NEUROCRINE BIOSCIENCES INC
Form 424B5
September 04, 2003

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The information in this prospectus supplement is not complete and may be changed. The registration statement filed with the Securities and Exchange Commission is effective. This prospectus supplement and the accompanying prospectus are not an offer to sell these securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

This filing is made pursuant to Rule 424(b)(5) under the Securities Act of 1933 in connection with Registration No. 333-105917

Prospectus Supplement (Subject to Completion)
(To Prospectus dated June 12, 2003)

Issued September 4, 2003

3,000,000 Shares
Common Stock

We are offering 3,000,000 shares of our common stock.

Our common stock is quoted on the Nasdaq National Market under the symbol NBIX. On September 2, 2003, the reported last sale price of our common stock on the Nasdaq National Market was $53.58 per share.

Investing in our common stock involves risks. See Risk Factors beginning on page S-6 of this prospectus supplement.

PRICE $ A SHARE

	Price to Public	Underwriting Discounts and Commissions	Proceeds to Neurocrine
Per Share	$	$	$
Total	$	$	$

We have granted the underwriters the right to purchase up to an additional 450,000 shares to cover over-allotments.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares to purchasers on , 2003.

Joint Book-Running Managers

Morgan Stanley **Merrill Lynch & Co.**

Deutsche Bank Securities

UBS Investment Bank
Bear, Stearns & Co. Inc.

CIBC World Markets

Banc of America Securities LLC

Credit Suisse First Boston

, 2003

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Prospectus Supplement

Prospectus

You should rely only on the information contained in this prospectus supplement and the accompanying prospectus and the information incorporated by reference in the accompanying prospectus. We have not authorized anyone to provide you with information that is different. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information in these documents is accurate only as of the date thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of our common stock.

This document is in two parts. The first part is this prospectus supplement, which describes the terms of the offering of common stock and also supplements and updates information contained in the accompanying prospectus and the documents incorporated by reference into the accompanying prospectus. The second part is the accompanying prospectus, which gives more general information, some of which may not apply to the common stock. If the description of the offering of common stock varies between this prospectus supplement and the accompanying prospectus, you should rely on the information in this prospectus supplement.

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PROSPECTUS SUPPLEMENT SUMMARY

You should read the following summary together with the entire prospectus supplement and accompanying prospectus carefully, including the documents identified under Where You Can Find More Information. You should carefully consider, among other things, the matters discussed under Risk Factors.

NEUROCRINE BIOSCIENCES

We discover, develop and intend to commercialize drugs for the treatment of neurological and endocrine-related diseases and disorders. Our product candidates address some of the largest pharmaceutical markets in the world, including insomnia, anxiety, depression, various female and male health disorders, multiple sclerosis, diabetes and other neuro-endocrine related diseases and disorders. We currently have 17 programs in various stages of research and development, including seven programs in clinical development. While we independently develop many of our product candidates, we have entered into collaborations for six of our programs. Our lead clinical development program, indiplon, is a drug for the treatment of insomnia and is currently being evaluated in Phase III clinical trials in collaboration with Pfizer Inc. We anticipate filing a new drug application, or NDA, for indiplon in the first half of 2004.

Indiplon

Insomnia is a neurological disorder with over 80 million adults in the United States reporting trouble sleeping a few nights per week or more according to Mattson Jack, which publishes an epidemiological database used to determine the prevalence of a disease or disorder. Despite this widespread prevalence, insomnia remains a disorder without a satisfactory therapeutic option. There is currently no approved therapy that induces and maintains sleep throughout the night without next-day residual effects. According to IMS Health, the United States insomnia market was $1.7 billion in 2002. However, insomnia remains significantly undertreated as only an estimated one-third of insomnia sufferers are diagnosed, and only one-half of those diagnosed receive prescription drug treatment. In addition, according to the National Sleep Foundation, frequent sleep problems in individuals that are 55 to 84 years old, if ignored, can complicate the treatment of other medical conditions, including arthritis, diabetes, heart and lung disease and depression. A class of drugs known as non-benzodiazepines represents the current standard of care in the United States for the treatment of insomnia.

Indiplon acts via the same mechanism as currently marketed non-benzodiazepine therapeutics, including Sanofi-Synthelabo s Ambien® and Wyeth-Ayerst Laboratories Sonata®. Ambien® is the current market leader, with approximately $1.3 billion in worldwide sales in 2002, according to Sanofi-Synthelabo. Non-benzodiazepines target a specific site of action on a natural brain chemical involved in promoting and maintaining sleep. This chemical is called gamma-amino-butyric acid, or GABA, and the site of action is called the GABA-A receptor. Preclinical studies suggest that indiplon, a GABA-A receptor agonist, has fewer side effects than the currently marketed non-benzodiazepines, including Ambien® and Sonata®. In our Phase II and III clinical studies, indiplon demonstrated efficacy with no significant effects of next-day residual sedation at clinically relevant doses.

We are developing both a short and a longer acting formulation of indiplon. The short acting formulation can be used by patients who have trouble falling asleep or who wake up in the middle of the night and cannot get back to sleep. The longer acting formulation can be used by patients to rapidly induce sleep and maintain sleep through the night. If approved by the Food and Drug Administration, or FDA, the longer acting formulation would represent the first non-benzodiazepine GABA-A receptor agonist approved for maintaining, rather than simply inducing, sleep. In addition, if both formulations are approved by the FDA, indiplon will be the first non-benzodiazepine on the market to offer two formulations.

To date, we have completed approximately 30 clinical trials including three Phase III clinical trials. The results of these trials demonstrated that indiplon was safe, well tolerated and effective in achieving rapid sleep induction without next-day residual effects. In addition, these clinical trials have shown that indiplon users do not exhibit tolerance, which is the need for increasing dosages after chronic use, or rebound liability, which is a

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worsening of the pre-treatment condition after use of the product candidate is discontinued. In total, our Phase III program will consist of 13 studies with approximately 4,000 subjects, all of which are currently underway or completed. At completion, we will have included over 6,000 subjects with insomnia in our studies.

In December 2002, we announced an exclusive worldwide collaboration with Pfizer to develop and commercialize indiplon. Pfizer made an upfront payment to us of $100 million and agreed to make additional pre-commercialization milestone payments of up to $300 million. Under the terms of the agreement, Pfizer is also responsible for all future third-party development, marketing and commercialization costs, with the exception of $30 million for specified development costs which we will bear. Following the filing of an NDA, Pfizer is obligated to pay for and support the creation of a 200-person Neurocrine sales force that will initially promote Pfizer s leading antidepressant drug, Zoloft®, to psychiatrists in the United States and, upon approval of the indiplon NDA, will co-promote indiplon in the United States. We will be entitled to a percentage of worldwide sales of indiplon for the longer of 10 years or the life of the indiplon patent rights as well as co-promotion payments on sales of indiplon and Zoloft® in the United States. In addition, subject to FDA approval of indiplon and various other conditions, Pfizer has committed to loan us up to $175 million, at commercial terms, pursuant to a secured credit facility. We have granted Pfizer an exclusive license to develop and market indiplon in all markets outside the United States. In June 1998, we sublicensed exclusive worldwide rights to indiplon from DOV Pharmaceutical, Inc.

Our Other Product Candidates

We have an extensive product pipeline focused on neurological and endocrine-related diseases and disorders.

GnRH Antagonist We completed two Phase I clinical studies for our gonadotropin-releasing hormone, or GnRH, antagonist, NBI-42902, for the treatment of endometriosis. The results of these trials demonstrated that GnRH reduced gonadotropin production, which is a surrogate parameter for efficacy, and that the product candidate was safe and well tolerated. We have selected a second development candidate that we expect to advance into clinical trials during the second half of 2003 for the treatment of uterine fibroids. According to Med Ad News, these markets had worldwide sales in 2002 of approximately $2.5 billion.

Altered Peptide Ligand We are currently conducting a Phase II study and have recently completed enrollment in another Phase II study to access safety and efficacy of our novel altered peptide ligand, NBI-6024, for new onset Type 1 diabetes. We also have initiated a Phase II study to determine the optimal dosing and frequency of administration of NBI-5788 in the treatment of relapsing multiple sclerosis. Diabetes and multiple sclerosis represented $4.5 billion and $2.9 billion markets, respectively, in 2002.

D_2 Receptor Agonist In the first quarter of 2003, we acquired the rights from Pharmacia to develop a selective dopamine D_2 receptor agonist, which is now designated as NBI-69733, for the treatment of male and female sexual dysfunction. We plan to conduct a Phase II proof of concept clinical study in erectile dysfunction to determine potential efficacy in early 2004. Viagra, which acts via a different mechanism of action than our product candidate, is the market leader for erectile dysfunction with 2002 sales of $1.7 billion according to Pfizer.

Corticotropin-Releasing Factor Receptor We are currently in advanced preclinical development in preparation for Phase I clinical trials for our corticotropin-releasing factor receptor-1, or CRF-R_1, antagonist for the treatment of neurological disorders such as depression and anxiety. In July 2001, we announced a worldwide collaboration with GlaxoSmithKline PLC to develop and commercialize CRF antagonists for psychiatric, neurological and gastrointestinal diseases. In 2003, the market for depression therapeutics alone is expected to be approximately $14.0 billion according to Datamonitor.

IL-4 Fusion Toxin Our interleukin 4, or IL-4, product candidate, NBI-3001, has completed Phase I/ II trials for solid tumor cancers and malignant glioma. In October 1999, the FDA granted us fast track designation for NBI-3001. We currently plan to outsource the development and commercialization of NBI-3001 to allow us to focus on neurological and endocrine-related diseases and disorders.

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Research Our research focus addresses diseases and disorders of the central nervous system and endocrine system, which includes stress-related disorders and neurodegenerative diseases, as well as prostate cancer, eating disorders and cardiovascular diseases. Central nervous system drug therapies represent the second largest sector of the worldwide drug market, accounting for over $55 billion in worldwide drug sales in 2002 according to Datamonitor.

Our Strategy

Our goal is to become the leading biopharmaceutical company focused on discovering, developing and commercializing therapeutics for the treatment of neurological and endocrine diseases and disorders. The key elements of our business strategy to realize this goal include:

- completing the development and commercialization of our lead product candidate, indiplon;
- continuing to advance and build our product portfolio focused on neurological and endocrine-related diseases and disorders;
- identifying novel drug targets to address large unmet market opportunities;
- selectively establishing corporate collaborations with global pharmaceutical companies to assist in the development of our products and mitigate financial risk while retaining significant commercial upside; and
- acquiring rights to complementary drug candidates and technologies.

Other Information

We were incorporated in California in 1992 and reincorporated in Delaware in 1996. Our common stock began trading publicly in May 1996. As of June 30, 2003, we had 326 employees, consisting of 293 full-time and 33 part-time employees. Of the full-time employees, approximately 105 hold Ph.D., M.D. or equivalent degrees. Our headquarters are located at 10555 Science Center Drive, San Diego, California 92121. Our telephone number is (858) 658-7600. Our website is www.neurocrine.com, but the information on our website does not constitute a part of this prospectus supplement.

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THE OFFERING

Common stock offered	3,000,000 shares
Common stock to be outstanding after this offering	34,461,943 shares
Over-allotment option	450,000 shares
Use of proceeds	For research and product development, including late-stage clinical trials, potential acquisitions of companies and technologies, working capital and general corporate purposes.
Nasdaq National Market symbol	NBIX

The number of shares of our common stock outstanding after the offering is based on the number of shares outstanding as of June 30, 2003, and excludes as of June 30, 2003:

- 4,980,233 shares of common stock reserved for the exercise of options outstanding at a weighted average exercise price of $30.76 per share;
- 376,021 shares of common stock reserved for the exercise of warrants outstanding at a weighted average exercise price of $16.81 per share;
- 171,360 shares of common stock reserved for issuance under our employee stock purchase plan; and
- 5,455,083 shares of common stock reserved for issuance under our stock incentive plans.

Unless otherwise indicated, the information in this prospectus supplement assumes no exercise of the underwriters over-allotment option.

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SUMMARY CONSOLIDATED FINANCIAL DATA

The following table is a summary of our consolidated financial data for the periods presented. You should read this data along with Management s Discussion and Analysis of Financial Condition and Results of Operations included in this prospectus supplement, and our financial statements and related notes in our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, each filed with the Securities and Exchange Commission and incorporated by reference in this prospectus supplement and the accompanying prospectus. Historical results are not necessarily indicative of results to be expected for any future period.

	Six Months Ended June 30,		Year Ended December 31,				
	2003	2002	2002	2001	2000	1999[1]	1998[1][2]
	(Unaudited)		(In thousands, except per share data)				
Consolidated Statement of Operations Data:							
Revenues:							
Sponsored research and development	$ 64,071	$ 7,138	$ 12,364	$ 16,880	$ 6,881	$ 12,662	$ 12,361
Milestones and license fees	17,987	1,166	3,516	22,937	6,345	3,000	2,500
Grant income and other revenues	626	880	2,165	1,425	1,362	1,129	1,176
Total revenues	82,684	9,184	18,045	41,242	14,588	16,791	16,037
Operating expenses:							
Research and development	100,647	43,143	108,939	74,267	40,227	29,169	21,803
General and administrative	9,879	5,882	12,721	10,857	9,962	7,476	6,594
Write-off of acquired in-process research and development and licenses							4,910
Total operating expenses	110,526	49,025	121,660	85,124	50,189	36,645	33,307
Loss from operations	(27,842)	(39,841)	(103,615)	(43,882)	(35,601)	(19,854)	(17,270)
Other income and (expenses):							
Interest income, net	4,276	4,135	8,864	6,662	6,048	2,851	4,000
Other income, net	104	191	215	430	1,047	1,066	504
Equity in NPI losses and other adjustments, net						(885)	(7,188)
Total other income and (expenses)	4,380	4,326	9,079	7,092	7,095	3,032	(2,684)
Loss before income taxes	(23,462)	(35,515)	(94,536)	(36,790)	(28,506)	(16,822)	(19,954)
Income taxes	153			120	302		1
Net loss	$ (23,615)	$ (35,515)	$ (94,536)	$ (36,910)	$ (28,808)	$ (16,822)	$ (19,955)
Net loss per share:							
Basic and diluted	$ (.76)	$ (1.17)	$ (3.10)	$ (1.42)	$ (1.30)	$ (.88)	$ (1.10)
Shares used in calculation of net loss per share:							
Basic and diluted	31,063	30,408	30,488	26,028	22,124	19,072	18,141

	As of June 30, 2003	
	Actual	As Adjusted[3]
	(Unaudited) (In thousands)	
Consolidated Balance Sheet Data:		
Cash, cash equivalents and short-term investments	$ 272,814	$ 424,313
Working capital	212,686	364,185
Total assets	372,762	524,261
Long-term debt, net of current portion	19,123	19,123
Accumulated deficit	(225,541)	(225,541)
Stockholders equity	209,969	361,468

(1) Sponsored research and development includes $491,000 and $3,610,000 in revenues from a related party for the years ended December 31, 1999 and 1998, respectively.

(2) Includes results of operations and financial position of Northwest NeuroLogic, Inc. from May 28, 1998, the date of acquisition.

(3) The as adjusted balance sheet data summarized above reflects the application of the net proceeds from the sale of the 3,000,000 shares of common stock offered by us at an assumed public offering price of $53.58 per share after deducting the underwriting discounts and commissions and estimated offering expenses.

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RISK FACTORS

You should consider carefully the risks described below, together with the other information in this prospectus supplement, the accompanying prospectus and the information incorporated by reference therein, before you make a decision to invest in our securities. If any of the following risks actually occur, our business, operating results, prospects or financial condition could be harmed. Additional risks not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks Relating to Our Business

Our clinical trials may fail to demonstrate the safety and efficacy of our product candidates, which could prevent or significantly delay their regulatory approval.

Any failure or substantial delay in completing clinical trials for our product candidates may severely harm our business. Before obtaining regulatory approval for the sale of any of our potential products, we must subject these product candidates to extensive preclinical and clinical testing to demonstrate their safety and efficacy for humans. Clinical trials are expensive, time-consuming and may take years to complete. We are currently conducting Phase III clinical trials in our indiplon development program for insomnia. This is our most advanced clinical program and represents a significant portion of our total clinical development activities and expenditures. If our Phase III indiplon program is significantly delayed or fails to demonstrate that indiplon is safe and efficacious for the targeted patient populations or if the FDA does not approve the proposed indiplon product labeling, our business and reputation would be harmed and our stock price would be negatively affected.

In connection with the clinical trials of indiplon and our other product candidates, we face the risks that:

the product may not prove to be effective;

we may discover that a product candidate may cause harmful side effects;

the results may not replicate the results of earlier, smaller trials;

we or the FDA may suspend the trials;

the results may not be statistically significant;

patient recruitment may be slower than expected; and

patients may drop out of the trials.

Also, late stage clinical trials are often conducted with patients having the most advanced stages of disease. During the course of treatment, these patients can die or suffer other adverse medical effects for reasons that may not be related to the pharmaceutical agent being tested but which can nevertheless adversely affect clinical trial results.

We expect to rely on our collaboration with Pfizer for the funding of the completion of our indiplon clinical program and for commercialization of indiplon.

Pfizer has agreed to:

fund substantially all third-party costs related to future indiplon development, manufacturing and commercialization activities;

fund a 200-person Neurocrine sales force that will initially promote Zoloft® and, upon approval of the indiplon NDA, will co-promote indiplon in the Unites States;

be responsible for obtaining all regulatory approvals outside of the United States and regulatory approvals in the United States after approval of the first indiplon NDA; and

be responsible for sales and marketing of indiplon worldwide.

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While our agreement with Pfizer requires them to use commercially reasonable efforts in the development and commercialization of indiplon, we cannot control the amount and timing of resources Pfizer may devote to our collaboration following FDA approval in the United States nor can we control when Pfizer will seek regulatory approvals outside of the United States. In addition, if Pfizer s development activities in pursuing new indications and uses of indiplon are not successful or Pfizer s sales and marketing activities for indiplon are not effective, indiplon sales and our business may be harmed.

Pfizer may terminate the collaboration at any time upon 180-days written notice, subject to payment of specified amounts related to ongoing clinical development activities. If Pfizer elects to terminate the collaboration prior to FDA approval, we will be responsible for Phase III indiplon development expenses while we seek another partner to assist us in the worldwide development and commercialization of indiplon. This could cause delays in obtaining marketing approvals and sales, and negatively impact our business. If Pfizer elects to terminate the collaboration after receipt of FDA approval, we would be forced to fund the Neurocrine sales force and/or seek new marketing partners for indiplon. This could lead to loss of sales and negatively impact our business. In the event the collaboration is terminated by Pfizer, we may not be successful in finding another collaboration partner on favorable terms, or at all, and any failure to obtain a new partner on favorable terms could adversely affect indiplon development and commercialization and our business.

We may not receive regulatory approvals for our product candidates or approvals may be delayed.

Regulation by government authorities in the United States and foreign countries is a significant factor in the development, manufacture and marketing of our proposed products and in our ongoing research and product development activities. Any failure to receive the regulatory approvals necessary to commercialize our product candidates would harm our business. The process of obtaining these approvals and the subsequent compliance with federal and state statutes and regulations require spending substantial time and financial resources. If we fail or our collaborators or licensees fail to obtain or maintain, or encounter delays in obtaining or maintaining, regulatory approvals, it could adversely affect the marketing of any products we develop, our ability to receive product or royalty revenues and our liquidity and capital resources. All of our products are in research and development and we have not yet requested or received regulatory approval to commercialize any product from the FDA or any other regulatory body. In addition, we have limited experience in filing and pursuing applications necessary to gain regulatory approvals, which may impede our ability to obtain such approvals.

