As filed with the Securities and Exchange Commission on November 22, 2000

Registration No. 333-47252

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

AMENDMENT NO. 2
TO
FORM S-3

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

NEUROCRINE BIOSCIENCES, INC.
(Exact name of registrant as specified in its charter)

Delaware	10555 Science Center Drive	33-0525145
(State of incorporation)	San Diego, California 92121	(I.R.S. Employer Identification No.)
	(858) 658-7600	

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Gary A. Lyons
President, Chief Executive Officer and Director
Neurocrine Biosciences, Inc.
10555 Science Center Drive
San Diego, California 92121
(858) 658-7600
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

John M. Newell, Esq. Andrew S. Williamson, Esq. Robert W. Phillips, Esq. Latham & Watkins 505 Montgomery Street, Suite 1900 San Francisco, California 94111-2562 (415) 391-0600	Peter T. Healy, Esq. Steven L. Pickering, Esq. Natasha L. Ell, Esq. O'Melveny & Myers LLP 275 Battery Street, Suite 2600 San Francisco, California 94111-3305 (415) 984-8700

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this Registration Statement.

If the only securities being registered on this Form are to be offered pursuant to dividend or interest reinvestment plans, please check the following box. [_]

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended (the "Securities Act"), other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. [_]

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. [_]

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. [_]

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. [_]

The Registrant hereby amends this Registration Statement on such date or

dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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EXPLANATORY NOTE

This registration statement contains two forms of prospectus front cover page: (a) one to be used in connection with an offering in the United States and Canada and (b) one to be used in connection with a concurrent offering outside of the United States and Canada. The U.S./Canadian prospectus and the international prospectus are otherwise identical in all respects. The international version of the front cover page is included immediately before Part II of this registration statement.

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

SUBJECT TO COMPLETION, DATED NOVEMBER 22, 2000

[LOGO OF NEUROCRINE BIOSCIENCES]

3,000,000 Shares
Common Stock

Neurocrine Biosciences, Inc. is offering 3,000,000 shares of its common stock. Neurocrine Biosciences, Inc.'s common stock is traded on the Nasdaq National Market under the symbol "NBIX." The last reported sale price of the common stock on the Nasdaq National Market on November 21, 2000 was $33.13 per share.

Investing in our common stock involves risks.
See "Risk Factors" beginning on page 5.

	Per Share	Total
Public Offering Price	$	$
Underwriting Discounts and Commissions	$	$
Proceeds to Neurocrine Biosciences, Inc.	$	$

The Securities and Exchange Commission and state securities regulators have not approved or disapproved these securities, or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Neurocrine Biosciences, Inc. has granted the underwriters a 30-day option to purchase up to an additional 450,000 shares of common stock to cover over-allotments.

Robertson Stephens Salomon Smith Barney

The date of this prospectus is , 2000.

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PROSPECTUS SUMMARY

You should read the following summary together with the more detailed information in this prospectus, including risk factors regarding our company and the common stock being sold in this offering.

Our Company

Neurocrine Biosciences, Inc. is a product-based biopharmaceutical company focused on neurologic and endocrine diseases and disorders. Our product candidates address some of the largest pharmaceutical markets in the world including insomnia, anxiety, depression, cancer and diabetes. We currently have 15 programs in various stages of research and development, including four programs in clinical development and four programs in advanced preclinical development which we expect to progress into human clinical trials in the near future. While we independently develop the majority of our product candidates, we utilize collaborators in four of our 15 programs, including Janssen Pharmaceutica, a subsidiary of Johnson & Johnson, Wyeth-Ayerst, a division of American Home Products, Taisho Pharmaceutical and Eli Lilly.

Our Product Candidates

Our four product candidates in clinical trials address insomnia, cancer, multiple sclerosis and diabetes:

Insomnia. Insomnia is a prevalent neurological disorder in the United States, with up to 62% of the adult population reporting trouble sleeping a few nights per week or more, according to the National Sleep Foundation. Worldwide sedative sales in 1999 totaled over $1.1 billion. However, most sedatives have side effects such as amnesia and hangover-type effects, especially when combined with alcohol. As a result, we believe there is a significant unmet medical need for an improved sedative.

