product approval submitted to the FDA for RebeccamycinS. Moreover, although Bristol Myers-Squibb has provided the NCI with sufficient quantities of Rebeccamycin, development necessary for 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 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

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decisions impacting resource allocation may not lead to the development of viable commercial products and may divert resources from more profitable market opportunities.

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.

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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.

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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 Food and Drug Administration, or 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

Explanation of Responses:

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; and

general and industry-specific economic conditions that may affect our collaborators' research and development expenditures.

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.

Explanation of Responses:

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; 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.

Currency fluctuations may impair our financial results.

With our acquisition of Artemis, some of our operating expenses are denominated in foreign currencies. To the extent that our operating expenses are denominated in foreign currencies, our operating results may be adversely affected by changes in exchange rates. Given the substantial volatility of currency exchange rates, and constantly changing currency exposures, we cannot predict the effect of exchange rate fluctuations on our future operating results. Although we engage in foreign currency hedging transactions from time to time, these hedging transactions can be costly, and therefore, we do not attempt to cover all potential foreign currency exposures. These hedging techniques do not eliminate all of the effects of foreign currency fluctuations on anticipated revenue.

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 our common stock held by existing stockholders could cause the market price of our common stock to decline. In addition, up to 1.7 million shares of our common stock held by former investors in Artemis will become freely tradable in August 2001 following the expiration of a 90-day lock-up for shares acquired in the Artemis acquisition.

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

Unless otherwise indicated in the prospectus supplement, the net proceeds from the sale of common stock offered by this prospectus will be used for general corporate purposes, including capital expenditures and to meet working capital needs. These purposes may also include repaying indebtedness. In addition, from time to time we may evaluate the acquisition of businesses,

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products and technologies for which a portion of the net proceeds may be used; however, we currently are not planning or negotiating any such transactions. Pending such uses, we may invest the net proceeds in interest-bearing securities.

PLAN OF DISTRIBUTION

We may sell the common stock offered under this prospectus:

through one or more underwriters or dealers in a public offering and sale by them;

directly to investors; or

through agents.

We may sell the common stock offered under this prospectus from time to time in one or more transactions:

at a fixed price or prices, which may be changed from time to time;

at market prices prevailing at the times of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

We will describe the method of distribution of the securities in the prospectus supplement.

Underwriters, dealers or agents may receive compensation in the form of discounts, concessions or commissions from us or our purchasers (as their agents in connection with the sale of securities). These underwriters, dealers or agents may be considered to be underwriters under the Securities Act. As a result, discounts, commissions or profits on resale received by the underwriters, dealers or agents may be treated as underwriting discounts and commissions. The prospectus supplement will identify any such underwriter, dealer or agent, and describe any

compensation received by them from us. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may be changed from time to time.

Underwriters, dealers and agents may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments made by the underwriters, dealers or agents, under agreements between us and the underwriters, dealers and agents.

We may grant underwriters who participate in the distribution of our common stock an option to purchase additional shares of common stock to cover over- allotments, if any, in connection with the distribution.

Underwriters or agents and their associates may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock of consists of 100,000,000 shares of common stock, \$0.001 par value per share, and 10,000,000 shares of preferred stock, \$0.001 par value per share.

Common Stock

As of May 31, 2001, there were 48,533,903 shares of Exelixis common stock outstanding, held of record by approximately 923 stockholders. The holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders. Accordingly, holders of a majority of the shares of common stock entitled to vote in any election of directors

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may elect all of the directors standing for election. Subject to preferences that may be applicable to any preferred stock outstanding at the time, the holders of outstanding shares of common stock are entitled to receive ratably any dividends out of assets legally available therefor as our board of directors may from time to time determine. Upon liquidation, dissolution or winding up of Exelixis, holders of common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any then outstanding shares of preferred stock. Holders of common stock have no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of Exelixis common stock are, and all shares of Exelixis common stock to be outstanding upon the closing of this offering will be, fully paid and nonassessable.

Preferred Stock

Our board of directors has the authority to issue up to 10,000,000 shares of Exelixis preferred stock, in one or more series and to determine the rights, preferences, privileges and restrictions of the preferred stock, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. The issuance of Exelixis preferred stock could diminish the voting power of holders of Exelixis common stock, and the likelihood that holders of Exelixis preferred stock will receive dividend payments and payments upon liquidation may have the effect of delaying, deferring or preventing a change in control of Exelixis. We have no present plans to issue any shares of Exelixis preferred stock.