In particular, human therapeutic products are subject to rigorous preclinical testing and clinical trials and other approval procedures of the FDA and similar regulatory authorities in foreign countries. The FDA regulates, among other things, the development, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale and distribution of biopharmaceutical products. Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information to the FDA for each indication to establish the product candidate s safety and efficacy. The approval process may take many years to complete and may involve ongoing requirements for post-marketing studies. Any FDA or other regulatory approval of our product candidates, once obtained, may be withdrawn. If our potential products are marketed abroad, they will also be subject to extensive regulation by foreign governments.

We plan to file an NDA for indiplon in the first half of 2004. We face the risk that the FDA could force us to delay our filing, reject our NDA filing, find it incomplete or find it insufficient for marketing approval for indiplon, which may cause our business and reputation to be harmed and likely would cause our stock price to decrease. In addition, even if our indiplon NDA is approved, the FDA could require Phase IV, or post-marketing, trials to study the long-term effects of indiplon and could withdraw its approval based on the results of those trials.

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We have a history of losses and expect to incur substantial losses and negative operating cash flows for the foreseeable future, and we may never achieve sustained profitability.

Since our inception, we have incurred significant net losses, including net losses of $23.6 million and $94.5 million for the six months ended June 30, 2003 and the year ended December 31, 2002, respectively. As a result of ongoing operating losses, we had an accumulated deficit of $225.5 million and $201.9 million as of June 30, 2003 and December 31, 2002, respectively. We were not profitable for the year ended December 31, 2002, and we do not expect to be profitable in 2003. We have not yet completed the development, including obtaining regulatory approvals, of any products and, consequently, have not generated revenues from the sale of products. Even if we succeed in developing and commercializing one or more of our drugs, we expect to incur substantial losses for the foreseeable future. We also expect to continue to incur significant operating and capital expenditures and anticipate that our expenses will increase substantially in the foreseeable future as we:

seek regulatory approvals for our product candidates;

develop, formulate, manufacture and commercialize our drugs;

implement additional internal systems and infrastructure; and

hire additional clinical and scientific personnel.

We also expect to experience negative cash flow for the foreseeable future as we fund our operating losses and capital expenditures. We will need to generate significant revenues to achieve and maintain profitability and positive cash flow. We may not be able to generate these revenues, and we may never achieve profitability in the future. Our failure to achieve or maintain profitability could negatively impact the market price of our common stock. Even if we become profitable, we cannot assure you that we would be able to sustain or increase profitability on a quarterly or annual basis.

Because our operating results may vary significantly in future periods, our stock price may decline.

Our quarterly revenues, expenses and operating results have fluctuated in the past and are likely to fluctuate significantly in the future. Our revenues are unpredictable and may fluctuate, among other reasons, due to our achievement of product development objectives and milestones, clinical trial enrollment and expenses, research and development expenses and the timing and nature of contract manufacturing and contract research payments. A high proportion of our costs are fixed, due in part to our significant research and development costs. Thus, small declines in revenue could disproportionately affect operating results in a quarter. Because of these factors, our operating results in one or more future quarters may fail to meet the expectations of securities analysts or investors, which could cause our stock price to decline.

We depend on continuing our current strategic alliances and developing additional strategic alliances to develop and commercialize our product candidates.

We depend upon our corporate collaborators to provide adequate funding for a number of our programs. Under these arrangements, our corporate collaborators are responsible for:

selecting compounds for subsequent development as drug candidates;

conducting preclinical studies and clinical trials and obtaining required regulatory approvals for these drug candidates; and

manufacturing and commercializing any resulting drugs.

Our strategy for developing and commercializing our products is dependent upon maintaining our current arrangements and establishing new arrangements with research collaborators, corporate collaborators and others. We have collaborations with Pfizer, GlaxoSmithKline, Wyeth and Eli Lilly and Company. Because we

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rely heavily on our corporate collaborators, the development of our projects would be substantially delayed if our collaborators:

fail to select a compound that we have discovered for subsequent development into marketable products;

fail to gain the requisite regulatory approvals of these products;

do not successfully commercialize products that we originate;

do not conduct their collaborative activities in a timely manner;

do not devote sufficient time and resources to our partnered programs or potential products;

terminate their alliances with us;

develop, either alone or with others, products that may compete with our products;

dispute our respective allocations of rights to any products or technology developed during our collaborations; or

merge with a third party that may wish to terminate the collaboration.

These issues and possible disagreements with our corporate collaborators could lead to delays in the collaborative research, development or commercialization of many of our product candidates. Furthermore, disagreements with these parties could require or result in litigation or arbitration, which would be time-consuming and expensive. If any of these issues arise, it may delay the filing of our NDAs and, ultimately, our generation of product revenues.

We license some of our core technologies and drug candidates from third parties. If we default on any of our obligations under those licenses, we could lose our rights to those technologies and drug candidates.

We are dependent on licenses from third parties for some of our key technologies. These licenses typically subject us to various commercialization, reporting and other obligations. If we fail to comply with these obligations, we could lose important rights. For example, we have licensed indiplon from DOV Pharmaceutical and IL-4 fusion toxin, which we call NBI-3001, from the National Institutes of Health, or NIH. In addition, we license some of the core research tools used in our collaborations from third parties, including the CRF receptor we license from The Salk Institute and use in our CRF program collaboration with GlaxoSmithKline and the excitatory amino acid transporters we license from Oregon Health Sciences University and use in our collaboration with Wyeth. Other in-licensed technologies, such as the GnRH receptor we license from Mount Sinai School of Medicine and melanocortin subtype 4 we license from the University of Michigan, will be important for future collaborations for our GnRH and melanocortin programs. If we were to default on our obligations under any of our product licenses, such as our license to indiplon, we could lose some or all of our rights to develop, market and sell the product. Likewise, if we were to lose our rights under a license to use proprietary research tools, it could adversely affect our existing collaborations or adversely affect our ability to form new collaborations. We also face the risk that our licensors could, for a number of reasons, lose patent protection or lose their rights to the technologies we have licensed, thereby impairing or extinguishing our rights under our licenses with them.

Because the development of our product candidates is subject to a substantial degree of technological uncertainty, we may not succeed in developing any of our product candidates.

All of our product candidates are in research or development and we do not expect any of our product candidates to be commercially available within a year, if at all. Only a small number of research and development programs ultimately result in commercially successful drugs. Potential products that appear to be promising at early stages of development may not reach the market for a number of reasons. These reasons include the possibilities that the potential products may:

be found ineffective or cause harmful side effects during preclinical studies or clinical trials;

fail to receive necessary regulatory approvals on a timely basis or at all;

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be precluded from commercialization by proprietary rights of third parties;

be difficult to manufacture on a large scale; or

be uneconomical or fail to achieve market acceptance.

If any of our products encounters any of these potential problems, we may never successfully market that product.

We are currently conducting Phase III clinical trials for indiplon. Since this is our most advanced product program, our business and reputation would be particularly harmed, and our stock price likely would be harmed, if the product does not prove to be efficacious in these clinical trials or we fail to receive necessary regulatory approvals on a timely basis or achieve market acceptance.

If we cannot raise additional funding, we may be unable to complete development of our product candidates.

We may require additional funding to continue our research and product development programs, including preclinical testing and clinical trials of our product candidates, for operating expenses and to pursue regulatory approvals for product candidates. We also may require additional funding to establish manufacturing and marketing capabilities in the future. We believe that our existing capital resources, together with interest income, and future payments due under our strategic alliances, will be sufficient to satisfy our current and projected funding requirements for at least the next 12 months. However, these resources might be insufficient to conduct research and development programs as planned. If we cannot obtain adequate funds, we may be required to curtail significantly one or more of our research and development programs or obtain funds through additional arrangements with corporate collaborators or others that may require us to relinquish rights to some of our technologies or product candidates.

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

continued scientific progress in our research and development programs;

the magnitude of our research and development programs;

progress with preclinical testing and clinical trials;

the time and costs involved in obtaining regulatory approvals;

the costs involved in filing and pursuing patent applications and enforcing patent claims;

competing technological and market developments;

the establishment of additional strategic alliances;

the cost of commercialization activities and arrangements, including manufacturing of our product candidates; and

the cost of product in-licensing and any possible acquisitions.

We intend to seek additional funding through strategic alliances, and may seek additional funding through public or private sales of our securities, including equity securities. In addition, we have leased equipment and may continue to pursue opportunities to obtain additional debt financing in the future. However, additional equity or debt financing might not be available on reasonable terms, if at all, and any additional equity financings will be dilutive to our stockholders.

We have no marketing experience, sales force or distribution capabilities, and if our products are approved, we may not be able to commercialize them successfully.

Although we do not currently have any marketable products, our ability to produce revenues ultimately depends on our ability to sell our products if and when they are approved by the FDA. We currently have no experience in marketing or selling pharmaceutical products. We are currently initiating marketing activities for indiplon by hiring staff with experience in pharmaceutical sales, marketing and distribution. We will

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on Pfizer to co-promote indiplon with us in the United States and rely exclusively on Pfizer to market indiplon outside of the United States. We will also rely on Pfizer to provide distribution, customer service, order entry, shipping, billing, customer reimbursement assistance and managed care sales support related to indiplon. If we fail to establish successful marketing and sales capabilities or fail to enter into successful marketing arrangements with third parties, our product revenues will suffer.

The independent clinical investigators and contract research organizations that we rely upon to conduct our clinical trials may not be diligent, careful or timely, and may make mistakes, in the conduct of our trials.

We depend on independent clinical investigators and contract research organizations, or CROs, to conduct our clinical trials under their agreements with us. The investigators are not our employees, and we cannot control the amount or timing of resources that they devote to our programs. If independent investigators fail to devote sufficient time and resources to our drug development programs, or if their performance is substandard, it will delay the approval of our FDA applications and our introductions of new drugs. The CROs we contract with for execution of our clinical trials play a significant role in the conduct of the trials and the subsequent collection and analysis of data. Failure of the CROs to meet their obligations could adversely affect clinical development of our products. Moreover, these independent investigators and CROs may also have relationships with other commercial entities, some of which may compete with us. If independent investigators and CROs assist our competitors at our expense, it could harm our competitive position.

We have no manufacturing capabilities. If third-party manufacturers of our product candidates fail to devote sufficient time and resources to our concerns, or if their performance is substandard, our clinical trials and product introductions may be delayed and our costs may rise.

We have in the past utilized, and intend to continue to utilize, third-party manufacturers to produce the drug compounds we use in our clinical trials and for the potential commercialization of our future products. We have no experience in manufacturing products for commercial purposes and do not currently have any manufacturing facilities. Consequently, we depend on several contract manufacturers for all production of products for development and commercial purposes. If we are unable to obtain or retain third-party manufacturers, we will not be able to commercialize our products. The manufacture of our products for clinical trials and commercial purposes is subject to specific FDA regulations. Our third-party manufacturers might not comply with FDA regulations relating to manufacturing our products for clinical trials and commercial purposes or other regulatory requirements now or in the future. Our reliance on contract manufacturers also exposes us to the following risks:

- contract manufacturers may encounter difficulties in achieving volume production, quality control and quality assurance, and also may experience shortages in qualified personnel. As a result, our contract manufacturers might not be able to meet our clinical schedules or adequately manufacture our products in commercial quantities when required;

- switching manufacturers may be difficult because the number of potential manufacturers is limited. It may be difficult or impossible for us to find a replacement manufacturer quickly on acceptable terms, or at all;

- our contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to successfully produce, store or distribute our products;

- drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Agency, and corresponding state agencies to ensure strict compliance with good manufacturing practices and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers compliance with these regulations and standards; and

- if our primary contract manufacturer should be unable to manufacture indiplon for any reason, or should fail to receive FDA approval or Drug Enforcement Agency approval, commercialization of indiplon could be delayed, which would delay indiplon sales and negatively impact our business.

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Our current dependence upon third parties for the manufacture of our products may harm our profit margin, if any, on the sale of our future products and our ability to develop and deliver products on a timely and competitive basis.

If we are unable to retain and recruit qualified scientists or if any of our key senior executives discontinues his or her employment with us, it may delay our development efforts.

We are highly dependent on the principal members of our management and scientific staff. The loss of any of these people could impede the achievement of our development objectives. Furthermore, recruiting and retaining qualified scientific personnel to perform research and development work in the future is critical to our success. We may be unable to attract and retain personnel on acceptable terms given the competition among biotechnology, pharmaceutical and health care companies, universities and non-profit research institutions for experienced scientists. In addition, we rely on members of our Scientific Advisory Board and a significant number of consultants to assist us in formulating our research and development strategy. All of our consultants and members of the Scientific Advisory Board are employed by employers other than us. They may have commitments to, or advisory or consulting agreements with, other entities that may limit their availability to us.

We may be subject to claims that we or our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is commonplace in the biotechnology industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Governmental and third-party payors may impose sales and pharmaceutical pricing controls on our products that could limit our product revenues and delay profitability.

The continuing efforts of government and third-party payors to contain or reduce the costs of health care through various means may reduce our potential revenues. These payors efforts could decrease the price that we receive for any products we may develop and sell in the future. In addition, third-party insurance coverage may not be available to patients for any products we develop. If government and third-party payors do not provide adequate coverage and reimbursement levels for our products, or if price controls are enacted, our product revenues will suffer.

If physicians and patients do not accept our products, we may not recover our investment.

The commercial success of our products, if they are approved for marketing, will depend upon the acceptance of our products as safe and effective by the medical community and patients.

The market acceptance of our products could be affected by a number of factors, including:

- the timing of receipt of marketing approvals;
- the safety and efficacy of the products;
- the success of existing products addressing our target markets or the emergence of equivalent or superior products; and
- the cost-effectiveness of the products.

In addition, market acceptance depends on the effectiveness of our marketing strategy, and, to date, we have very limited sales and marketing experience or capabilities. If the medical community and patients do not ultimately accept our products as being safe and effective, we may not recover our investment.

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Risks Related to Our Industry

We face intense competition, and if we are unable to compete effectively, the demand for our products, if any, may be reduced.

The biotechnology and pharmaceutical industries are subject to rapid and intense technological change. We face, and will continue to face, competition in the development and marketing of our product candidates from academic institutions, government agencies, research institutions and biotechnology and pharmaceutical companies. Competition may also arise from, among other things:

- other drug development technologies;
- methods of preventing or reducing the incidence of disease, including vaccines; and
- new small molecule or other classes of therapeutic agents.

Developments by others may render our product candidates or technologies obsolete or noncompetitive.

We are performing research on or developing products for the treatment of several disorders including insomnia, anxiety, depression, various female and male disorders, multiple sclerosis, diabetes and other neuro-endocrine related diseases and disorders, and there are a number of competitors to products in our research pipeline. If one or more of our competitors products or programs are successful, the market for our products may be reduced or eliminated.

Compared to us, many of our competitors and potential competitors have substantially greater:

- capital resources;
- research and development resources, including personnel and technology;
- regulatory experience;
- preclinical study and clinical testing experience;
- manufacturing and marketing experience; and
- production facilities.

Any of these competitive factors could reduce demand for our products.

If we are unable to protect our intellectual property, our competitors could develop and market products based on our discoveries, which may reduce demand for our products.

Our success will depend on our ability to, among other things:

- obtain patent protection for our products;
- preserve our trade secrets;
- prevent third parties from infringing upon our proprietary rights; and
- operate without infringing upon the proprietary rights of others, both in the United States and internationally.

Because of the substantial length of time and expense associated with bringing new products through the development and regulatory approval processes in order to reach the marketplace, the pharmaceutical industry places considerable importance on obtaining patent and trade secret protection for new technologies, products and processes. Accordingly, we intend to seek patent protection for our proprietary technology and compounds. However, we face the risk that we may not obtain any of these patents and that the breadth of claims we obtain, if any, may not

provide adequate protection of our proprietary technology or compounds.

We also rely upon unpatented trade secrets and improvements, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our commercial collaborators, employees and consultants. We also have

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invention or patent assignment agreements with our employees and some, but not all, of our commercial collaborators and consultants. However, if our employees, commercial collaborators or consultants breach these agreements, we may not have adequate remedies for any such breach, and our trade secrets may otherwise become known or independently discovered by our competitors.

In addition, although we own a number of patents, the issuance of a patent is not conclusive as to its validity or enforceability, and third parties may challenge the validity or enforceability of our patents. We cannot assure you how much protection, if any, will be given to our patents if we attempt to enforce them and they are challenged in court or in other proceedings. It is possible that a competitor may successfully challenge our patents or that challenges will result in limitations of their coverage. Moreover, competitors may infringe our patents or successfully avoid them through design innovation. To prevent infringement or unauthorized use, we may need to file infringement claims, which are expensive and time-consuming. In addition, in an infringement proceeding a court may decide that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the ground that our patents do not cover its technology. Interference proceedings declared by the United States Patent and Trademark Office may be necessary to determine the priority of inventions with respect to our patent applications or those of our licensors. Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and be a distraction to management. We cannot assure you that we will be able to prevent misappropriation of our proprietary rights, particularly in countries where the laws may not protect such rights as fully as in the United States.

The technologies we use in our research as well as the drug targets we select may infringe the patents or violate the proprietary rights of third parties.

We cannot assure you that third parties will not assert patent or other intellectual property infringement claims against us or our collaboration partners with respect to technologies used in potential products. Any claims that might be brought against us relating to infringement of patents may cause us to incur significant expenses and, if successfully asserted against us, may cause us to pay substantial damages. Even if we were to prevail, any litigation could be costly and time-consuming and could divert the attention of our management and key personnel from our business operations. Furthermore, if a patent infringement suit were brought against us or our collaboration partners, we or our collaboration partners could be forced to stop or delay developing, manufacturing or selling potential products that are claimed to infringe a third party s intellectual property unless that party grants us or our collaboration partners rights to use its intellectual property. In such cases, we could be required to obtain licenses to patents or proprietary rights of others in order to continue to commercialize our products. However, we may not be able to obtain any licenses required under any patents or proprietary rights of third parties on acceptable terms, or at all. Even if our collaboration partners or we were able to obtain rights to the third party s intellectual property, these rights may be non-exclusive, thereby giving our competitors access to the same intellectual property. Ultimately, we may be unable to commercialize some of our potential products or may have to cease some of our business operations as a result of patent infringement claims, which could severely harm our business.

We face potential product liability exposure far in excess of our limited insurance coverage.

The use of any of our potential products in clinical trials, and the sale of any approved products, may expose us to liability claims. These claims might be made directly by consumers, health care providers, pharmaceutical companies or others selling our products. We have obtained limited product liability insurance coverage for our clinical trials in the amount of $10 million per occurrence and $10 million in the aggregate. However, our insurance may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. We intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. On occasion, juries have awarded large judgments in class action lawsuits based on drugs that had unanticipated side

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effects. A successful product liability claim or series of claims brought against us would decrease our cash reserves and could cause our stock price to fall.

Our activities involve hazardous materials and we may be liable for any resulting contamination or injuries.

Our research activities involve the controlled use of hazardous materials. We cannot eliminate the risk of accidental contamination or injury from these materials. If an accident occurs, a court may hold us liable for any resulting damages, which may reduce our cash reserves and force us to seek additional financing.