We are developing NBI-34060, our most advanced drug candidate, for the treatment of insomnia. We completed an initial placebo-controlled efficacy trial, known as a Phase II clinical trial, in 228 subjects in November 1999. Our results demonstrated that the compound was safe and effective in helping subjects with insomnia to fall asleep rapidly without adverse side effects as compared to a placebo. The average time to fall asleep, the primary clinical goal, was 16 minutes with the drug as compared to 34 minutes with a placebo. These results were highly statistically significant and clinically meaningful.

Based on the positive results from this Phase II trial, we have initiated multiple Phase II trials, and we expect to enroll an additional 300 subjects by year-end. We are currently designing large-scale efficacy trials, known as Phase III trials, which are required for commercial approval. We expect these pivotal trials to begin in the second half of 2001.

Brain Cancer. Our drug candidate NBI-3001 treats malignant glioma, a very aggressive form of brain cancer. The Food and Drug Administration has awarded fast track designation for this drug candidate. We completed a safety and efficacy trial in February 2000, and found that this compound was safe and had acceptable tolerability. In addition, of the 27 patients who completed therapy, 63% showed complete or partial reduction in tumor size. We plan to initiate an additional trial in the fourth quarter of 2000 to better establish dosing, safety and efficacy. We also plan to initiate a Phase III trial in mid-2001.

Multiple Sclerosis. We designed NBI-5788, our multiple sclerosis compound, utilizing proprietary technology to treat autoimmune diseases, in which the body's own immune system attacks normal tissue. We have completed safety and preliminary efficacy trials in patients with a recurring form of multiple sclerosis, and we plan to initiate a confirmatory efficacy trial to determine the optimal dose and frequency of administration.

Diabetes. Utilizing our proprietary technology to treat autoimmune diseases, we designed a drug candidate, NBI-6024, to treat a type of diabetes. We recently completed a safety trial in 20 diabetic patients which showed that our compound was safe and well tolerated. We have a safety trial currently underway with an additional 30 patients involving multiple doses, and we plan to initiate several Phase II efficacy trials in 2001. We recently entered into a worldwide development collaboration for this compound with Taisho Pharmaceutical.

In addition to our clinical programs, we have four programs in advanced preclinical development. We expect these programs to progress into human clinical trials in the near future:

Depression and Anxiety--Janssen. We have developed compounds that are blockers of a brain chemical called corticotropin-releasing factor, which has been shown to be involved in both depression and anxiety. We have strong intellectual property and collaborations with experts in this area. We licensed our first corticotropin-releasing factor program to Janssen Pharmaceutica, which then demonstrated efficacy in depression in a 1998 trial. Due to adverse side effects, Janssen decided to discontinue development of its lead compound in favor of another of our earlier-stage backup compounds. We believe Janssen will move this program forward with the clinical development of the backup compound shortly.

Depression and Anxiety--Neurocrine. We are also independently pursuing a second corticotropin-releasing factor program in which we expect to enter into clinical trials to assess safety in late 2000 and early 2001.

Additional Cancers. We believe our NBI-3001 compound discussed above may have therapeutic potential in cancers in addition to brain cancer. We plan to initiate a clinical trial in early 2001 to investigate the safety and preliminary efficacy of our drug in kidney cancer and some types of lung cancer.

Prostate Cancer and Endometriosis. Gonadotropin-releasing hormone is a hormone that regulates sex steroid production. Researchers have linked it to hormone-dependent diseases such as prostate cancer and a common uterine disease known as endometriosis. We have developed blockers of this hormone, and expect to select a final development compound by the end of 2000. We plan to initiate clinical safety trials in the second half of 2001.

We also have seven additional research programs in areas such as neurodegenerative disease, gastrointestinal disorders, obesity, sleep disorders and eating disorders. We believe that these research programs will supply clinical development candidates in the future.

Our Business Strategy

Our business strategy has six major components:

- pursue a large and diversified product portfolio to mitigate clinical and technical risk;
- target market opportunities with clear clinical and regulatory paths;
- collaborate with global pharmaceutical companies for development, regulatory and commercialization expertise while retaining North American commercial participation;
- selectively acquire complementary drug candidates in our areas of expertise;
- collaborate with leading platform technology companies to supplement our research capabilities; and
- outsource capital intensive, non-strategic activities to focus on our core discovery and development programs.

Other Information

We have no FDA-approved products, and any of our programs may be delayed or terminated for any number of reasons. To date, we have not generated any revenues from the sale of products, and we do not expect to generate any product revenues in the foreseeable future. Since our inception, we have incurred significant net losses, including net losses of $19.4 million in the first nine months of 2000. As of September 30, 2000, we had an accumulated deficit of $61.0 million.