Warrants

As of May 31, 2001, the following warrants to purchase an aggregate of 496,220 shares of Exelixis common stock were outstanding:

a warrant to purchase 71,428 shares of common stock at an exercise price of \$1.13 per share. The warrant expires on April 14, 2005;

three warrants to purchase an aggregate of 106,875 shares of common stock at an exercise price of \$4.00 per share. The warrants expire on April 14, 2005;

three warrants to purchase an aggregate of 78,750 shares of common stock at an exercise price of \$13.00 per share. The warrants expire on April 14, 2005;

13 warrants to purchase an aggregate of 166,251 shares of common stock at an exercise price of \$20.00 per share. The warrants expire on December 31, 2001;

a warrant to purchase 29,167 shares of common stock at an exercise price of \$20.98 per share. The warrant expires on December 31, 2001; and

two warrants to purchase an aggregate of 43,750 shares of common stock at an exercise price of \$20.00 per share. The warrants expire on September 30, 2004.

The warrants contain provisions for the adjustment of the exercise price and the aggregate number of shares that may be issued upon the exercise of the warrants if a stock dividend, stock split, reorganization, reclassification or consolidation occurs.

Registration Rights

Holders of an aggregate of 23,199,818 shares of common stock and holders of warrants to purchase an aggregate of 71,428 shares of common stock will be entitled to rights to register these shares under the Securities Act. These rights are provided under the fourth amended and restated securityholders' agreement, dated January 28, 1999, under the fourth amended and restated

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registration rights agreement, dated February 26, 1999, and under agreements with similar registration rights. If we propose to register any of our securities under the Securities Act, either for our own account or for the account of others, the holders of these shares with registration rights are entitled to notice of the registration and are entitled to include, at our expense, their shares of common stock in the registration and any related underwriting, provided, among other conditions, that the underwriters may limit the number of shares to be included in the registration and in some cases, exclude these shares entirely. In addition, the holders of these shares may require us, at our expense and on not more than two occasions, to file a registration statement under the Securities Act with respect to their shares of common stock, and we will be required to use our best efforts to effect the registration. Further, the holders may require us, at our expense, to register their shares on Form S-3 when this form is available. In addition, in connection with our sale of shares of common stock to Bristol-Myers Squibb on July 17, 2001 we have agreed to file a resale registration statement on Form S-3 for the 600,600 shares purchased by Bristol-Myers Squibb within 45 days of the purchase date.

Delaware General Corporation Law and Certain Charter Provisions.

In general, Section 203 of the Delaware General Corporation Law prohibits a publicly-held Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years following the date that the stockholder became an interested stockholder unless:

prior to that date, the corporation's board of directors approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;

upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding those shares owned by persons who are directors and also officers, and by employee stock plans in which shares held subject to the plan will be tendered in a tender or exchange offer; or

on or subsequent to that date, the business combination is approved by the corporation's board of directors and is authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least two-thirds of the outstanding voting stock not owned by the interested stockholder.

Section 203 defines "business combination" to include:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;

subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; and

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

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Our certificate of incorporation requires that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and may not be effected by a consent in writing. Additionally, our certificate of incorporation:

substantially limits the use of cumulative voting in the election of directors;

provides that the authorized number of directors may be changed only by resolution of its board of directors; and

authorizes its board of directors to issue blank check preferred stock to increase the amount of outstanding shares.

Our bylaws provide that candidates for director may be nominated only by our board of directors or by a stockholder who gives written notice to us no later than 60 days prior, nor earlier than 90 days prior, to the first anniversary of the last annual meeting of stockholders. Our board of directors currently consists of ten members, divided into three classes. As a result, a portion of the board of directors will be elected each year. The board of directors may appoint new directors to fill vacancies or newly created directorships. The restated bylaws also limit who may call a special meeting of stockholders.

Delaware law and these charter provisions may have the effect of deterring hostile takeovers or delaying changes in control of our management, which could depress the market price of our common stock.

Transfer Agent and Registrar

The transfer agent and registrar for Exelixis common stock is Mellon Investor Services LLC.

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 or any prospectus supplement. 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 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

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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.

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 Current Reports on Form 8-K, filed on May 15, 2001 pursuant to Item 2 of such report, on July 18, 2001 and on July 26, 2001 pursuant to Item 5 of such report; and
4	•	The description of our common stock set forth in our registration statement on Form 8-A, filed with the SEC on April 6,

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.

2000.

No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in the prospectus and the prospectus supplement. You must not rely on any unauthorized information or representations. The prospectus and the prospectus supplement are an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in the prospectus supplement is current only as of their respective dates.

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