Risks Related to this Offering

The price of our common stock is volatile.

The market prices for securities of biotechnology and pharmaceutical companies historically have been highly volatile, and the market has from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. Over the course of the last 12 months, the price of our common stock has ranged from approximately $34 per share to approximately $60 per share. The market price of our common stock may fluctuate in response to many factors, including:

the results of our clinical trials;

developments concerning our strategic alliance agreements;

announcements of technological innovations or new therapeutic products by us or others;

developments in patent or other proprietary rights;

future sales of our common stock by existing stockholders;

comments by securities analysts;

general market conditions;

fluctuations in our operating results;

government regulation;

health care reimbursement;

failure of any of our product candidates, if approved, to achieve commercial success; and

public concern as to the safety of our drugs.

If any of the risks described in this Risk Factors section occurs, it could cause our stock price to fall dramatically and may expose us to class action securities lawsuits which, even if unsuccessful, would be costly to defend and a distraction to management.

We have broad discretion in how we use the net proceeds of this offering, and we may not use these proceeds effectively.

We have not designated the amount of net proceeds we will use for any particular purpose. Accordingly, our management will have broad discretion as to the application of the net proceeds and could use them for purposes other than those contemplated at the time of this offering. Our stockholders may not agree with the manner in which our management chooses to allocate and spend the net proceeds. Moreover, our management may use the net proceeds for corporate purposes that may not increase our profitability or our market value.

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FORWARD-LOOKING STATEMENTS

Any statements in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference in the accompanying prospectus about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and are forward-looking statements. You can identify these forward-looking statements by the use of words or phrases such as believe, may, could, will, estimate, continue, anticipate, intend, seek, plan, expect, should and would. These forward-looking statements number of risks, uncertainties and assumptions, including the risks outlined under Risk Factors and elsewhere in this prospectus supplement, that may cause actual results, levels of activity, performance or achievements to differ materially from any results, levels of activity, performance or achievements expressed or implied by any forward-looking statement.

Although we believe that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee future results, events, levels of activity, performance or achievement. We undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.

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USE OF PROCEEDS

We estimate that our net proceeds from the offering of our common stock will be approximately $151.5 million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters option to purchase up to 450,000 shares in this offering is exercised in full, we estimate that our net proceeds will be approximately $174.3 million. These numbers are based on an assumed offering price to the public of $53.58, which was the reported last sale price of our common stock on the Nasdaq National Market on September 2, 2003.

We expect to use the net proceeds from this offering for general corporate purposes, including clinical trials, research and development expenses, general and administrative expenses, manufacturing expenses, and potential acquisitions of companies and technologies that complement our business. The amounts and timing of our actual expenditures will depend significantly upon a number of factors, including future revenues from licensing and corporate collaborations. As a result, we will retain broad discretion in determining how we will allocate the net proceeds from this offering. Pending these uses, we intend to invest the net proceeds in interest-bearing, investment-grade corporate and government securities.

PRICE RANGE OF COMMON STOCK

Our common stock is quoted on the Nasdaq National Market under the symbol NBIX. The following table sets forth, for the periods indicated, the high and low sales prices per share of our common stock as reported on the Nasdaq National Market:

	High	Low
Year ended December 31, 2001:		
First Quarter	$36.50	$14.25
Second Quarter	39.99	16.75
Third Quarter	40.71	27.93
Fourth Quarter	54.26	30.36
Year ended December 31, 2002:		
First Quarter	$52.21	$32.15
Second Quarter	43.88	23.25
Third Quarter	42.65	24.04
Fourth Quarter	50.00	37.92
Year ended December 31, 2003:		
First Quarter	$48.53	$37.38
Second Quarter	60.27	41.45
Third Quarter (through September 2, 2003)	57.50	48.49

On September 2, 2003, the reported last sale price of our common stock on the Nasdaq National Market was $53.58 per share. As of September 2, 2003, there were approximately 102 stockholders of record of our common stock.

DIVIDEND POLICY

We have not declared or paid any cash dividends since our inception. We currently intend to retain our future earnings, if any, for use in the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future.

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CAPITALIZATION

You should read this table together with our consolidated financial statements and related notes and the other financial data appearing elsewhere or incorporated by reference into this prospectus supplement and accompanying prospectus.

The following table sets forth our capitalization and other financial data as of June 30, 2003 on:

an actual basis; and

an as adjusted basis, which gives effect to our sale of 3,000,000 shares of common stock in this offering at an assumed public offering price of $53.58 per share, after deducting underwriting discounts and commissions and estimated offering expenses.

	June 30, 2003	
	Actual	As Adjusted
	(In thousands)	
Cash, cash equivalents and short-term investments	$ 272,814	$ 424,313
Long-term debt, net of current portion	$ 19,123	$ 19,123
Stockholders equity:		
Preferred stock, $0.001 par value, 5,000,000 shares authorized; no shares issued and outstanding		
Common stock, $0.001 par value, 50,000,000 shares authorized; 31,461,943 shares issued and outstanding, actual; 34,461,943 shares issued and outstanding, as adjusted	31	34
Additional paid-in capital	432,279	583,775
Deferred compensation	(1,008)	(1,008)
Notes receivable from stockholders	(208)	(208)
Accumulated other comprehensive gain	4,416	4,416
Accumulated deficit	(225,541)	(225,541)
Total stockholders equity	209,969	361,468
Total capitalization	$ 229,092	$ 380,591

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DILUTION

Our net tangible book value as of June 30, 2003 was $210.0 million or approximately $6.67 per share. The per share amount results from dividing total assets less intangible assets and total liabilities by the 31,461,943 shares of our common stock outstanding on June 30, 2003. After giving effect to the sale of the 3,000,000 shares of common stock at the assumed public offering price of $53.58 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses, our net tangible book value as of June 30, 2003 would have been $361.5 million, or $10.49 per share. This represents an immediate increase in net tangible book value of $3.82 per share to existing stockholders and an immediate dilution of $43.09 per share to new investors in this offering. The following table illustrates this dilution on a per share basis:

Assumed public offering price per share		$53.58
Net tangible book value per share as of June 30, 2003	$6.67	
Increase per share attributable to new investors	3.82	
Net tangible book value per share after this offering		$10.49
Dilution per share to new investors		$43.09

The outstanding share information in the table above excludes as of June 30, 2003:

4,980,233 shares of common stock reserved for the exercise of options outstanding at a weighted average exercise price of $30.76;

376,021 shares of common stock reserved for the exercise of warrants outstanding at a weighted average exercise prices of $16.81;

171,360 shares of common stock reserved for issuance under our employee stock purchase plan; and

5,455,083 shares of common stock reserved for issuance under our stock incentive programs.

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SELECTED CONSOLIDATED FINANCIAL DATA

The following selected consolidated financial data should be read in conjunction with our consolidated financial statements and the related notes and Management s Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this prospectus supplement or incorporated by reference. The selected consolidated statement of operations and balance sheet data for the years ended December 31, 1998, 1999, 2000, 2001 and 2002 are derived from our audited consolidated financial statements. In the opinion of management, our unaudited financial statements include all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of this information. The operating results for the six months ended June 30, 2003 are not necessarily indicative of results that may be expected for the year ended December 31, 2003 or any other interim period or future year.

	Six Months Ended June 30,		Year Ended December 31,				
	2003	2002	2002	2001	2000	1999[1]	1998[1][2]
	(Unaudited)		(In thousands, except per share data)				
Consolidated Statement of Operations Data:							
Revenues:							
Sponsored research and development	$ 64,071	$ 7,138	$ 12,364	$ 16,880	$ 6,881	$ 12,662	$ 12,361
Milestones and license fees	17,987	1,166	3,516	22,937	6,345	3,000	2,500
Grant income and other revenues	626	880	2,165	1,425	1,362	1,129	1,176
Total revenues	82,684	9,184	18,045	41,242	14,588	16,791	16,037
Operating expenses:							
Research and development	100,647	43,143	108,939	74,267	40,227	29,169	21,803
General and administrative	9,879	5,882	12,721	10,857	9,962	7,476	6,594
Write-off of acquired in-process research and development and licenses							4,910
Total operating expenses	110,526	49,025	121,660	85,124	50,189	36,645	33,307
Loss from operations	(27,842)	(39,841)	(103,615)	(43,882)	(35,601)	(19,854)	(17,270)
Other income and (expenses):							
Interest income, net	4,276	4,135	8,864	6,662	6,048	2,851	4,000
Other income, net	104	191	215	430	1,047	1,066	504
Equity in NPI losses and other adjustments, net						(885)	(7,188)
Total other income and (expenses)	4,380	4,326	9,079	7,092	7,095	3,032	(2,684)
Loss before income taxes	(23,462)	(35,515)	(94,536)	(36,790)	(28,506)	(16,822)	(19,954)
Income taxes	153			120	302		1
Net loss	$ (23,615)	$ (35,515)	$ (94,536)	$ (36,910)	$ (28,808)	$ (16,822)	$ (19,955)
Net loss per share:							
Basic and diluted	$ (.76)	$ (1.17)	$ (3.10)	$ (1.42)	$ (1.30)	$ (.88)	$ (1.10)
Shares used in calculation of net loss per share:							

Basic and diluted	31,063	30,408	30,488	26,028	22,124	19,072	18,141

	June 30, 2003	December 31,				
		2002	2001	2000	1999	1998
	(Unaudited)	(In thousands)				
Consolidated Balance Sheet Data:						
Cash, cash equivalents and short-term investments	$ 272,814	$ 244,710	$ 319,982	$ 164,670	$ 91,098	$ 62,670
Working capital	212,686	215,615	306,754	157,446	86,168	60,064
Total assets	372,762	266,539	346,350	185,962	109,222	80,529
Long-term debt, net of current portion	19,123	5,277	3,600	2,283	2,139	2,247
Accumulated deficit	(225,541)	(201,926)	(107,390)	(70,480)	(41,672)	(24,850)
Stockholders equity	209,969	224,254	310,393	163,208	96,354	71,958

(1) Sponsored research and development includes $491,000 and $3,610,000 in revenues from a related party for the years ended December 31, 1999 and 1998, respectively.

(2) Includes results of operations and financial position of Northwest NeuroLogic from May 28, 1998, the date of acquisition.

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MANAGEMENT S DISCUSSION AND ANALYSIS

OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following Management s Discussion and Analysis of Financial Condition and Results of Operations section contains forward-looking statements, which involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth under Risk Factors in this prospectus supplement and incorporated by reference in the accompanying prospectus. This discussion should be read in conjunction with our consolidated financial statements and related notes and the related Management s Discussion and Analysis of Financial Condition and Results of Operations incorporated by reference into the prospectus supplement and prospectus.

Overview

We incorporated in California in 1992 and reincorporated in Delaware in 1996. Since inception, we have been engaged in the discovery and development of novel pharmaceutical products for neurological and endocrine-related diseases and disorders. Our product candidates address some of the largest pharmaceutical markets in the world including insomnia, anxiety, depression, various female and male health disorders, multiple sclerosis, diabetes and other neuro-endocrine related diseases and disorders. To date, we have not generated any revenues from the sale of products, and we do not expect to generate any product revenues until the FDA approves one of our drug candidates. Our lead clinical development program, indiplon, is a drug candidate for the treatment of insomnia and is currently being evaluated in Phase III clinical trials in collaboration with Pfizer. We currently anticipate filing an NDA for indiplon in the first half of 2004. We have funded our operations primarily through private and public offerings of our common stock and payments received under research and development agreements. We are developing a number of products with corporate collaborators and will rely on existing and future collaborators to meet funding requirements. We expect to generate future net losses in anticipation of significant increases in operating expenses as product candidates are advanced through the various stages of clinical development. As of June 30, 2003, we have incurred an accumulated deficit of $225.5 million and expect to incur operating losses in the future.

Critical Accounting Policies

Our discussion and analysis of our financial condition and results of operations is based upon our financial statements, which we have prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires management to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses, and related disclosures. On an ongoing basis, we evaluate these estimates, including those related to revenues under collaborative research agreements and grants, clinical trial accruals (which affect research and development expenses), and fixed assets. Estimates are based on historical experience, information received from third parties and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. The items in our financial statements requiring significant estimates and judgments are as follows:

Revenues under collaborative research agreements and grants are recognized as research costs are incurred over the period specified in the related agreement or as the services are performed. These agreements are on a best-efforts basis and do not require scientific achievement as a performance obligation and provide for payment to be made when costs are incurred or the services are performed. All fees are nonrefundable to the collaborators. Up-front, nonrefundable payments for license fees and advance payments for sponsored research and for sponsored development received in excess of amounts earned are classified as deferred revenue and recognized as revenue over the contract or development period. Estimating the duration of the development period includes continual assessment of development stages and regulatory requirements. Milestone payments are recognized as revenue upon achievement of pre-defined scientific events which require substantive effort. Revenues from government grants are recognized based on a percentage-of-completion basis as the related costs are incurred.

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Research and development, or R&D, expenses include related salaries, contractor fees, facilities costs, administrative expenses and allocations of corporate costs. All such costs are charged to R&D expense as incurred. These expenses result from our independent R&D efforts as well as efforts associated with collaborations, grants and in-licensing arrangements. In addition, we fund R&D at other companies and research institutions under agreements, which are generally cancelable. We review and accrue clinical trials expenses based on work performed, which relies on estimates of total hours incurred based on completion of patient studies and other events. We follow this method since reasonably dependable estimates of the costs applicable to various stages of a research agreement or clinical trial can be made. Accrued clinical costs are subject to revisions as trials progress to completion. Revisions are charged to expense in the period in which the facts that give rise to the revision become known.

We review long-lived assets, including leasehold improvements and property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Long-lived assets and certain identifiable intangible assets to be disposed of are reported at the lower of the carrying amount or fair value less the cost to dispose.

Results of Operations

Six Months Ended June 30, 2003 and 2002

Revenues for the six months ended June 30, 2003 were $82.7 million compared with $9.2 million in 2002. The increase in revenues for the six months ended June 30, 2003, compared with the respective period in 2002, is primarily from revenues recognized under our collaboration agreement with Pfizer. During the first half of 2003, we recognized revenue of $61.2 million in sponsored development funding and $16.1 million of revenue from amortization of up-front license fees from Pfizer. Under our agreement with GlaxoSmithKline, we recognized $3.6 million in year to date revenues through June 30, 2003 and $3.7 million for the same six-month period last year. Revenues recognized under the Taisho agreement totaled $1.1 million for the six-month period ended June 30, 2003 and $3.9 million for the same period last year. This $2.7 million decrease in Taisho revenue is due to the restructuring of our collaboration agreement whereby we reacquired worldwide rights to our diabetes drug candidate.

Research and development expenses increased to $100.6 million for the first six months of 2003 compared with $43.1 million for the respective period in 2002. Increased expenses primarily reflect higher costs associated with expanding development activities, in particular the indiplon Phase III program. Additionally, personnel and laboratory costs related to the expansion of research activities have increased during the same period. We expect to incur significant increases in research and development expenses in future periods as later phases of development typically involve an increase in the scope of studies, the number of patients treated and the number of scientific personnel required to manage the clinical trials.

General and administrative expenses increased to $9.9 million for the six months ended June 30, 2003 compared with $5.9 million during the same period last year. The increased cost resulted primarily from increased market research and marketing related costs, increased professional fees associated with business development, increased insurance costs and the addition of administrative personnel needed to support expanding research and development activities. We expect general and administrative costs to increase this year to provide continued support on development and clinical trials and collaborative relationships.

Interest income increased to $4.8 million for the six months ended June 30, 2003 compared to $4.3 million for the same period last year. The increase primarily resulted from higher overall investment balances offset slightly by lower interest rates.

Net loss for the first six months of 2003 was $23.6 million, or $0.76 per share, compared to $35.5 million, or $1.17 per share, for the same period in 2002. The decrease in the net loss resulted primarily from the revenue recognized under the licensing and collaboration agreements with Pfizer. Net losses are expected to continue this year as our programs continue to advance through the various stages of the research and clinical development processes.

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To date, our revenues have primarily come from funded research and achievements of milestones under corporate collaborations. The nature and amount of these revenues may fluctuate substantially from period to period, which would affect our quarterly revenues and earnings. Accordingly, results and earnings of one period are not predictive of future periods. Revenues from collaborations accounted for 99% and 90% of total revenues for the six months ended June 30, 2003 and 2002, respectively.

Years Ended December 31, 2002, 2001 and 2000

Our revenues for the year ended December 31, 2002 were $18.0 million compared with $41.2 million in 2001, and $14.6 million in 2000. The $23.2 million decrease in revenues from 2001 to 2002 resulted primarily from $21.0 million of milestones achieved in 2001 under the Taisho and GlaxoSmithKline collaborations. The increase in revenues from 2000 to 2001 was primarily the result of the Taisho and GlaxoSmithKline collaborations, which were effective July 2000 and July 2001, respectively. Under the Taisho agreement, we recognized $16.6 million during 2001, which included a $5.5 million milestone achievement, compared with $7.1 million in 2000. Under the GlaxoSmithKline agreement, we recognized $19.2 million during 2001, which included a $15.5 million milestone achievement. The increase in revenues from these agreements was partially offset by the completion of the sponsored research portion of an agreement with Janssen Pharmaceutical, N.V. that concluded, as scheduled, in February 2001. Under the Janssen agreement, we recognized $525,000 during 2001 and $3.0 million during 2000.

Research and development expenses increased to $108.9 million during 2002 compared with $74.3 million during 2001 and $40.2 million in 2000. Increased expenses over the three years primarily reflect advancement of our drug candidates through progressive clinical development phases and the higher costs associated with expanding development activities and increased enrollment in clinical trials, in particular, the indiplon Phase III program. Additionally, personnel and laboratory costs related to the expansion of research and development activities have increased over the same period. We expect to incur significant increases in research and development expense in future periods as later phases of development typically involve an increase in the scope of studies, the number of patients treated and the number of scientific personnel required to manage the trials.

General and administrative expenses increased to $12.7 million during 2002 compared with $10.9 million during 2001 and $10.0 million during 2000. The increase in administrative expenses from 2001 to 2002 resulted primarily from increased marketing research and marketing-related costs, increased recruiting and relocation costs for new employees, increased insurance costs and the addition of administrative personnel needed to support expanding research and development activities. The increase in expenses from 2000 to 2001 resulted primarily from additional patent-related legal expenses, marketing research and the addition of administrative personnel needed to support expanding research and development activities.

Interest income increased to $9.3 million during 2002 compared with $7.0 million during 2001 and $6.3 million during 2000. The increase in 2002, compared with 2001 and 2000, primarily resulted from higher investment balances achieved through public and private offerings of our common stock offset by lower investment yields. In December 2001, we sold 4.0 million shares of our common stock in a public offering resulting in net proceeds of $175.6 million. In December 2000, we sold 3.2 million shares of our common stock in a public offering resulting in net proceeds of $90.4 million.

Other income consists primarily of sublease income from unrelated parties. The fluctuations in sublease income from year to year reflect facility capacity in excess of our needs. Excess space is subleased until it is needed to support our growth. During 2002, sublease income decreased significantly as we ceased subleasing portions of our facility to enable us to use all of our laboratory and office space in conjunction with increased research and development activities.