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

THE OFFERING

The following summarizes our offering of common stock. Unless otherwise noted, we are presenting all information in this prospectus as if the underwriters do not exercise the over-allotment option.

Common stock offered by Neurocrine Biosciences	3,000,000 shares
Common stock to be outstanding after the offering	25,066,248 shares
Use of proceeds	Working capital and general corporate purposes.
Nasdaq National Market symbol	"NBIX"

The number of shares of our common stock to be outstanding after the offering is based on 22,066,248 shares outstanding as of October 31, 2000. Unless otherwise stated, all share information in this prospectus excludes:

- 4,179,466 shares of common stock issuable upon exercise of options and warrants outstanding on October 31, 2000 at a weighted average exercise price of $12.14; and
- 341,409 shares of common stock available for awards under our stock incentive plans as of October 31, 2000.

Summary Consolidated Financial Data
(in thousands, except per share 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, and our consolidated financial statements and related notes incorporated by reference in this prospectus.

	Year Ended December 31,					Nine Months Ended September 30,	
	1995	1996	1997	1998	1999	1999	2000
Statement of Operations Data:							
Revenues:							
Sponsored research and development	$ 3,000	$ 9,092	$14,985	$ 8,751	$ 12,171	$ 9,760	$ 4,943
Sponsored research and development from related party	--	--	--	3,610	491	501	--
Milestones and license fees	2,750	9,000	10,250	2,500	3,000	1,500	5,050
Grant income and other revenues	356	1,124	909	1,176	1,129	831	1,050
Total revenues	6,106	19,216	26,144	16,037	16,791	12,592	11,043
Operating expenses:							
Research and development	7,740	12,569	18,758	21,803	29,169	21,893	28,404
General and administrative	2,728	3,697	5,664	6,594	7,476	5,587	6,930
Write-off of acquired in-process research and development and licenses	--	--	--	4,910	--	--	--
Total operating expenses	10,468	16,266	24,422	33,307	36,645	27,480	35,334
Income (loss) from operations	(4,362)	2,950	1,722	(17,270)	(19,854)	(14,888)	(24,291)
Interest income, net	839	2,598	3,931	4,000	2,851	2,040	4,293
Other income	177	574	818	504	1,066	889	973
Equity in NPI net losses and other adjustments, net	--	--	(1,130)	(7,188)	(885)	(1,174)	(47)
Net income (loss) before income taxes	(3,346)	6,122	5,341	(19,954)	(16,822)	(13,133)	(19,072)
Income taxes	--	248	214	1	--	--	302
Net income (loss)	$(3,346)	$ 5,874	$ 5,127	$(19,955)	$(16,822)	$(13,133)	$(19,374)
Earnings (loss) per share:							
Basic	$ (0.29)	$ 0.39	$ 0.30	$ (1.10)	$ (0.88)	$ (0.69)	$ (0.88)
Diluted	$ (0.29)	$ 0.36	$ 0.28	$ (1.10)	$ (0.88)	$ (0.69)	$ (0.88)
Shares used in calculation of earnings (loss) per share:							
Basic	11,684	14,971	16,930	18,141	19,072	18,975	21,900
Diluted	11,684	16,127	18,184	18,141	19,072	18,975	21,900

	September 30, 2000	
	Actual	As Adjusted(1)
Balance Sheet Data:		

Cash, cash equivalents and short-term investments	$79,448	$172,366
Working capital	72,241	165,159
Total assets	96,260	189,178
Long-term debt and capital lease obligations, net of current portion	1,910	1,910
Accumulated deficit	(61,046)	(61,046)
Total stockholders' equity	81,435	174,353

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(1) The As Adjusted Consolidated 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 price of $33.13 per share and after deducting the underwriting discounts and commissions and our estimated offering expenses.

RISK FACTORS

This offering involves a high degree of risk. You should consider carefully the risks described below, together with the other information in this prospectus, before you make a decision to invest in our common stock. If any of the following risks actually occur, our business, operating results, prospects or financial condition could be materially adversely affected. This could cause the market price of our common stock to decline, and could cause you to lose all or part of your investment.

Risks Related to the Company

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 or maintain profitability.