Our net loss for 2002 was $94.5 million, or $3.10 per share, compared with $36.9 million, or $1.42 per share, in 2001 and $28.8 million, or $1.30 per share, in 2000. The increase in net loss primarily resulted from an increase in scientific personnel and expanded clinical development activities, primarily related to the indiplon program. We expect operating losses to increase for the foreseeable future as we continue to expand our clinical development efforts.

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Liquidity and Capital Resources

At June 30, 2003, our cash, cash equivalents, and short-term investments totaled $272.8 million compared with $244.7 million at December 31, 2002. The increase in cash balances at June 30, 2003 resulted primarily from the receipt of the initial license and collaboration payments from Pfizer totaling $100.0 million, offset by capital acquisitions and operating losses.

Net cash provided by (used in) operating activities during the first two quarters of 2003 was $45.1 million compared with ($31.9) million during the same period last year. The increase in cash provided by operations is a result of the receipt of the initial payment under the collaboration agreement with Pfizer, offset by a $32.0 million increase in accounts receivable from collaborators due to increased clinical development costs.

Net cash used in investing activities during the first two quarters of 2003 was $61.7 million compared to $85.5 million for the same period in 2002. This fluctuation resulted primarily from timing differences in investment purchases, sales and maturities and the fluctuations in our portfolio mix between cash equivalents and short-term investment holdings. We expect similar fluctuations to continue in future periods. In addition, undeveloped real property in San Diego, California was acquired for approximately $17 million to construct a new corporate facility. Capital equipment purchases for 2003 are expected to be approximately $6.0 million and will be financed primarily through debt arrangements.

Net cash provided by financing activities during the first two quarters of 2003 was $7.2 million compared to $1.3 million for the respective period last year. Cash proceeds from the issuance of common stock upon exercise of outstanding stock options and employee stock purchase plans increased by $5.3 million for the first six months of 2003 compared to the same period last year. We expect similar fluctuations to occur throughout the year, as the amount and frequency of stock-related transactions are dependent upon the market performance of our common stock. Additionally, we obtained financing for $1.8 million of capital equipment purchases during the first half of 2003.

We believe that our existing capital resources, together with interest income and future payments due under our strategic alliances, will be sufficient to satisfy our current and projected funding requirements for at least the next 12 months. However, we cannot guarantee that these capital resources and payments will be sufficient to conduct all of our research and development programs as planned. The amount and timing of expenditures will vary depending upon a number of factors, including progress of our research and development programs.

We will require additional funding to continue our research and product development programs, to conduct preclinical studies and clinical trials, for operating expenses, to pursue regulatory approvals for our product candidates, for the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims, if any, the cost of product in-licensing and any possible acquisitions, and we may require additional funding to establish manufacturing and marketing capabilities in the future. We may also seek to access the public or private equity markets whenever conditions are favorable. We may also seek additional funding through strategic alliances and other financing mechanisms, such as debt financing for equipment, our new headquarters, or general corporate purposes. We cannot assure you that adequate funding will be available on terms acceptable to us, if at all. If adequate funds are not available, we may be required to curtail significantly one or more of our research or development programs or obtain funds through arrangements with collaborators or others. This may require us to relinquish rights to certain of our technologies or product candidates.

We expect to incur operating losses over the next several years as our research, development, preclinical studies and clinical trial activities increase. To the extent that we are unable to obtain third-party funding for such expenses, we expect that increased expenses will result in increased losses from operations. We cannot assure you that we will be successful in the development of our product candidates, or that, if successful, any products marketed will generate sufficient revenues to enable us to earn a profit.

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Subsidiaries

In May 1997, we along with two unrelated parties formed Science Park Center LLC in order to construct an office and laboratory facility which we subsequently leased. Science Park is a California limited liability company, of which we, prior to April 2003, only owned a nominal minority interest. In May 2003, we became the majority owner of Science Park with an effective date of April 1, 2003, and accordingly we now consolidate Science Park in our financial statements. The net effect of the transaction on our consolidated financial statements was to increase property and equipment and long term debt on our consolidated balance sheet by approximately $14.0 million each at June 30, 2003.

We also recently formed Neurocrine International LLC, a Delaware limited liability company in which we hold a 99% ownership interest and Science Park holds a 1% interest.

Real Estate Transactions

During April 2003, Science Park, at our direction, entered into an agreement with a third party to sell our current research and administrative facility and an undeveloped parcel of land adjacent to the facility for approximately $40 million. We anticipate closing the sale of both parcels during the fourth quarter of 2003, and have negotiated a leaseback provision, as part of the sale agreements, to allow for the completion of the construction of our new facility.

In May 2003, Science Park, at our direction, entered into an agreement to acquire undeveloped real property in San Diego, California for approximately $17 million to construct a new corporate facility. Science Park has also placed a deposit of $3.5 million and a $4.4 million irrevocable standby letter of credit for an adjacent parcel of land, which it intends to purchase in early 2004. The letter of credit is secured by a $4.4 million cash deposit with the issuer and expires in February 2004.

Additional costs we expect to incur in connection with these two properties include design and construction costs as well as the purchase and installation of equipment and furnishings for these facilities. We estimate these costs at $43 million and expect to finance these costs through the net proceeds of the sale of the existing facility, a construction loan and a subsequent permanent financing. Construction of the new facility commenced in June 2003 and is expected to be completed in July 2004.

Quantitative and Qualitative Disclosures About Market Risk

We are exposed to interest rate risk on our short-term investments. The primary objective of our investment activities is to preserve principal while at the same time maximizing yields without significantly increasing risk. To achieve this objective, we invest in highly liquid and high quality government and other debt securities. To minimize our exposure due to adverse shifts in interest rates, we invest in short-term securities and ensure that the maximum average maturity of our investments does not exceed 40 months. If a 10% change in interest rates were to have occurred on June 30, 2003, this change would not have had a material effect on the fair value of our investment portfolio as of that date. Due to the short holding period of our investments, we have concluded that we do not have a material financial market risk exposure.

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BUSINESS

We discover, develop and intend to commercialize drugs for the treatment of neurological and endocrine-related diseases and disorders. Our product candidates address some of the largest pharmaceutical markets in the world, including insomnia, anxiety, depression, various female and male health disorders, multiple sclerosis, diabetes and other neuro-endocrine related diseases and disorders. We currently have 17 programs in various stages of research and development, including seven programs in clinical development. While we independently develop many of our product candidates, we have entered into collaborations for six of our programs. Our lead clinical development program, indiplon, is a drug for the treatment of insomnia and is currently being evaluated in Phase III clinical trials in collaboration with Pfizer. We anticipate filing an NDA for indiplon in the first half of 2004.

Our Product Pipeline

The following table summarizes our most advanced product candidates currently in clinical development and those currently in research, and is followed by detailed descriptions of each program:

Program	Targeted Indication	Status	Commercial Rights
Products under clinical development:			
Indiplon	Insomnia	Phase III	Pfizer/ Neurocrine
GnRH Antagonist (NBI-42902)	Endometriosis, Fibroids	Phase I	Neurocrine
Altered Peptide Ligand (NBI-5788)	Multiple Sclerosis	Phase II	Neurocrine
Altered Peptide Ligand (NBI-6024)	Type 1 Diabetes	Phase II	Neurocrine
D_2 Receptor Agonist (NBI-69733)	Male and Female Sexual Dysfunction	Phase II	Neurocrine
CRF R_1 Antagonist	Anxiety, Depression, Gastrointestinal Disorders	Development	GlaxoSmithKline/ Neurocrine
IL-4 Fusion Toxin (NBI-3001)	Solid Tumors, Malignant Glioma	Phase I & II	Neurocrine
Research:			
CRF R_1 Antagonist	Anxiety, Depression, Gastrointestinal Disorders	Research	GlaxoSmithKline/ Neurocrine
CRF R_2 Antagonist	Psychiatric Disorders, Eating Disorders	Research	GlaxoSmithKline/ Neurocrine
GnRH Antagonist	Endometriosis, Fibroids, Prostate Cancer	Research	Neurocrine
CRF R_2 Agonist	Obesity	Research	Eli Lilly/ Neurocrine
Melanocortin Receptor Agonist/ Antagonist	Obesity	Research	Neurocrine
Melanin Concentrating Hormone Antagonist	Depression, Obesity, Anxiety	Research	Neurocrine
Excitatory Amino Acid Transporters	Neurodegenerative Diseases, Schizophrenia	Research	Wyeth/ Neurocrine
CRF R_2 Peptide Agonist Urocortin II	Cardiovascular	Research	Neurocrine
Fractalkine	Pain	Research	Neurocrine
H_1 Receptor Antagonist	Sleep	Research	Neurocrine

Phase III indicates that we or our collaborators are conducting large-scale, comparative clinical trials on groups of patients afflicted with a specific disease in order to determine safety and efficacy as primary support for regulatory approval by the FDA to market a product for a specific disease or condition.

Phase II indicates that we or our collaborators are conducting clinical trials on groups of patients afflicted with a specific disease in order to determine preliminary efficacy, optimal dosages and expanded evidence of safety.

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Phase I indicates that we or our collaborators are conducting clinical trials with a smaller number of patients to determine early safety profile, maximally tolerated dose and pharmacological properties of the product in human volunteers.

Development indicates lead compound(s) have been selected and are undergoing good laboratory practices toxicology studies to prepare for Phase I clinical trials.

Research indicates identification and evaluation of compound(s) in laboratory and preclinical models.

R_1 and R_2 refer to two CRF receptor subtypes.

Products under Clinical Development

Indiplon

Insomnia is a neurological disorder with over 80 million adults in the United States reporting trouble sleeping a few nights per week or more, according to Mattson Jack. Mattson Jack also states that 24 million adults in the United States experience chronic insomnia, having trouble sleeping every night or almost every night. Studies have indicated that an estimated 80% of affected individuals have insomnia for more than a year and an estimated 40% have the condition for more than five years. Despite this widespread prevalence, insomnia remains a disorder without a satisfactory therapeutic option. There is currently no approved therapy that induces and maintains sleep throughout the night without next-day residual effects. According to IMS Health, the United States insomnia market was $1.7 billion in 2002. However, insomnia remains significantly undertreated as only an estimated one-third of insomnia sufferers are diagnosed, and only one-half of those diagnosed receive prescription drug treatment. In addition, according to the National Sleep Foundation, frequent sleep problems in individuals that are 55 to 84 years old, if ignored, can complicate the treatment of other medical conditions, including arthritis, diabetes, heart and lung disease and depression.

Researchers have found that insomnia can be treated by drugs that interact with the site of action of a natural brain chemical involved in promoting and maintaining sleep. This chemical is called gamma amino-butyric acid, or GABA, and the site of action is called the GABA-A receptor. During the 1980s, drugs that non-selectively target the GABA-A receptor, known as benzodiazepines, were used as sedatives to treat insomnia. This class of drugs produces several undesirable side effects, including negative interactions with other central nervous system depressants, such as alcohol, the development of tolerance upon repeat dosing, and rebound insomnia, or the worsening of insomnia following discontinuation of dosing. Additional side effects, due to the long half-life, or the duration of action of a compound, associated with this class of drugs include next-day residual sedation effects and impairment of coordination and memory. Memory impairment, which can include amnesia for events occurring prior to and after drug administration, is of particular concern in the elderly who comprise approximately 20% of the total insomnia population according to Mattson Jack.

During the late 1980s, a class of drugs known as non-benzodiazepines was developed to target a specific site on the GABA-A receptor. The non-benzodiazepines have a reduced incidence of side effects that are believed to be attributable to binding more selectively on a GABA-A receptor subtype than the benzodiazepines. The most popular of the non-benzodiazepines are marketed in the United States as Ambien® and Sonata®. Ambien® is the current market leader, with approximately $1.3 billion in worldwide sales in 2002, according to Sanofi-Synthelabo, with sales growing in excess of 20% per year.

We obtained the rights to indiplon for the treatment of insomnia through an exclusive worldwide sublicense that we entered into with DOV Pharmaceutical in June 1998. Indiplon, a non-benzodiazepine GABA-A receptor agonist, acts via the same mechanism as the currently marketed non-benzodiazepine therapeutics. However, preclinical studies suggest that indiplon has fewer side effects than the currently marketed non-benzodiazepines, including Ambien® and Sonata®. In our Phase II and III clinical studies, indiplon demonstrated efficacy with no significant next-day residual sedation effects at clinically relevant doses.

We are developing both an immediate release, or short acting, formulation and a modified release, or longer acting, formulation of indiplon to address the different needs of the insomnia patient population. To

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develop these two different formulations, we have capitalized on important features of indiplon, its rapid absorption and its short half-life in the body. Based on our clinical studies, we have determined that the concentration of indiplon in the bloodstream reaches levels high enough to induce sedation approximately 15 minutes after the patient takes the tablet. Indiplon is then rapidly metabolized and eliminated. This results in rapid sleep onset followed by rapid elimination of the drug from the body, reducing the risk of next-day residual sedation effects.

We believe that both formulations of indiplon will address the most prevalent forms of insomnia difficulty falling asleep; difficulty staying asleep; and middle of the night awakenings, with difficulty getting back to sleep. The immediate release formulation can be used by patients who have trouble falling asleep or who wake up in the middle of the night and cannot get back to sleep. The modified release formulation can be used by patients to rapidly induce sleep and maintain sleep through the night. There are currently no non-benzodiazepine GABA-A receptor agonists approved for maintaining, rather than simply inducing, sleep.

We have completed three Phase III clinical trials of indiplon. The results of these trials demonstrated that indiplon was safe, well tolerated and effective in achieving rapid sleep induction without next-day residual effects. In addition, these clinical trials have shown that indiplon users do not exhibit tolerance or rebound liability after using the product candidate. Our entire Phase III program will consist of 13 studies with approximately 4,000 subjects, all of which are underway or completed.

We have also completed 27 Phase I and Phase II clinical trials of indiplon for efficacy and safety involving approximately 2,000 subjects. In our Phase II clinical studies, indiplon was also shown to be safe and effective in helping subjects with both chronic and transient insomnia to fall asleep rapidly without adverse side effects as compared to a placebo. Results of a single dose Phase II clinical trial in 35 healthy volunteers comparing an immediate release formulation of indiplon, 10 mg Ambien® and 7.5 mg zopiclone, a sedative available in Europe and under development in the United States, relative to placebo during middle of the night dosing demonstrated that indiplon does not lead to next-day residual sedation effects, while both Ambien® and zopiclone exhibited statistically significant measures of next-day adverse side effects of residual sedation when compared with placebo. Our gender and age studies to date have indicated that indiplon works with no major differences between male and female subjects or young adult and elderly subjects. In two studies of transient insomnia involving an aggregate of 559 patients, the median time to fall asleep, the primary clinical goal, was reduced by 40% to 59% compared to a placebo. In a study of chronic insomnia, subjects receiving indiplon compared to a placebo showed a statistically significant decrease in time to sleep onset and increase in sleep duration as well as quality of sleep.

GnRH Antagonist

Gonadotropin-releasing hormone, or GnRH, is a brain peptide that stimulates the secretion of the pituitary hormones that are responsible for sex steroid production and normal reproductive function. Researchers have found that chronic administration of GnRH agonists reversibly shuts down this transmitter pathway and is clinically useful in treating hormone-dependent diseases such as endometriosis, uterine fibroids and prostate cancer. Other companies have developed several peptide drugs on this principle, such as Lupron® and Zoladex®, and according to market analyst reports by Med Ad News, the annual worldwide sales in 2002 for these drugs were approximately $2.5 billion. However, since these drugs are peptides, they must be injected rather than taken orally. In addition, these types of agonists take up to several weeks to exert their effect, a factor not seen with direct gonadotropin-releasing hormone antagonists, and until these drugs exert their effects, they have shown a tendency to exacerbate the condition. We believe that there is a large potential market for an orally delivered gonadotropin-releasing hormone antagonist.

Our GnRH clinical efforts are focused on providing new treatments for endometriosis, uterine fibroids and prostate cancer. According to Mattson Jack, there are more than 5.7 million women in the United States who are clinically recognized as having chronic endometriosis. Of those afflicted, approximately 200,000 patients are treated in a hospital setting, and approximately 250,000 are treated in an outpatient setting, according to a 1998 National Patient Profile audit. We believe that the availability of an oral treatment lacking the side effect profile of the currently available peptide agonists may be an alternative to surgery and

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encourage a higher treatment rate. Additionally, approximately 2.8 million women are symptomatic for uterine fibroids, according to the article Medical Treatment of Uterine Fibroids published in 2001 in the journal *Clinical Obstetrics and Gynecology.* We also believe our drug will have utility on the treatment of prostate cancer, of which there are expected to be approximately 221,000 new cases in 2003 in the United States, according to the American Cancer Society.

We selected NB1-42902, our lead clinical candidate, in early 2001 and initiated our Phase I clinical program in November 2001 for the treatment of endometriosis. The results of the first Phase I clinical trial demonstrated that GnRH reduced gonadotropin production, which is a surrogate parameter for efficacy. In June 2003, the results of the second Phase I clinical trial demonstrated that the product candidate was safe and well tolerated. We have selected a second development candidate that we expect to move into clinical trials during the second half of 2003 for the treatment of uterine fibroids.

Altered Peptide Ligand

The American Autoimmune Related Diseases Association estimates that approximately 50 million people in the United States suffer from autoimmune diseases such as multiple sclerosis, rheumatoid arthritis, Type 1 diabetes, systemic lupus erythematosus and thyroiditis. Scientists believe that the body s immune system causes these diseases. The immune system protects an individual from disease agents, such as viruses, by recognizing and destroying those foreign substances using specialized blood cells, called lymphocytes. Occasionally, however, some lymphocytes arise that inappropriately recognize the body s own tissues as an invader and begin to attack normal healthy tissue, resulting in an autoimmune disease like Type 1 diabetes. While the mechanism through which the lymphocyte initiates the autoimmune disease is still unknown, the development of drugs that specifically suppress the action of self-reactive lymphocytes or restore the function of regulatory cells may prove advantageous for the prevention, cure or treatment of autoimmune disease.

One type of lymphocyte involved in the immune response to self or foreign substances is the T cell. T cells detect antigens, which are foreign substances, such as viruses or bacteria, and destroy them. Experiments conducted by our scientists determined that specific amino acid residues within a peptide sequence of an antigen are required for T cell recognition and subsequent cellular activation. Scientists can specifically alter the structure of such a peptide fragment so that it will not properly activate the T cell. This altered peptide ligand can thus prevent the T cell from destroying its target, or in the case of an autoimmune reaction, prevent the T cell from destroying the healthy tissue.

Multiple Sclerosis. Multiple sclerosis is a chronic autoimmune disease characterized by recurrent attacks of neurologic dysfunction due to damage in the central nervous system. The classic clinical features of multiple sclerosis include impaired vision and weakness or paralysis of one or more limbs. In a recent study of multiple sclerosis patients, the peak age of onset was between the ages of 20 and 25 with approximately 10% of these patients experiencing their first symptoms after the age of 50. According to the National Multiple Sclerosis Society, there are approximately 400,000 cases of multiple sclerosis in the United States. Currently available treatments for multiple sclerosis offer only limited efficacy. Doctors often prescribe steroids to reduce the severity of acute flare-ups and speed recovery. Experimental therapy with other immune-suppressive agents has shown limited success. Nevertheless, worldwide sales of multiple sclerosis therapies reached $2.9 billion in 2002.

We designed a novel altered peptide ligand based on myelin basic protein that would target the autoreactive T cells that cause neurological damage in multiple sclerosis. Together with Novartis Pharmaceuticals Corporation, our former collaborative partner for this program, we filed an investigational new drug, or IND, application with the FDA and received approval in 1996 to commence clinical trials. We subsequently completed Phase I clinical trials and two Phase II clinical trials of our altered peptide ligand for the treatment of multiple sclerosis, NBI-5788.

One of the Phase II trials was a multi-center, placebo-controlled, randomized, parallel design study in which patients received one of three doses of NBI-5788, and the other Phase II trial was an open label, unblinded, non-placebo-controlled study in eight patients conducted in collaboration with the NIH. While allergic reactions were seen in approximately 10% of patients in these trials, suggesting that optimal dosing

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may be at lower levels than those selected for the trials, of the patients completing the placebo-controlled study, the total volume of enhancing lesions was reduced in the lowest dose group compared to the placebo control. Moreover, in this study 57% of the patients in the lowest dose group experienced reductions in the volume of new enhancing lesions compared to 25% in the placebo group. In the open label study, a higher incidence of new brain lesions was found in two patients who received the highest dose and the one patient who received the low dose. As a result, the trial was stopped.

In July 2003 we initiated a Phase II clinical trial with NBI-5788 for the treatment of relapsing multiple sclerosis. This multicenter, randomized, double-blind, placebo-controlled trial will evaluate optimal dose and frequency of administration. Our aim for future trials will be to further establish the benefit of altered peptide ligand therapy in patients with multiple sclerosis.

Type 1 Diabetes. Utilizing our experience in the development of altered peptide ligands for multiple sclerosis, we have extended this approach to Type 1 or insulin dependent diabetes mellitus, which is a metabolic disease in which the body does not produce enough insulin. Like multiple sclerosis, in Type 1 diabetes the immune system erroneously targets healthy tissue, in this case the pancreatic cells responsible for the production of insulin. According to the International Diabetes Federation, Type 1 diabetes is one of the most prevalent chronic childhood conditions worldwide, afflicting approximately 5 million patients in 2002. Diabetics often suffer from a number of complications of the disease including heart disease, circulatory problems, kidney failure, neurologic disorders and blindness. Current therapy for Type 1 diabetes consists of daily insulin injections to regulate blood glucose levels. This therapy does not cure nor does it prevent the disease. Worldwide sales of diabetes therapies reached $4.5 billion in 2002 according to ASInsights.

We believe that an altered peptide ligand specific for autoimmune T cells involved in diabetes may stop the destruction of the insulin-secreting cells in early onset Type 1 diabetic patients, thus allowing them to delay or avoid chronic insulin therapy. In preclinical studies, this altered peptide ligand, NBI-6024, was capable of eliciting a protective immune response and reducing the incidence of diabetes. In addition, experiments using immune cells derived from the blood of Type 1 diabetes patients indicate that patients immune cells recognize NBI-6024. This suggests that NBI-6024 may have the potential to intervene in the disease process in humans. We have completed four Phase I/IIa safety and dose escalating clinical trials in approximately 120 diabetic patients. Data from these trials indicates that NBI-6024 is safe and well tolerated. A Phase IIb clinical trial was initiated consisting of a randomized, double blind, placebo-controlled, multi-center, multi-national study in adolescent and adult patients with new onset Type 1 diabetes. This study will involve approximately 20 medical sites in Canada, Europe and South America and approximately 200 patients.

In 2000, we entered into agreements with Taisho providing them with worldwide rights to NBI-6024. Pursuant to the collaboration agreement, we received licensing and option fees, payments for certain development milestones, and reimbursement of a significant portion of worldwide development expenses. In September 2002, the collaboration agreement with Taisho was restructured to provide that Taisho s monetary and development obligations under the collaboration agreement would terminate effective September 30, 2002 and that we would reacquire worldwide rights to our diabetes drug candidate, excluding Japan. On March 31, 2003, we reacquired the Japanese rights to our diabetes drug candidate.

D_2 Receptor Agonist

In the first quarter of 2003, we acquired the rights from Pharmacia to develop a selective dopamine D_2 receptor agonist, which is now designated as NBI-69733, for the treatment of male and female sexual dysfunction. As a condition to the closing of the Pharmacia-Pfizer merger, the Federal Trade Commission required Pharmacia to divest this product candidate, to enhance competition in the market for human sexual dysfunction. Dopamine receptors in the brain are involved in sexual motivation, performance, and motor activity in rodents and monkeys. Neuroleptic dopamine receptor antagonists suppress both male and female sexual behavior in human patients while L-DOPA exerts pro-sexual effects in both sexes. Based on the results of animal studies, dopamine does not appear to elicit sexual behavior directly, but rather allows sexual stimuli to more readily activate neural circuits that have been primed by sex hormones. Our product candidate has

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demonstrated high intrinsic activity in animal models of sexual dysfunction and has been tested in Phase I clinical studies. Accordingly, we plan to conduct a Phase II proof of concept clinical study in the area of erectile dysfunction, or ED, with NBI-69733 to determine its potential efficacy in early 2004. Pharmacia is currently transferring to us the technology and manufacturing know-how to support such a study.

According to Mattson Jack, ED affects nearly 85 million men in the seven major pharmaceutical markets. However, less than 20% of the prevalent population is diagnosed with the condition according to a Decision Resources July 2002 study. Over the next decade, as the number of men 55 and older increases considerably, the number of ED sufferers in the United States is projected to increase by nearly one million or 14% according to a 2001 Gallup study of ED. This far outpaces the population growth of men which is likely to increase by only 9% by the year 2010. Currently, PDE-5 inhibitors such as Viagra are the only effective oral treatment. We believe that our approach to ED may have significantly fewer side effects than the currently marketed PDE-5 inhibitors. We also believe that the mechanism of action of our product candidate would enable it to be used in combination with existing therapies for the treatment of ED.

Corticotropin-Releasing Factor

According to Mattson Jack, in 2002 over 45 million people in the United States had symptoms of depression. The National Institute of Mental Health has also indicated that over 16% of the United States population has an anxiety disorder. In 2003, the market for depression therapeutics is expected to be approximately $14.0 billion according to Datamonitor. However, there remain significant unmet medical needs. The leading drug class, known as the selective serotonin reuptake inhibitors, is ineffective or intolerable in one-third of patients. These drugs frequently require as long as three weeks to take effect and have significant adverse side effects such as sexual dysfunction. Therefore, a rapid acting antidepressant with fewer side effects would represent a major advance in the treatment of depression.

Researchers have identified what they believe to be the central mediator of the body s stress responses or stress-induced disorders. This mediator is a brain chemical known as corticotropin-releasing factor, or CRF. CRF is overproduced in clinically depressed patients and individuals with anxiety disorders. Current research indicates that clinically depressed patients and patients with anxiety experience dysfunction of the hypothalamic-pituitary-adrenal axis, which is the system that manages the body s overall response to stress. When the body detects a threat to physical or psychological well-being, the region of the brain called the hypothalamus amplifies production of CRF, which induces the physical effects that are associated with stress which can lead to depression or anxiety.

The novelty and specificity of the CRF mechanism of action and the prospect of improving upon selective serotonin reuptake inhibitor therapy is a topic of interest throughout the psychiatric community and pharmaceutical industry, representing a market opportunity both to better serve patients and expand overall treatment for this life threatening disease.

We have a strategic position in the CRF field through our intellectual property portfolio and relationship with experts in the neuropsychiatric field. We have further characterized the CRF receptor system and have identified additional members of the CRF receptor family. We have patent rights on two receptor subtypes called CRF R_1 and CRF R_2, and we have pending patent applications on small molecule organic compounds modulating the CRF receptors.

Depression. Depression is one of a group of neuropsychiatric disorders that is characterized by extreme feelings of elation and despair, loss of body weight, decreased aggressiveness and sexual behavior, and loss of sleep. Researchers believe that depression results from a combination of environmental factors, including stress, as well as an individual s biochemical vulnerability, which is genetically predetermined. Researchers believe that the biochemical basis of depression involves elevated secretion of CRF and abnormally low levels of other neurotransmitters in the brain such as serotonin. The most frequently prescribed antidepressant therapies are selective serotonin reuptake inhibitors such as Zoloft®, Paxil®, Celexa® and Prozac® which act to increase the levels of serotonin and several other chemicals in the brain. However, because these drugs affect a wide range of neurotransmitters, they have been associated with a number of adverse side effects. While

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newer, more selective drugs offer some safety improvement, side effects remain problematic. In addition, one of the biggest limitations of most existing antidepressant therapies is their slow onset of action.

The first clinical trial to offer evidence of proof of concept of CRF antagonists in addressing depression was a Phase IIa open label trial conducted with our NBI-30775 product candidate in 1999 pursuant to two collaborations with Janssen in the field of CRF antagonists. Results from this trial indicated that NBI-30775 was safe and well tolerated and demonstrated anti-depressant activity as measured by a widely-accepted depression scale known as the Hamilton Depression Scores. In this trial, NBI-30775 was administered to 20 patients with major depressive disorders. Results from the trial, as reported in the Journal of Psychiatric Research, showed that treatment response, as defined by more than a 50% reduction in Hamilton Depression Scores, occurred in 50% of the patients in the low dose group and 80% of the patients in the higher dose group. While development of NBI-30775 was discontinued for safety reasons by our collaborator, Janssen, we were encouraged by these results, which we believe support the hypothesized mechanism of action. In March 2002, Janssen notified us that it had elected to terminate the 1995 and 1999 agreements with us. As a result, exclusive rights to these first generation CRF antagonist compounds have reverted to us.

In 1998, we initiated a proprietary CRF R_1 antagonist program independent of Janssen. This program led to the discovery of a novel class of second generation CRF R_1 antagonist compounds of a chemical class distinct from the class of compounds that were subject to the Janssen collaboration. In July 2001, we announced our second CRF antagonist collaboration, a worldwide collaboration with GlaxoSmithKline, to develop and commercialize CRF antagonists for psychiatric, neurological and gastrointestinal diseases. Under the terms of this agreement, we and GlaxoSmithKline will conduct a collaborative research program for up to five years and collaborate in the development of our current lead compounds, as well as novel back-up candidates and second generation compounds identified through the collaborative research. As part of the collaboration agreement with GlaxoSmithKline, we continue to perform research and discovery in CRF.

Anxiety. Anxiety is among the most commonly observed group of central nervous system disorders, which includes phobias or irrational fears, panic attacks, obsessive-compulsive disorders and other fear and tension syndromes. Of the pharmaceutical agents that other companies currently market for the treatment of anxiety disorders, benzodiazepines, such as Valium® and Xanax®, and the anxiolytic BuSpar® and their generic equivalents are the most frequently prescribed. Several side effects, however, limit the utility of these anti-anxiety drugs. Most problematic among these are drowsiness, the inability to stand up, amnesia, drug dependency and withdrawal reactions following the termination of therapy. In view of significant evidence implicating CRF in anxiety-related disorders, we are developing small molecule CRF R_1 receptor antagonists as anti-anxiety agents that block the effects of overproduction of CRF. We believe that these compounds utilize a novel mechanism of action that may offer the advantage of being more selective, thereby providing increased efficacy with reduced side effects as compared to benzodiazepines.

As a co-examined variable in the NBI-30775 open label Phase IIa clinical trial for depression described above, the anti-anxiety effects of the CRF R_1 receptor antagonist NBI-30775 showed a reduction in Hamilton Anxiety Scores from baseline in both treatment groups at all times after dosing. In addition, in preclinical studies used to evaluate anti-anxiety drugs, our scientists have demonstrated with statistical significance that clinical compound candidates from our independent CRF R_1 antagonist program are effective following oral administration. We did not observe any evidence of clinically relevant side effects. These results are encouraging because they suggest that compounds blocking the CRF R_1 receptor may be effective in treating anxiety-related disorders.

Irritable Bowel Syndrome. Research has also suggested that CRF plays a role in the control or modulation of the gastrointestinal system. Studies have demonstrated that central administration of CRF acts in the brain to inhibit emptying of the stomach while stimulating bowel activity, and suggest that overproduction of CRF in the brain may be a main contributor to stress-related gastrointestinal disorders.

Irritable bowel syndrome is a gastrointestinal inflammatory disease that affects approximately 110 million people worldwide. Irritable bowel syndrome can be a lifelong, intermittent disease, involving chronic or recurrent abdominal pain and frequent diarrhea or constipation. Some patients with irritable bowel syndrome report the onset of symptoms of the disease following a major life stress event, such as death in the family,

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which suggests that the causes of irritable bowel syndrome may be related to stress. In addition, most irritable bowel syndrome sufferers also experience anxiety and depression.

IL-4 Fusion Toxin

Interleukin 4, or IL-4, is a natural chemical that modulates cell growth. Proteins that bind to IL-4, known as IL-4 receptors, are highly concentrated on the cells of malignant brain tumors as well as many other cancers, including some types of kidney and lung cancer. Targeted toxins are a novel form of anticancer therapy under investigation in a variety of clinical settings. Targeted toxin therapeutics carry a toxin to a target site on the cancer cell and subsequently kill the cancer cell. Many scientists believe that targeted toxins have several potential advantages over conventional chemotherapy in that they are more selective and effective in the treatment of chemotherapy-resistant cancer cells.

Our IL-4 product candidate, NBI-3001, has completed a Phase I trial for solid tumor cancers and a Phase II trial for malignant glioma. In October 1999, the FDA granted us fast track designation for NBI-3001. We currently plan to outsource the development and commercialization of NBI-3001 to allow us to focus on neurological and endocrine-related diseases and disorders.

Research

Our research focus is on addressing diseases and disorders of the central nervous system and endocrine system, which includes stress-related disorders and neurodegenerative diseases, as well as prostate cancer, eating disorders and cardiovascular diseases. Central nervous system drug therapies represent the second largest sector of the worldwide drug market, accounting for over $55 billion in worldwide drug sales in 2002 according to Datamonitor.

CRF R_1 Antagonist

As mentioned previously, the CRF R_1 antagonist has been identified by researchers to be the central mediator of the body s stress responses or stress related disorders. Since researchers believe that CRF is the primary mediator of stress, they have suggested that CRF R_1 antagonists may provide a treatment for irritable bowel syndrome. Researchers have demonstrated the CRF R_1 antagonists demonstrate dose dependent effect with in vivo preclinical models of irritable bowel syndrome. Together with GlaxoSmithKline, we are evaluating our proprietary CRF R_1 antagonists for treatment of stress, anxiety, depression, and irritable bowel syndrome.

CRF R_2 Antagonist

Our scientists were the first to isolate a second CRF receptor, called CRF R_2. We believe the distribution of CRF R_2 in the brain suggests that CRF R_2 could play a role in some forms of anxiety and some eating disorders. Our researchers have demonstrated that administration of a CRF R_2 antagonist reduces measures of anxiety in studies of obsessive compulsive disorder and conditioned fear. We are also working with GlaxoSmithKline in evaluating our proprietary CRF R_2 antagonist for treatment of a variety of psychiatric and eating disorders. We have screened our small molecule library and conducted exploratory chemistry to identify a new series of compounds to undergo further study.

GnRH Antagonists

As previously mentioned, GnRH may be useful in treating some hormone dependent diseases. Our discovery work in GnRH has allowed us to select a backup compound to move into preclinical studies during 2003. This compound is expected to complete preclinical studies in mid-2003 and if successful, will advance to Phase I clinical trials. We continue to search for innovative formulations of GnRH that may lead to additional candidates for clinical trials.

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CRF R_2 Agonist

CRF R_2 agonists may also represent a therapeutic strategy for diseases and disorders of the central nervous system. Preliminary data indicates that CRF may act as a central regulator of both appetite and metabolism and may play a role in neurodegenerative diseases. In 1996, we initiated a three-year research collaboration with Eli Lilly to screen and optimize CRF R_2 agonists. In October 1999, the funded research portion of the program was completed as scheduled, and Eli Lilly has retained control of the program and exclusive rights to the compounds.

Melanocortin Receptor Agonist/ Antagonist

Melanocortin receptors are proteins on the surface of cells which help regulate some body functions such as eating and skin color. Researchers discovered that one of the melanocortin receptor subtypes, subtype 4, plays an important role in the mechanism regulating appetite and body weight. The subtype 4 receptor is activated by melanocyte stimulating hormone. When melanocyte stimulating hormone is injected into the brain, it reduces food intake and body weight. Responses have included the apparent increase in basal metabolic rate and lowering of serum insulin levels. We believe that an orally active subtype 4 agonist may produce the same effects and, thus, may provide a novel approach to the treatment of obesity. Conversely, the endogenous peptide antagonist of the central melanocortin subtype 4 receptor has been shown to have the reverse effect, increasing food intake over a sustained period of time after a single brain injection, and this observation has prompted significant interest in diseases such as cancer- and AIDS-related cachexia. For these reasons, we are also studying melanocortin subtype 4 receptor antagonists and have discovered novel, potent and selective compounds that are now being evaluated in relevant animal models. Additionally, researchers have recently suggested that melanocortin receptor subtype 4 agonists may also have a role in sexual dysfunction, and studies are underway to explore this further. We have screened our small molecule library and identified highly potent, selective orally active melanocortin subtype 4 receptor antagonist compounds.

Melanin Concentrating Hormone Antagonist

Recent studies suggest that melanin concentrating hormone, or MCH, plays a role in the regulation of eating behavior. Based on these findings, we believe that blocking the effect of MCH with a small molecule antagonist may represent a novel approach to the treatment of obesity. Additional indications include anxiety and depression. Through our research efforts, we have identified and screened small-molecule, orally-active compounds which will block the activity of MCH at its receptor. We believe that these compounds may provide a novel therapeutic strategy for treating obesity and related disorders.

Excitatory Amino Acid Transporters

Some of the most successful central nervous system drugs, including selective serotonin reuptake inhibitors such as Prozac®, selectively target transporters of neurotransmitters in the brain. Similarly, we are targeting a set of proteins, called excitatory amino acid transporters, generally located in the brain, which transport glutamate in and out of cells, to selectively control the levels of this neurotransmitter. Drugs which alter the activity of these transporters are expected to produce a therapeutic benefit in disorders where glutamate levels are abnormal such as head trauma, schizophrenia, Lou Gehrig s Disease and other neurodegenerative and psychiatric disorders.

We collaborate with Wyeth to investigate controlling the glutamate transporter function as a novel strategy for the treatment of neurodegenerative and psychiatric disorders that include basic research to understand the function and regulation of the transporters, along with the identification and characterization of chemical and biological leads.

CRF R_2 Peptide Agonist Urocortin II

We have in-licensed Urocortin II, which is a 38 amino acid peptide ligand selective for the CRF R_2 receptor and is one member of a family of recently discovered peptides that are related to CRF. As a family,

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CRF is believed to modulate endocrine, automatic and behavioral responses to stress. As a result, Urocortin II may have therapeutic uses through pathways yet to be utilized in current research programs or marketed products. We will be exploring the utility of this compound in cardiovascular, endocrine and metabolic disorders.

Fractalkine

Fractalkine is a unique member of the chemokine family, which is highly expressed by neurons in the brain. Recent evidence suggests that blockade of $CX3CR_1$, the receptor for fractalkine, may be beneficial for prevention of chronic pain. We have initiated a research effort to identify small-molecule, orally-active compounds as fractalkine receptor antagonists. We believe that these compounds may provide a novel therapeutic strategy for treating pain and related disorders.

H_1 Receptor Antagonist

We are pursuing orally active small molecule antagonists of the H_1, or histamine, receptor. While histamine itself has no therapeutic applications, anti-histamines are used widely for the treatment of allergies. Since sedation is common among anti-histamines that target the H_1 receptor, we believe that small molecules that target this receptor may represent a novel approach to treat various sleep disorders.

Our Discovery Technology

We utilize a proprietary approach to small molecule drug design that we refer to as multi-channel technology.

Multi-Channel Discovery™. The advent of molecular biology, culminating recently in the cloning of the human genome, has opened up a vast array of receptors as potential targets for drug discovery. Over the past ten years, numerous new technologies have been developed to try to speed the identification of small molecule drugs. These technologies have mainly relied on the creation of large chemical libraries utilizing combinatorial chemistry, automated synthesis of compounds and ultra-high throughput screening machines to test hundreds of thousands of compounds against a particular receptor. While we utilize all of these technologies, we have taken the science to the next step, one we call Multi-Channel Discovery, or MCD™.

MCD is driven by the power of traditional medicinal chemistry accelerated by a suite of computational methodologies that guide the synthesis of highly active small molecules. At the core of MCD is our development of a virtual library containing over 100 million molecules. Utilizing this universe of compounds, our chemists sequentially apply computer generated molecular screens to filter compounds that will bind to the desired receptor. The unique feature of MCD is that chemists are no longer constrained by the physical properties of a particular compound but rather are free to work with thousands of shapes and charges to design compounds that will fit onto the receptor target.

The power of MCD, however, lies not in its application to a single receptor as a drug target but in the database of compounds that are characterized and isolated for the next target from the same class of receptors. Our current focus is on the most attractive receptor class in the pharmaceutical industry, G-protein-coupled receptors. MCD is not a static process, but one that becomes more powerful, more predictive, and more efficient with each subsequent use. It is an artificial intelligence system applied to drug design.

In connection with our multi-channel technology, we utilize other advanced technologies to enhance our drug discovery capabilities and to accelerate the drug development process. These technologies include:

High-Throughput Screening. We have assembled a chemical library of diverse, low molecular weight organic molecules for lead compound identification, and we have implemented robotic screening capabilities linked to our library of compounds that facilitate the rapid identification of new drug candidates for multiple drug targets. In addition, we have designed a 175,000-compound library focused on some of our molecular targets. We believe that our utilization of high-throughput screening and medicinal and peptide chemistry will enable us to rapidly identify and optimize lead molecules.

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Molecular Biology. Our scientists utilize novel techniques to examine gene expression in a variety of cellular systems. We have developed a sophisticated technique to evaluate the type and quantity of genes in various cellular systems prior to the isolation of genes. We have also developed unique expression vectors and cell lines that allow for the highly efficient protein expression of specific genes.

Our drug discovery program creates a significant amount of genetic sequence information. We have developed a bioinformatics system, which we believe will allow us to identify novel genes involved in neurodegeneration. We collect data with automated instruments, and we store and analyze the data using customized computational tools.

Gene Sequencing. We apply integrated automated DNA sequencing and gene identification technology in our drug discovery program, enabling us to perform extended gene analysis in a rapid, high-throughput format with independent linkage into a sequence identification database. We have optimized gene sequencing instrumentation for differential display, a technique that may facilitate the rapid identification of novel genes.

Our Business Strategy

Our goal is to become the leading biopharmaceutical company focused on neurological and endocrine-related diseases and disorders. The following are the key elements of our business strategy:

Completing the Development and Commercialization of Our Lead Product Candidate, Indiplon. We are working with our collaboration partner, Pfizer, to complete our Phase III clinical trials for indiplon as promptly as practicable. Our entire Phase III program will consist of 13 studies with approximately 4,000 patients, all of which are currently underway or completed. We anticipate filing an NDA for indiplon in the first half of 2004.

Continuing to Advance and Build Our Product Portfolio Focused on Neurological and Endocrine-Related Diseases and Disorders. We believe that by continuing to advance and build our product pipeline, we can mitigate some of the clinical development risks associated with drug development. We currently have 17 programs in various stages of research and development, with seven projects in clinical development. We take a portfolio approach to managing our pipeline that balances the size of the market opportunities with clear and defined clinical and regulatory paths to approval. We do this to ensure that we focus our internal development resources on innovative therapies with improved probabilities of technical and commercial success.

Identifying Novel Drug Targets to Address Large Unmet Market Opportunities. We seek to identify and validate novel drug targets for internal development or collaboration. For example, the novel drug candidates we have identified to regulate CRF, which is believed to be the central mediator of the body s stress response, may represent the first new breakthrough for anxiety and depression in over 20 years. GnRH antagonists, compounds designed to reduce the secretions of sex steroids, may represent the first novel non-injectible means of treatment of endometriosis, uterine fibroids and prostate cancer. Additionally, melanocortin and MCH modulators are compounds that affect proteins in the brain believed to be involved in many activities of the body. The creativity and productivity of our discovery research group will continue to be a critical component for our continued success. Our team of approximately 160 biologists and chemists has a goal of delivering three innovative clinical compounds over the next five years to fuel our research and development pipeline.

Selectively Establishing Corporate Collaborations with Global Pharmaceutical Companies to Assist in the Development of Our Products and Mitigate Financial Risk While Retaining Significant Commercial Upside. We leverage the development, regulatory and commercialization expertise of our corporate collaborators to accelerate the development of our potential products while typically retaining co-promotional rights, and at times commercial rights, in North America. We intend to further leverage our resources by selectively entering into additional strategic alliances to enhance our internal development and commercialization capabilities. We currently have strategic alliances with:

Pfizer, for indiplon for the treatment of insomnia;

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GlaxoSmithKline, for second generation corticotropin-releasing factor receptor antagonists to treat anxiety and depression and irritable bowel syndrome;

Wyeth, for compounds to treat neurodegenerative and psychiatric diseases; and

Eli Lilly, for treatments of central nervous system disorders, including obesity.

Acquiring Rights to Complementary Drug Candidates and Technologies. We plan to continue to selectively acquire rights to products in various stages of development to take advantage of our drug development capabilities. For example, in May 1998, we acquired Northwest NeuroLogic and thereby considerably expanded our research pipeline. Through this acquisition, we acquired the technology and intellectual property rights surrounding excitatory amino acid transporters, a portion of which is now in collaboration with Wyeth. We also acquired from Northwest NeuroLogic intellectual property relating to melanocortin technology and other technologies that we are developing. In June 1998, we licensed exclusive worldwide commercial rights for indiplon from DOV Pharmaceutical.

Our Strategic Alliances

One of our business strategies is to utilize strategic alliances to enhance our development and commercialization capabilities. To date, we have formed the following alliances:

Pfizer. In December 2002, we announced an exclusive worldwide collaboration with Pfizer to develop and commercialize indiplon. Pfizer made an upfront payment to us of $100 million and agreed to make additional pre-commercialization milestone payments of up to $300 million. Under the terms of the agreement, Pfizer is also responsible for all future third-party development, marketing and commercialization costs, with the exception of $30 million for specified development costs which we will bear. Following the filing of an NDA, Pfizer is obligated to pay for and support the creation of a 200-person Neurocrine sales force that will initially promote Pfizer s leading antidepressant drug, Zoloft®, to psychiatrists in the United States and, upon approval of the indiplon NDA, will co-promote indiplon in the United States. We will be entitled to a percentage of worldwide sales of indiplon for the longer of 10 years or the life of the indiplon patent rights as well as co-promotion payments on sales of indiplon and Zoloft® in the United States. In addition, subject to FDA approval of indiplon and various other conditions, Pfizer has committed to loan us up to $175 million, at commercial terms, pursuant to a secured credit facility. We have granted Pfizer an exclusive license to develop and market indiplon in all markets outside the United States. Pfizer may terminate the collaboration at its discretion upon 180-days written notice to us. In such event, we would be entitled to specified payments for ongoing clinical development and related activities and all indiplon product rights would revert to us. As of June 30, 2003, we had recorded revenues of $16.1 million in license fees and $61.2 million in sponsored development. We obtained rights to indiplon pursuant to a 1998 Sublicense and Development Agreement with DOV Pharmaceutical, and we are responsible for specified milestone payments and royalties on net sales to DOV Pharmaceutical under the license agreement. In addition, at June 30, 2003 we had $83.9 million of deferred revenue, which is being amortized over the estimated period to commercialization of indiplon.

GlaxoSmithKline. In July 2001, we announced a worldwide collaboration with an affiliate of GlaxoSmithKline to develop and commercialize CRF antagonists for psychiatric, neurological and gastrointestinal diseases. Under the terms of this agreement, we and GlaxoSmithKline will conduct a collaborative research program for up to five years and collaborate in the development of our current lead compounds, as well as novel back-up candidates and second generation compounds identified through the collaborative research. In addition, we will be eligible to receive milestone payments as compounds progress through the research and development process, royalties on future product sales and co-promotion rights in the U.S. in some circumstances. GlaxoSmithKline may terminate the agreement at its discretion upon 90-days prior written notice to us. In such event, we may be entitled to specified payments and all product rights would revert to us. As of June 30, 2003, we had recorded revenues of $2.9 million in license fees, $15.8 million in milestone payments, $11.0 million in sponsored research and $842,000 in reimbursement of development costs. In addition, at June 30, 2003 we had $1.6 million of deferred license fees that will be amortized over the remaining life of the agreement. GlaxoSmithKline also sponsors a portion of our research efforts related to

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CRF through annual payments, of which $1.8 million is deferred and will be amortized over the remaining sponsored research period.

Wyeth. Effective in January 1999, we entered into a collaboration and license agreement with Wyeth relating to the research, development and commercialization of compounds that control excitatory amino acid transporters for the treatment of neurodegenerative and psychiatric diseases. We have granted Wyeth exclusive and non-exclusive rights to our excitatory amino acid transporters technology as well as exclusive rights to any products developed during the collaboration. These licenses are for the term of the patents licensed. We will receive royalties on net product sales for the terms of the patents covering the collaboration products, subject to adjustments for royalties payable to other parties and for competition. We will also receive royalties for products that are not the subject of issued patents. Under specified conditions, we have the option to co-promote collaboration products in Canada and the United States. Wyeth may terminate the agreement if it decides that the research is not successful upon six months prior written notice to us. In addition, Wyeth may terminate the agreement if it decides to stop the program upon written notice to us. Wyeth may also terminate the agreement in certain circumstances if we are acquired by another company. The three-year sponsored research portion of the Wyeth agreement was completed on schedule in December 2001 and was subsequently extended on a smaller scale through December 2002.

As of June 30, 2003, we had recognized a total of $13.9 million under the Wyeth agreement consisting of $10.5 million in sponsored research and $3.4 million in milestone payments.

Eli Lilly. In October 1996, we entered into a research and license agreement with Eli Lilly to collaborate in the discovery, development and commercialization of CRF binding protein ligand inhibitors for the treatment of central nervous system disorders including obesity and dementias, such as Alzheimer s disease, and CRF $_2$ agonists for central nervous system diseases and disorders. Under the agreement, we are entitled to milestone payments for specified development and regulatory accomplishments. We will have the option to receive co-promotion rights and share profits from commercial sales of select products that result from the collaboration in the United States or receive royalties on United States net sales. We will receive royalties on net sales for the rest of the world.

In October 1999, the funded portion of the research program concluded as scheduled and, to our knowledge, Eli Lilly is not planning any specific future development efforts, and we do not expect to receive any additional payments under this agreement. During the funded portion of the research program, we received payments totaling $17.2 million.

Intellectual Property

We seek to protect our lead compounds, compound libraries, expressed proteins, synthetic organic processes, formulations, assays, cloned targets, screening technology and other technologies by filing, or by causing to be filed on our behalf, patent applications in the United States and abroad. We have approximately 35 issued United States patents, 45 pending United States patent applications and another 200 issued and pending foreign patents and applications. We have licensed, from institutions such as The Salk Institute, Stanford University, Oregon Health Sciences University, DOV Pharmaceutical and others the rights to approximately an additional 40 issued United States patents, 10 pending United States patent applications, and 55 issued and pending foreign filings. We face the risk that one or more of the above patent applications may be denied. We also face the risk that our issued patents may be challenged or circumvented or may otherwise not provide protection for any commercially viable products we develop.

The technologies we use in our research, as well as the drug targets we select, may infringe the patents or violate the proprietary rights of third parties. If this occurs, we may be required to obtain licenses to patents or proprietary rights of others in order to continue with the commercialization of our products. We are aware of a patent application controlled by another company, which if granted in its broadest scope and held to be valid, could impact the commercialization of our modified release insomnia formulation unless we obtain a license, which may not be available to us. We are also aware of pending and issued patent claims to melanin concentrating hormone ligand and receptor, and some uses of melanocortin subtype 4 agonists. We are conducting research in all of those areas and may ultimately need to license those patents in order to proceed.

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In addition, we are aware of two United States patents relating to IL-4 proteins that are controlled by other entities which, if construed very broadly, and if valid as so construed, could prevent us from commercializing our IL-4 fusion toxin products in the United States unless we obtain a license, which may not be available to us on commercially reasonable terms, or at all. We do not believe that our research and development activities as currently conducted infringe any valid issued patents.

Indiplon, our leading gamma amino-butyric acid agonist compound for the treatment of insomnia, is covered in an issued United States patent, which we sublicensed from DOV Pharmaceutical. The term of the United States patent is due to expire in 2020. Additional United States patents covering synthesis, formulations and forms of indiplon were issued in 2002 and do not expire until 2020. Indiplon is not currently covered by any foreign patents of which we are aware. We intend to seek additional protection of this compound through nine United States and foreign patent applications directed to the synthesis, formulations and various forms of indiplon, which could extend some patent protection to the year 2020. We face the risk that these patents may not issue, or may subsequently be challenged successfully. In addition to the granted and potential patent protection, the United States, the European Union and Japan all provide data protection for new medicinal compounds. If this protection is available, no competitor may use the original applicant s data as the basis of a generic marketing application during the period of data protection. This period of exclusivity is five years in the United States, six years in Japan and six to ten years in the European Union, measured from the date of FDA, or corresponding foreign, approval.

Manufacturing

We currently rely on contract manufacturers, and will continue to rely on contract manufacturers for at least the next few years, to produce sufficient quantities of our product candidates for use in our pre-clinical and anticipated clinical trials. We have established an internal pharmaceutical development group to develop manufacturing methods for our products, to optimize manufacturing processes, and to select and transfer these manufacturing technologies to our suppliers. We continue to contract with multiple manufacturers to ensure adequate product supply and to mitigate risk.

There is currently a limited number of these manufacturers. Furthermore, some of the contract manufacturers that we have identified to date only have limited experience at manufacturing, formulating, analyzing and packaging our product candidates in quantities sufficient for conducting clinical trials or for commercialization.

Marketing and Sales

We currently have no sales or distribution capabilities. In order to commercialize any of our product candidates, we must either internally develop sales and distribution capabilities or make arrangements with third parties to perform these services. Additionally, we currently have no experience in marketing or selling pharmaceutical products. We are currently initiating marketing activities for indiplon by hiring staff with experience in pharmaceutical sales, marketing and distribution.

As part of our collaboration agreement with Pfizer, we will receive funding from Pfizer for a 200 person United States sales force. This funding will commence upon our filing of an NDA for indiplon and the sales force will immediately focus on detailing Pfizer s antidepressant drug Zoloft® to psychiatrists. Upon approval of the indiplon NDA, the sales force will also co-promote indiplon to psychiatrists and sleep specialists. Pfizer will manage all aspects of distribution for both Zoloft® and indiplon.

Additionally, under our collaboration agreements with GlaxoSmithKline, Wyeth, and Eli Lilly, we may have the opportunity to co-promote some of our other products in the United States. To market any of our other products directly, we must develop a sales force with technical expertise and with supporting distributions capabilities, none of which we currently have.

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Government Regulation

Regulation by government authorities in the United States and foreign countries is a significant factor in the development, manufacture and marketing of our proposed products and in our ongoing research and product development activities. All of our products will require regulatory approval by government agencies prior to commercialization. In particular, human therapeutic products are subject to rigorous preclinical studies and clinical trials and other approval procedures of the FDA and similar regulatory authorities in foreign countries. Various federal and state statutes and regulations also govern or influence testing, manufacturing, safety, labeling, storage and record-keeping related to such products and their marketing. The process of obtaining these approvals and the subsequent compliance with appropriate federal and state statutes and regulations require the expenditure of substantial time and financial resources.

Preclinical studies generally are conducted in laboratory animals to evaluate the potential safety and the efficacy of a product. Drug developers submit the results of preclinical studies to the FDA as a part of an IND application that must be approved before clinical trials can begin in humans. Typically, clinical evaluation involves a time consuming and costly three-phase process.

Phase I	Clinical trials are conducted with a small number of patients to determine the early safety profile, maximum tolerated dose and pharmacological properties of the product in human volunteers.
Phase II	Clinical trials are conducted with groups of patients afflicted with a specific disease in order to determine preliminary efficacy, optimal dosages and expanded evidence of safety.
Phase III	Large-scale, multi-center, comparative clinical trials are conducted with patients afflicted with a specific disease in order to determine safety and efficacy as primary support for regulatory approval by the FDA to market a product candidate for a specific disease.

The FDA closely monitors the progress of each of the three phases of clinical trials that are conducted in the United States and may, at its discretion, reevaluate, alter, suspend or terminate the testing based upon the data accumulated to that point and the FDA s assessment of the risk/benefit ratio to the patient. To date we have also conducted some of our clinical trials in Europe and South Africa.

Once Phase III trials are completed, drug developers submit the results of preclinical studies and clinical trials to the FDA in the form of an NDA or a biologics licensing application for approval to commence commercial sales. In response, the FDA may grant marketing approval, request additional information or deny the application if the FDA determines that the application does not meet regulatory approval criteria. FDA approvals may not be granted on a timely basis, or at all. Furthermore, the FDA may prevent a drug developer from marketing a product under a label for its desired indications, which may impair commercialization of the product.

If the FDA approves the NDA, the drug becomes available for physicians to prescribe in the United States. After approval, the drug developer must submit periodic reports to the FDA, including descriptions of any adverse reactions reported. The FDA may request additional studies, known as Phase IV, to evaluate long-term effects.

In addition to studies requested by the FDA after approval, a drug developer may conduct other trials and studies to explore use of the approved compound for treatment of new indications. The purpose of these trials and studies and related publications is to broaden the application and use of the drug and its acceptance in the medical community.

We will also have to complete an approval process similar to that in the United States in virtually every foreign target market for our products in order to commercialize our product candidates in those countries. The approval procedure and the time required for approval vary from country to country and may involve

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additional testing. Foreign approvals may not be granted on a timely basis, or at all. In addition, regulatory approval of prices is required in most countries other than the United States. We face the risk that the resulting prices would be insufficient to generate an acceptable return to us or our corporate collaborators.

Competition

The biotechnology and pharmaceutical industries are subject to rapid and intense technological change. We face, and will continue to face, competition in the development and marketing of our product candidates from biotechnology and pharmaceutical companies, research institutions, government agencies and academic institutions. Competition may also arise from, among other things:

other drug development technologies;

methods of preventing or reducing the incidence of disease, including vaccines; and

new small molecule or other classes of therapeutic agents.

Developments by others may render our product candidates or technologies obsolete or noncompetitive. We are performing research on or developing products for the treatment of several disorders including insomnia, anxiety, depression, diabetes mellitus, multiple sclerosis, eating disorders, pain, irritable bowel syndrome, autoimmunity and various female and male health disorders.

We are developing indiplon for the treatment of insomnia. Ambien® and Sonata® are already marketed for the treatment of insomnia by Sanofi-Synthelabo and King Pharmaceuticals, Inc., respectively. Additionally, in early 2003, Sepracor filed an NDA for Estorra™ (eszopiclone) for the treatment of insomnia. Takeda Pharmaceuticals is developing TAK-375, a melatonin agonist, for insomnia, which is currently in Phase III clinical trials, and Sanofi-Synthelabo is developing a new formulation of Ambien®, which is currently in Phase III clinical trials.

Products that may compete with NBI-5788, our altered peptide ligand for multiple sclerosis, include Betaseron® and Avonex®, similar forms of beta-interferon marketed by Berlex BioSciences and Biogen, respectively, Rebif® marketed by Serono, Copaxone®, a peptide polymer marketed by Teva, and Rebif® marketed by Serono and Pfizer.

We are developing NBI-69733 for the treatment of sexual dysfunction. There are many approved products for this indication and we believe that this market will become increasingly competitive. These products include, Viagra®, marketed by Pfizer, and Levitra®, marketed by both GlaxoSmithKline and Bayer. We are aware that a number of companies are conducting research on molecules that act through the same mechanism of action as our product candidate.

In the area of anxiety disorders, our product candidates will compete with well-established products such as Valium®, marketed by Hoffman-La Roche, Xanax®, marketed by Pfizer, BuSpar®, marketed by Bristol-Myers Squibb, Zoloft® marketed by Pfizer, and Wellbutrin® marketed by GlaxoSmithKline among others, as well as generic alternatives for each of these products.

We are also developing products for depression, which will compete with well-established products in the antidepressant class, including Prozac®, marketed by Eli Lilly as well as its generic alternatives, Zoloft®, marketed by Pfizer, Paxil®, marketed by GlaxoSmithKline, and Celexa®, marketed by Forest Laboratories, among others. Some technologies under development by other pharmaceutical companies could result in additional commercial treatments for depression and anxiety. In addition, a number of companies also are conducting research on molecules to block CRF, which is the same mechanism of action employed by our compounds.

There are a number of competitors to products in our research pipeline. Lupron Depot®, marketed by Takeda-Abbott Pharmaceuticals, Zoladex®, marketed by AstraZeneca, and Synarel®, marketed by Pfizer, are gonadotropin-releasing hormone peptide agonists that have been approved for the treatment of prostate cancer, endometriosis, infertility, and central precocious puberty. These drugs may compete with any small molecule gonadotropin-releasing hormone antagonists we develop for these indications. Anti-obesity therapeu-

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tics currently available include Xenical® from Roche Laboratories and Meridia® from Abbott Laboratories. If one or more of these products or programs are successful, it may reduce or eliminate the market for our products.

Compared to us, many of our competitors and potential competitors have substantially greater:

capital resources;

research and development resources, including personnel and technology;

regulatory experience;

preclinical study and clinical testing experience;

manufacturing and marketing experience; and

production facilities.

Any of these competitive factors could harm our business, prospects, financial condition and results of operations, which could negatively affect our stock price.

Employees

As of June 30, 2003, we had 326 employees, consisting of 293 full-time and 33 part-time employees. Of the full-time employees, approximately 105 hold Ph.D., M.D. or equivalent degrees. None of our employees are represented by a collective bargaining arrangement, and we believe our relationship with our employees is good. Furthermore, recruiting and retaining qualified scientific personnel to perform research and development work in the future will also be critical to our success. We face the risk that we may not be able to attract and retain personnel on acceptable terms given the competition among biotechnology, pharmaceutical and health care companies, universities and non-profit research institutions for experienced scientists. In addition, we rely on members of our Scientific Advisory Board and a significant number of consultants to assist us in formulating our research and development strategies.

Insurance

We maintain product liability insurance for our clinical trials. We intend to expand our insurance coverage to include the sale of commercial products if marketing approval is obtained for products in development. However, insurance coverage is becoming increasingly expensive, and no assurance can be given that we will be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. There can also be no assurance that we will be able to obtain commercially reasonable product liability insurance for any products approved for marketing.

Properties

We currently have approximately 93,000 square feet of space at our headquarters in San Diego, California, of which approximately 65% is laboratory space dedicated to research and development. We have entered into an agreement to sell this facility and are currently in the process of constructing our new headquarters in San Diego, California, which is expected to be completed in July 2004. We believe that our property and equipment are generally well maintained and in good operating condition.

Legal Proceedings

The Salk Institute has notified us that it is Salk s belief that we have not complied with certain milestone payments for our CRF antagonists under the 1993 license agreement between Salk and us. On June 27, 2003, Salk filed a demand for arbitration with the American Arbitration Association seeking information and additional milestone payments from us. We believe that we have complied with the terms of the license agreement and that no additional milestone payments are owed to Salk. We intend to vigorously defend our interests in this matter. We expect that the resolution of this matter will not have a material adverse effect on

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our business, financial condition or results of operations. However, due to the uncertainties inherent in these types of matters, no assurance can be given as to the outcome of these proceedings.

Other than the above, we are not currently a party to any material legal proceedings, though we are currently participating in other litigation in the ordinary course of business.

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MANAGEMENT

Executive Officers and Directors

Our Executive Officers and Directors as of the date of this prospectus supplement are as follows:

Name	Age	Position
Gary A. Lyons	52	President, Chief Executive Officer and Director
Paul W. Hawran	51	Executive Vice President and Chief Financial Officer
Henry Y. Pan, M.B.B.S., Ph.D., F.A.C.C	56	Executive Vice President, Clinical Development and Chief Medical Officer
Wendell Wierenga, Ph.D.	55	Executive Vice President, Research and Development
D. Bruce Campbell, Ph.D.	58	Senior Vice President, International Development
Margaret E. Valeur-Jensen, J.D., Ph.D.	46	Senior Vice President, General Counsel and Corporate Secretary
Robert J. Little	54	Senior Vice President, Commercial Operations
Joseph A. Mollica, Ph.D.[(1)(2)(3)]	62	Chairman of the Board of Directors
W. Thomas Mitchell[(1)(3)]	57	Director
Richard F. Pops[(1)(2)]	41	Director
Stephen A. Sherwin, M.D.[(2)(3)]	54	Director
Lawrence Steinman, M.D.	55	Director
Wylie W. Vale, Ph.D.	62	Director

(1) Member of the Audit Committee

(2) Member of the Compensation Committee

(3) Member of the Nominating/ Corporate Governance Committee

Gary A. Lyons has served as our President, Chief Executive Officer and as a member of our Board of Directors since joining us in February 1993. Prior to joining us, Mr. Lyons held a number of senior management positions at Genentech including Vice President of Business Development and Vice President of Sales as well as being a member of Genentech s Executive Committee. He was responsible for international licensing, acquisitions and partnering, was responsible for Genentech s Corporate Venture Program and had operating responsibility for Genentech s two subsidiaries, Genentech Canada, Inc. and Genentech Limited (Japan). Previously he served as Vice President of Sales and was responsible for building the marketing and sales organization for the commercial introduction of Genentech s first two pharmaceutical products, Protropin (human growth hormone) and Activase (TPA). Mr. Lyons currently serves on the Board of Directors of Intrabiotics Pharmaceuticals, Inc. and Vical, Inc. Mr. Lyons holds a B.S. in marine biology from the University of New Hampshire and an M.B.A. from Northwestern University s J.L. Kellogg Graduate School of Management.

Paul W. Hawran became our Executive Vice President and Chief Financial Officer in January 2001 after having served as our Senior Vice President and Chief Financial Officer since February 1996 and Vice President and Chief Financial Officer from 1993 to 1996. In this capacity, Mr. Hawran directs strategic planning, finance, accounting, investor relations, human resources, information technologies and operations. Mr. Hawran was employed by SmithKline Beecham Corporation from July 1984 to May 1993, most recently as Vice President and Treasurer. Prior to joining SmithKline in 1984, Mr. Hawran held various financial positions at Warner Communications (now AOL Time Warner) where he was involved in corporate finance, financial planning and domestic and international budgeting and forecasting. Mr. Hawran received a B.S. in

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finance from St. John s University and an M.S. in taxation from Seton Hall University. He is a Certified Public Accountant and a member of the American Institute of Certified Public Accountants and California and Pennsylvania Institute of Certified Public Accountants.

Henry Y. Pan M.B.B.S., Ph.D., F.A.C.C. became our Executive Vice President, Clinical Development and Chief Medical Officer in October 2001. In this capacity, he is responsible for scientific and administrative leadership and management of our clinical development programs. Prior to joining us, he was the Managing Director of VennWorks LLC from 2000 to 2001, an operating company that creates, builds and operates companies in different technology areas. Prior to joining VennWorks, he was the co-founder, President, CEO and Managing Partner of Pharmacologics LLC from 1999 to 2000. From 1997 to 1999, he was President and CEO of the Pharmaceutical Services division of MDS Inc., an integrated contract research organization. He served as Executive Vice President, Drug Development and Medical Affairs at DuPont Merck Pharmaceutical Company from 1992 to 1997 and was at Bristol-Myers Squibb from 1985 to 1992, most recently as Vice President of Clinical Research and Development. He received his B.S. in genetics from McGill University in 1969, M.S. in toxicology in 1973 and Ph.D. in pharmacology in 1974 from the University of Hawaii, and M.B.B.S. from the University of Hong Kong in 1979. He completed his fellowship training in Clinical Pharmacology in 1985 at Stanford University and is a fellow of the American College of Cardiology, the American College of Clinical Pharmacology, the American Heart Association, the Institute of Biological and Clinical Investigation and the Academy of Medicine of New Jersey.

Wendell Wierenga, Ph.D. became our Executive Vice President, Research and Development in September 2003 and is responsible for all aspects of Research and Development including discovery research as well as preclinical and clinical development. From August 2000 to August 2003, Dr. Wierenga was Chief Executive Officer of Syrrx, Inc. Prior to joining Syrrx, from March 1997 to July 2000, he was Senior Vice President of Worldwide Pharmaceutical Sciences, Technologies and Development at Parke-Davis/ Warner Lambert (now Pfizer), where he was responsible for worldwide drug development, including toxicology, pharmacokinetics/drug metabolism, chemical development, pharmaceutics, clinical supplies, information systems and technology acquisition. Prior to Parke-Davis, Dr. Wierenga was at Upjohn Pharmaceuticals for 16 years, most recently as Executive Director of Discovery Research. Dr. Wierenga led/participated in the research and development of more than 50 INDs, over 10 NDAs and over 10 marketed products, including Lipitor® and Neurontin®. Dr. Wierenga earned his B.A. in chemistry from Hope College, his Ph.D. in chemistry from Stanford University and an American Cancer Society Postdoctoral Fellowship at Stanford.

D. Bruce Campbell, Ph.D. became our Senior Vice President, International Development in January 2003 after having served as our Senior Vice President of Development since January 2001. He joined us as Vice President, Development in February 1998. In his current capacity, he is responsible for our international drug development efforts. He joined us after 27 years at Servier United Kingdom, a subsidiary of an international pharmaceutical company based in France, where he served as Research and Development Director from 1972 to 1991 and Director of International Scientific Affairs from 1991 to 1997 and was involved in the development of a wide range of drugs and vaccines. Dr. Campbell is a visiting Professor in Pharmacology at Guys and Kings College London. He is recognized as one of the experts on the regulatory aspects of kinetics and toxicology in new drug development and has published over 100 papers. He is a Fellow of the Royal Society of Chemistry and received his B.S. in biochemistry from the University of Bangor in North Wales and his Ph.D. in biochemistry from Guys Hospital Medical School, London University.

Margaret Valeur-Jensen, J.D., Ph.D. became our Senior Vice President, General Counsel and Corporate Secretary in January 2000 after having joined us as Vice President, General Counsel and Secretary in October 1998. She is responsible for all of our corporate and patent law practices, serves as Corporate Secretary and is a member of the senior management committee. From 1995 to 1998, she served as Associate General Counsel, Licensing and Business Law of Amgen. From 1991 to 1995, she served first as Corporate Counsel and later as Senior Counsel, Licensing for Amgen. Prior to joining Amgen, she practiced law at Davis Polk & Wardwell, a leading corporate law firm. She earned a J.D. degree from Stanford University, a Ph.D. in biochemistry and molecular biology from Syracuse University and was a Post-Doctoral Fellow at Massachusetts General Hospital and Harvard Medical School.

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Robert J. Little joined us as Senior Vice President, Commercial Operations in June 2003 and is responsible for building and managing our sales and marketing functions. Before joining us, Mr. Little was at Pharmacia Inc. for 18 years where his most recent position was Group Vice President, Diversified Products. His responsibilities included managing Pharmacia s Diversified Products business, as well as forming a new business group merging pricing, reimbursement and health outcome groups into a global unit focused on current industry issues, pricing and drug values. Mr. Little previously held a number of positions within Pharmacia including Group Vice President Specialty Products, President and Managing Director of Pharmacia in Milan, Italy, President Pharmacia & UpJohn Canada and President Pharmacia Inc. Canada. Prior to joining Pharmacia he held positions at Adria Laboratories and Miles Laboratories/ Bayer A.G. in the U.K., Italy and the United States. He received a degree in economics and finance from the West London Business School, Ealing Technical College.

Joseph A. Mollica, Ph.D. has served on our Board of Directors since June 1997 and became Chairman of the Board in April 1998. Since February 1994, he has served as the Chairman of the Board of Directors, President and Chief Executive Officer of Pharmacopeia, Inc., a biopharmaceutical company focusing on combinatorial chemistry, high throughput discovery, molecular modeling and bioinformatics. From 1987 to December 1993, he served as Vice President, Medical Products of DuPont Company and then as President and Chief Executive Officer of DuPont Merck Pharmaceutical Company from 1991 to 1993. At Ciba-Geigy, where he was employed from 1966 to 1986, he served in a variety of positions of increasing responsibility, rising to Senior Vice President of Ciba-Geigy s Pharmaceutical Division. He is currently on the Board of Directors of Impath, Inc., Genencor International, Inc. and Pharmacopeia. He received his B.S. from the University of Rhode Island and his M.S. and Ph.D. from the University of Wisconsin and Sc.D.h.c. from the University of Rhode Island.

W. Thomas Mitchell was appointed to our Board of Directors in November 2002. He is the former Chairman of the Board and Chief Executive Officer of Genencor International. Under his guidance, Genencor s revenues grew from under $30 million to over $325 million. In addition, he successfully managed the acquisition and integration of three major businesses to build the global enterprise that is now Genencor. Mr. Mitchell has participated in a number of important policy initiatives including the 1999 federal executive order that created the national bioenergy initiative. Mr. Mitchell also served as a member of the Governor s Council on Biotechnology in California, which was responsible for helping to improve the state s competitiveness in the mid-1990 s. He also served on the Advisory Boards of the Chemical Engineering School at Cornell University and the University of Iowa s School of Engineering. He received his B.S. in chemical engineering from Drexel University. He also completed the Executive Development Program at the University of Michigan.

Richard F. Pops was elected to our Board of Directors in April 1998. Mr. Pops has been Chief Executive Officer of Alkermes, Inc. since February 1991. Under his leadership, Alkermes has grown from a privately held company with 25 employees to a publicly traded, emerging pharmaceutical company with more than 400 employees in multiple locations in the United States. He currently serves on the Board of Directors of the following entities: Alkermes; Reliant Pharmaceuticals, LLC; CombinatoRx, Inc.; the Biotechnology Industry Organization, where he is the current Chairman; the Massachusetts Biotechnology Council; the New England Healthcare Institute and Harvard Medical School Board of Fellows. He also serves as Chair for the Harvard Medical School Advisory Council for Biological Chemistry & Molecular Pharmacology. He received a B.A. in economics from Stanford University in 1983.

Stephen A. Sherwin, M.D. was elected to our Board of Directors in April 1999. Since March 1990, Dr. Sherwin has served as Chief Executive Officer and Director of Cell Genesys, Inc., a biotechnology company. In March 1994, he was elected as Chairman of the Board of Cell Genesys. From 1983 to 1990, Dr. Sherwin held various positions at Genentech, most recently as Vice President of Clinical Research. Prior to 1983, Dr. Sherwin held various positions on the staff of the National Cancer Institute. Dr. Sherwin also serves as Chairman of the Board of Ceregene, Inc., a majority-owned subsidiary of Cell Genesys, and as a Director of Rigel Pharmaceuticals, Inc. Dr. Sherwin holds a B.A. in biology from Yale and an M.D. from Harvard Medical School.

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Lawrence Steinman, M.D. is one of our academic co-founders. He was elected to our Board of Directors in January 2001. He received his M.D. from Harvard University in 1973 and has served more than 20 years at Stanford University School of Medicine as a Professor of Neurology and Pediatrics, as well as serving as Professor of Immunology at the Weizmann Institute. Dr. Steinman is Chair of the Interdepartmental Program in Immunology at Stanford. Dr. Steinman became Chief Scientist, Neuroimmunology and a member of our Founding Board of Scientific and Medical Advisors and our Executive Committee in September 1992. He has been honored with the Weir Mitchell Award of the American Academy of Neurology and the Senator Jacob Javits Neuroscience Investigators Award from the United States Congress as well as The Dr. Friedrich Sasse Award for Outstanding Contributions in Immunology from the Free University of Berlin. He is Board Certified with the American Board of Psychiatry and Neurology and holds seven different patents in the United States, Europe and Australia.

Wylie W. Vale, Ph.D. is one of our academic co-founders, a member of our Board of Directors, Chief Scientific Advisor, Neuroendocrinology, and a member of our Founding Board of Scientific and Medical Advisors. Dr. Vale was elected to our Board of Directors in September 1992. He is the Helen McLoraine Professor of Molecular Neuroscience and Head of The Clayton Foundation Laboratories for Peptide Biology at The Salk Institute for Biological Studies, where he is currently Chairman of the Faculty and a member of the Board of Trustees. He is also an Adjunct Professor of Medicine at the University of California, San Diego. Dr. Vale is recognized for his work on the molecular, pharmacological and biomedical characterization of neuroendocrine peptides, growth factors and their receptors. In recognition of his discoveries, he has received numerous awards and is a member of the National Academy of Arts and Sciences, the Institute of Medicine and the National Academy of Sciences. He is a past President of the American Endocrine Society and is the current President of the International Society of Endocrinology. Dr. Vale received a B.A. in biology from Rice University and a Ph.D. in physiology and biochemistry from the Baylor College of Medicine.

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UNDERWRITERS

Under the terms and subject to the conditions contained in an underwriting agreement dated the date of this prospectus supplement, the underwriters named below, for whom Morgan Stanley & Co. Incorporated, Merrill Lynch, Pierce, Fenner & Smith Incorporated, Deutsche Bank Securities Inc., UBS Securities LLC, Bear, Stearns & Co. Inc., CIBC World Markets Corp., Banc of America Securities LLC and Credit Suisse First Boston LLC are acting as representatives, have severally agreed to purchase, and we have agreed to sell to them the number of shares indicated below:

Name	Number of Shares
Morgan Stanley & Co. Incorporated	
Merrill Lynch, Pierce, Fenner & Smith Incorporated	
Deutsche Bank Securities Inc.	
UBS Securities LLC	
Bear, Stearns & Co. Inc.	
CIBC World Markets Corp.	
Banc of America Securities LLC	
Credit Suisse First Boston LLC	
Total	3,000,000

The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus supplement and the accompanying prospectus are subject to the approval of various legal matters by their counsel and to other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus supplement and the accompanying prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters over-allotment option described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the public offering price listed on the cover page of this prospectus supplement and part to dealers at a price that represents a concession not in excess of $ a share under the public offering price. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to an aggregate of 450,000 additional shares of common stock at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the shares of common stock offered by this prospectus supplement and the accompanying prospectus. To the extent the option is exercised, each underwriter will become obligated, subject to various conditions, to purchase approximately the same percentage of the additional shares of common stock as the number listed next to the underwriter s name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

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The following table provides information regarding the amount of the discount to be paid by us to the underwriters:

		Total	
	Per Share	Without Over-Allotment	With Over-Allotment
Underwriting discounts and commissions to be paid by us	$	$	$

The estimated offering expenses payable by us, in addition to the underwriting discounts and commissions, are approximately $400,000, which includes legal, accounting and printing costs and various other fees associated with registering and listing the common stock.

The underwriters have informed us that they do not intend sales to discretionary accounts to exceed five percent of the total number of shares of common stock offered by them.

We and our directors and executive officers have agreed that, without the prior written consent of each of Morgan Stanley & Co. Incorporated and Merrill Lynch, Pierce, Fenner & Smith Incorporated on behalf of the underwriters, we and they will not, during the period ending 90 days after the date of this prospectus supplement:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock; or

- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock;

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. The restrictions described in this paragraph do not apply to:

- the sale of shares to the underwriters;

- the issuance by us of shares of common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of this prospectus supplement;

- the grant of options to purchase common stock under our employee benefit plans;

- transfers to immediate family members or to a trust the sole beneficiaries of which are the transferor and/or its immediate family members, provided that the recipient of the shares agrees to be subject to the restrictions described in this paragraph; or

- transactions by any person other than us relating to shares of common stock or other securities acquired in open market transactions after the completion of the offering of the shares.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the over-allotment option. The underwriters can close out a covered short sale by exercising the over-allotment option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the over-allotment option. The underwriters may also sell shares in excess of the over-allotment option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. As an additional means of facilitating the offering, the underwriters may bid for, and purchase, shares of common

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stock in the open market to stabilize the price of the common stock. The underwriting syndicate may also reclaim selling concessions allowed to an underwriter or a dealer for distributing the common stock in the offering, if the syndicate repurchases previously distributed common stock to cover syndicate short positions or to stabilize the price of the common stock. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. The underwriters are not required to engage in these activities, and may end any of these activities at any time.

Merrill Lynch will be facilitating Internet distribution for this offering to certain of its Internet subscription customers. Merrill Lynch intends to allocate a limited number of shares for sale to its online brokerage customers. An electronic prospectus is available on the Website maintained by Merrill Lynch. Other than the prospectus in electronic format, the information on the Merrill Lynch Website relating to this offering is not a part of this prospectus supplement.

From time to time, certain of the underwriters have provided, and continue to provide, investment banking services to us.

We and the underwriters have agreed to indemnify each other against specified liabilities, including liabilities under the Securities Act of 1933, as amended.

LEGAL MATTERS

Latham & Watkins LLP, San Diego, California will pass upon the validity of the common stock offered under this prospectus supplement and the accompanying prospectus and other legal matters. Davis Polk & Wardwell, Menlo Park, California, is representing the underwriters.

EXPERTS

Ernst & Young LLP, independent auditors, have audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2002, as set forth in their report, which is incorporated by reference in this prospectus supplement and the accompanying prospectus. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP s report, given on their authority as experts in accounting and auditing.

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PROSPECTUS

Neurocrine Biosciences, Inc.

$200,000,000

PREFERRED STOCK

COMMON STOCK

We may offer and sell from time to time in one or more classes or series and in amounts, at prices and on the terms that we will determine at the time of offering, with an aggregate initial offering price of up to $200,000,000:

- shares of preferred stock; and
- shares of common stock.

We will provide the specific terms of these securities in supplements to this prospectus. You should read this prospectus and any supplement carefully before you invest.

Our common stock is quoted and traded on the Nasdaq National Market under the symbol NBIX.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

We will sell these securities directly to our stockholders or to purchasers or through agents on our behalf or through underwriters or dealers as designated from time to time. If any agents or underwriters are involved in the sale of any of these securities, the applicable prospectus supplement will provide the names of the agents or underwriters and any applicable fees, commissions or discounts.

June 12, 2003

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You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate as of the date on the front cover of this prospectus only. Our business, financial condition, results of operations and prospects may have subsequently changed.

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Whenever we refer to Neurocrine, we, our or us in this prospectus, we mean Neurocrine Biosciences, Inc. and its consolidated subsidiaries unless the context suggests otherwise. When we refer to you or yours, we mean the holders of the applicable series of securities.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a shelf registration process. Under this shelf registration process, we may sell any combination of the securities described in this prospectus in one or more offerings up to a total dollar amount of $200,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer to sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. To the extent that any statement that we make in a prospectus supplement is inconsistent with statements made in this prospectus, the statements made in this prospectus will be deemed modified or superseded by those made in a prospectus supplement. You should read both this prospectus and any prospectus supplement together with additional information described under the next heading, Where You Can Find More Information.

WHERE YOU CAN FIND MORE INFORMATION

Neurocrine is subject to the informational requirements of the Securities Exchange Act of 1934, as amended, and files annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any reports, proxy statements and other information we file at the SEC s public reference room at 450 Fifth Street, N.W., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room. You may also access filed documents at the SEC s web site at www.sec.gov.

We are incorporating by reference some information about us that we file with the SEC. We are disclosing important information to you by referencing those filed documents. Any information that we reference this way is considered part of this prospectus. The information in this prospectus supersedes information incorporated by reference that we have filed with the SEC prior to the date of this prospectus, while information that we file with the SEC after the date of this prospectus that is incorporated by reference will automatically update and supersede this information.

We incorporate by reference the following documents we have filed, or may file, with the SEC:

Neurocrine s Annual Report on Form 10-K for its fiscal year ended December 31, 2002;

Neurocrine s Quarterly Report on Form 10-Q for its quarterly period ended March 31, 2003;

Neurocrine s Current Report on Form 8-K filed on April 9, 2003;

Neurocrine s Current Report on Form 8-K filed on June 3, 2003;

the description of Neurocrine s common stock contained in the Registration Statement on Form 8-A filed on April 3, 1996; and

all documents filed by Neurocrine with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and before termination of this offering.

You may request a free copy of any of the documents incorporated by reference in this prospectus by writing or telephoning us at the following address:

Neurocrine Biosciences, Inc.

10555 Science Center Drive
San Diego, California 92121
(858) 658-7600

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FORWARD-LOOKING STATEMENTS

Any statements in this prospectus about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and are forward-looking statements. You can identify these forward-looking statements by the use of words or phrases such as believe, may, could, will, estimate, continue, anticipate, intend, seek, plan, expect, should or would. Among the facto results to differ materially from those indicated in the forward-looking statements are risks and uncertainties associated with our development programs and business and finances including, but not limited to, the risk that our drug candidates will not successfully proceed through clinical trials or that later stage clinical trials will not show that they are effective in treating humans; adverse determinations by regulatory and governmental authorities; dependence on corporate collaborators who could terminate their relationships with us at any time; uncertainties relating to patent protection and intellectual property rights of third parties; the impact of competitive products and technological changes; our ability to raise additional capital and the cost of the capital; and other material risks described under the heading Risk Factors in our quarterly report on Form 10-Q for the quarterly period ended March 31, 2003.

Although we believe that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee future results, events, levels of activity, performance or achievement. We undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.

NEUROCRINE

We develop and intend to commercialize drugs for the treatment of neurologic and endocrine system-related diseases and disorders. Our product candidates address some of the largest pharmaceutical markets in the world, including insomnia, anxiety, depression, diabetes mellitus, multiple sclerosis, irritable bowel syndrome, eating disorders, pain, auto immunity and certain female and male health disorders. We currently have 16 programs in various stages of research and development, including seven programs in clinical development. Our lead clinical development program is a drug for the treatment of insomnia currently being evaluated in Phase III clinical trials.

While we independently develop the majority of our product candidates, we have entered into collaborations for seven of our 16 programs. We currently have product development collaborations with Pfizer, GlaxoSmithKline and Wyeth.

Our headquarters are located at 10555 Science Center Drive, San Diego, California 92121. Our telephone number is (858) 658-7600.

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RATIO OF EARNINGS TO FIXED CHARGES AND PREFERRED STOCK DIVIDENDS

Our ratios of earnings to fixed charges and preferred stock dividends are as follows for the periods indicated:

	Three Months Ended March 31,		Year Ended December 31,				
	2003	2002	2002	2001	2000	1999	1998
Ratio of Earnings to Fixed Charges and Preferred Stock Dividends							

For the years ended December 31, 2002, 2001, 2000, 1999 and 1998 and the three-month period ended March 31, 2003 and 2002, our earnings were insufficient to cover fixed charges by $813,000, $746,000, $847,000, $914,000, $746,000, $255,000 and $202,000, respectively. Fixed charges consist of interest expense, including capitalized interest, amortized premiums, discounts and capitalized expenses related to indebtedness and estimated interest included in rental expense. For the periods indicated above, we had no outstanding shares of preferred stock with required dividend payments.

USE OF PROCEEDS

Unless otherwise indicated in the prospectus supplement, we intend to use the net proceeds from the sale of the securities under this prospectus for general corporate purposes, including clinical trials, research and development expenses, general and administrative expenses, manufacturing expenses, and potential acquisitions of companies and technologies that complement our business. When a particular series of securities is offered, the prospectus supplement relating thereto will set forth our intended use for the net proceeds we receive from the sale of the securities. Pending the application of the net proceeds, we expect to invest the proceeds in short-term, interest-bearing instruments or other investment-grade securities.

DESCRIPTION OF CAPITAL STOCK

General

This prospectus describes the general terms of our capital stock. For a more detailed description of these securities, you should read the applicable provisions of Delaware law and our certificate of incorporation and bylaws. When we offer to sell a particular series of these securities, we will describe the specific terms of the series in a supplement to this prospectus. Accordingly, for a description of the terms of any series of securities, you must refer to both the prospectus supplement relating to that series and the description of the securities described in this prospectus. To the extent the information contained in the prospectus supplement differs from this summary description, you should rely on the information in the prospectus supplement.

Under our certificate of incorporation, the total number of shares of all classes of stock that we have authority to issue is 55,000,000, consisting of 5,000,000 shares of preferred stock, par value $0.001 per share, and 50,000,000 shares of common stock, par value $0.001 per share.

Common Stock

As of June 4, 2003, we had 31,362,536 shares of our common stock outstanding held of record by approximately 98 stockholders.

The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, and do not have cumulative voting rights. Subject to preferences that may be applicable to any of our outstanding preferred stock, the holders of common stock are entitled to receive ratably the dividends, if any, that may be declared from time to time by our board of directors out of funds legally available for such dividends. In the event of a liquidation, dissolution or winding up of

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Neurocrine, the holders of our common stock would be entitled to share ratably in all assets remaining after payment of liabilities and the satisfaction of any liquidation preferences granted to the holders of any outstanding shares of preferred stock. Holders of our common stock have no preemptive rights and no conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to our common stock. All the outstanding shares of common stock are, and the shares offered by this prospectus, when issued and paid for, will be validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of any shares of our outstanding preferred stock.

Preferred Stock

We currently have no outstanding shares of preferred stock. Under our certificate of incorporation, our board of directors is authorized to issue shares of our preferred stock from time to time, in one or more classes or series, without stockholder approval. Prior to the issuance of shares of each series, the board of directors is required by the General Corporation Law of the State of Delaware, known as the DGCL, and our certificate of incorporation to adopt resolutions and file a certificate of designation with the Secretary of State of the State of Delaware. The certificate of designation fixes for each class or series the designations, powers, preferences, rights, qualifications, limitations and restrictions, including the following:

- the number of shares constituting each class or series;
- voting rights;
- rights and terms of redemption, including sinking fund provisions;
- dividend rights and rates;
- dissolution;
- terms concerning the distribution of assets;
- conversion or exchange terms;
- redemption prices; and
- liquidation preferences.

All shares of preferred stock offered by this prospectus will, when issued, be fully paid and nonassessable and will not have any preemptive or similar rights. Our board of directors could authorize the issuance of shares of preferred stock with terms and conditions that could have the effect of discouraging a takeover or other transaction that might involve a premium price for holders of the shares or that holders might believe to be in their best interests.

We will describe in a prospectus supplement relating to the class or series of preferred stock being offered the following terms:

- the title and stated value of the preferred stock;
- the number of shares of the preferred stock offered, the liquidation preference per share and the offering price of the preferred stock;
- the dividend rate(s), period(s) or payment date(s) or method(s) of calculation applicable to the preferred stock;
- whether dividends are cumulative or non-cumulative and, if cumulative, the date from which dividends on the preferred stock will accumulate;
- the procedures for any auction and remarketing, if any, for the preferred stock;

the provisions for a sinking fund, if any, for the preferred stock;

the provision for redemption, if applicable, of the preferred stock;

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any listing of the preferred stock on any securities exchange;

the terms and conditions, if applicable, upon which the preferred stock will be convertible into common stock, including the conversion price or manner of calculation and conversion period;

voting rights, if any, of the preferred stock;

whether interests in the preferred stock will be represented by depositary shares;

a discussion of any material or special United States federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights upon the liquidation, dissolution or winding up of our affairs;

any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the class or series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of our affairs; and

any other specific terms, preferences, rights, limitations or restrictions of the preferred stock.

Unless we specify otherwise in the applicable prospectus supplement, the preferred stock will rank, relating to dividends and upon our liquidation, dissolution or winding up:

senior to all classes or series of our common stock and to all of our equity securities ranking junior to the preferred stock;

on a parity with all of our equity securities the terms of which specifically provide that the equity securities rank on a parity with the preferred stock; and

junior to all of our equity securities the terms of which specifically provide that the equity securities rank senior to the preferred stock.

The term equity securities does not include convertible debt securities.

Anti-Takeover Provisions

As a corporation organized under the laws of the State of Delaware, we are subject to Section 203 of the DGCL, which restricts our ability to enter into business combinations with an interested stockholder or a stockholder owning 15% or more of our outstanding voting stock, or that stockholder s affiliates or associates, for a period of three years. These restrictions do not apply if:

prior to becoming an interested stockholder, our board of directors approves either the business combination or the transaction in which the stockholder becomes an interested stockholder;

upon consummation of the transaction in which the stockholder becomes an interested stockholder, the interested stockholder owns at least 85% of our voting stock outstanding at the time the transaction commenced, subject to exceptions; or

on or after the date a stockholder becomes an interested stockholder, the business combination is both approved by our board of directors and authorized at an annual or special meeting of our stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock not owned by the interested stockholder.

Some provisions of our certificate of incorporation and bylaws could also have anti-takeover effects. These provisions:

provide for a board comprised of three classes of directors with each class serving a staggered three-year term;

authorize the issuance of preferred stock in one or more series; and

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require the approval of at least two-thirds of the outstanding voting stock to amend certain provisions of our certificate of incorporation and bylaws.

These provisions are intended to enhance the likelihood of continuity and stability in the composition of the policies formulated by the board of directors. These provisions are also intended to discourage some tactics that may be used in proxy fights.

Stockholder Rights Plan

On April 10, 1997, our board of directors adopted a stockholder rights plan, which was amended and restated on January 11, 2002. Under the rights plan, a dividend of one preferred share purchase right was declared for each outstanding share of our common stock. The common stock currently trades with a right to purchase Series A Participating preferred stock. A preferred share purchase right will be attached to each share of common stock issued during the term of the rights plan. Each right entitles the holder to buy one one-thousandth of a share of our Series A preferred stock at an exercise price of $350.00, subject to anti-dilution adjustments, upon the triggering event of a person acquiring, or making a tender or exchange offer for, 15% or more of our outstanding common stock. Each right entitles its holder, other than the person acquiring 15% or more of the outstanding common stock, to purchase shares of our common stock with a market value of twice the right s exercise price. In addition, if a company acquires us in a merger or other business combination, or if we sell more than 50% of our consolidated assets or earning power, these rights will entitle our stockholders, other than the acquirer, to purchase, for the exercise price, shares of the common stock of the acquiring company having a market value of two times the exercise price. At any time prior to these events, the board of directors may redeem the rights at one cent per right.

The rights plan is intended to protect stockholders in the event of an unsolicited attempt to acquire us. The right is transferred automatically with the transfer of the common stock until separate rights certificates are distributed upon the occurrence of certain events. The rights plan could have the effect of delaying, deferring or preventing a person from acquiring us or accomplishing a change in control of the board of directors. This description of the rights plan is intended as a summary only and is qualified in its entirety by reference to the amended and restated rights agreement dated as of January 11, 2002 between Neurocrine and American Stock Transfer & Trust Company. To obtain a copy of the amended and restated rights agreement see the section of this prospectus entitled Where You Can Find More Information.

Classified Board of Directors

The certificate of incorporation provides for the board of directors to be divided into three classes of directors, with each class as nearly equal in number as possible, serving staggered three-year terms. As a result, approximately one-third of the board of directors will be elected each year. The classified board provision will help to assure the continuity and stability of the board of directors and the business strategies and policies of Neurocrine as determined by the board of directors. The classified board provision could have the effect of discouraging a third party from making a tender offer or attempting to obtain control of us. In addition, the classified board provision could delay stockholders who do not agree with the policies of the board of directors from removing a majority of the board of directors for two years.

Special Meetings

The bylaws also provide that special meetings of stockholders may be called only by the board of directors, its chairman, the president or by one or more stockholders holding 10% of the votes at that meeting.

Number of Directors; Removal

The bylaws provide that the board of directors will consist of seven members. The bylaws provide that directors may be removed with or without cause by the affirmative vote of holders of a majority of the total voting power of all outstanding securities.

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Transfer Agent and Registrar

The Transfer Agent and Registrar for our common stock is American Stock Transfer & Trust Corporation.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities (1) through underwriters or dealers, (2) through agents and/or (3) directly to one or more purchasers. We may distribute the securities from time to time in one or more transactions at:

a fixed price or prices, which may be changed;

market prices prevailing at the time of sale;

prices related to the prevailing market prices; or

negotiated prices.

We may solicit directly offers to purchase the securities being offered by this prospectus. We may also designate agents to solicit offers to purchase the securities from time to time. We will name in a prospectus supplement any agent involved in the offer or sale of our securities.

If we utilize a dealer in the sale of the securities being offered by this prospectus, we will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If we utilize an underwriter in the sale of the securities being offered by this prospectus, we will execute an underwriting agreement with the underwriter at the time of sale and we will provide the name of any underwriter in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we, or the purchasers of securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and the underwriter may compensate those dealers in the form of discounts, concessions or commissions.

We will provide in the applicable prospectus supplement any compensation we pay to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof.

The securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involves the sale by persons participating in the offering of more securities than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

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The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for Neurocrine by Latham & Watkins LLP, San Diego, California.

EXPERTS

Ernst & Young LLP, independent auditors, have audited Neurocrine s consolidated financial statements included in its Annual Report on Form 10-K for the year ended December 31, 2002, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Neurocrine s financial statements are incorporated by reference in reliance on Ernst & Young LLP s report, given on their authority as experts in accounting and auditing.

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