Since our inception, we have incurred significant net losses, including net losses of $19.4 million in the period from January 1, 2000 through September 30, 2000. As a result of ongoing operating losses, we had an accumulated deficit of $61.0 million as of September 30, 2000. We are not currently profitable. Even if we succeed in developing and commercializing one or more of our drugs, we expect to incur substantial losses for the foreseeable future and may never become profitable. 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. As a result, we will need to generate significant revenues to achieve and maintain profitability. 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.

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

We may require additional funding in order 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 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 manufacturing facilities and of commercialization activities and arrangements; 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.

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 for the foreseeable future, 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;

- .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 these potential problems occurs, we may never successfully market any products.

We may not receive regulatory approvals for our product candidates.

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 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. The process of obtaining these approvals and the subsequent substantial compliance with appropriate 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 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.

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. Various federal and state statutes and regulations also govern or influence testing, manufacturing, safety, labeling, storage and record-keeping related to these products and their marketing. Any delay in, or suspension of, our clinical trials will delay the filing of our new drug applications with the FDA and, ultimately, our ability to commercialize our drugs and generate product revenues.

In connection with our clinical trials, we face the risks that:

.we or the FDA may suspend the trials;

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

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

.the results may not be statistically significant;

.patient recruitment may be slower than expected; and

.patients may drop out of the trials.

In addition, we depend on independent clinical investigators to conduct our clinical trials under their agreements with us. These 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. These investigators may also have relationships with other commercial entities, some of which may compete with us. If independent investigators assist our competitors at our expense, it could harm our competitive position.

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 depend on continuing our current strategic alliances and developing additional strategic alliances to develop and commercialize our compounds.

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 currently have collaborations with Janssen Pharmaceutica, Wyeth-Ayerst, Taisho Pharmaceutical and Eli Lilly. Because we rely heavily on our corporate collaborators, our development of our projects would be substantially delayed if our collaborators:

. fail to select a compound 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 new drug applications and, ultimately, our generation of product revenues.

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. In addition, our third-party manufacturers may 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.

- 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 and 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.

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 discontinue their employment with us, it will 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 will also be 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.

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 and we do not have a marketing and sales staff or distribution capabilities. 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.

Governmental and third-party payors may subject our products to sales and pharmaceutical pricing controls 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 medical community and patients accepting our products as being safe and effective. 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 emergence of equivalent or superior products; and
- the cost-effectiveness of the products.

If the medical community and patients do not ultimately accept our products as being safe and effective, we may not recover our investment.

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 anxiety, depression, insomnia, malignant glioma, other forms of cancer and multiple sclerosis, and there are a number of competitors to products in our research pipeline. If one or more of these 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. For more specific information about the competition we face, please see the section "Business" under the subheading "Competition" beginning on page 42.

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 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.

We may not be able to adequately enforce any of our patents to protect our proprietary technology and compounds. Litigation may be necessary to defend against or assert infringement claims to enforce our issued patents and to protect our trade secrets or know-how, or to determine the scope and validity of the proprietary rights of others. Two of our European patents are subject to opposition proceedings which, if successful, could reduce the breadth of some of our proprietary rights. These proceedings relate to our corticotropin-releasing factor receptor patent and our broad patent covering immune therapeutics in diabetes. In addition, 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.

The technologies we use in our research as well as the drug targets we select may unintentionally infringe the patents or violate the proprietary rights of third parties. In such cases, we may 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. If we do not obtain those licenses, we could encounter delays in product introductions while we attempt to design around those patents, or we could find that we are unable to develop, manufacture or sell products requiring those licenses. We are aware of pending and issued patent claims to certain uses of some of the types of compounds we are developing.

If we are unable to resolve third-party disputes regarding the validity of our patents or our alleged infringement of other third parties' patents, we may not be able to sell some or all of our products. For more information about our intellectual property, please see the section "Business" under the subheading "Intellectual Property" beginning on page 38.

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 $5 million per occurrence and $5 million in the aggregate. However, 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 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 $6 per share to approximately $47 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; 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.

FORWARD-LOOKING STATEMENTS

This prospectus and the information incorporated by reference contain forward-looking statements that involve a number of risks and uncertainties. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. Consequently, forward-looking statements are inherently subject to risks and uncertainties, and actual results and outcomes may differ materially from results and outcomes discussed in the forward-looking statements.

Forward-looking statements can be identified by the use of forward-looking words such as "believes," "expects," "hopes" "may," "will," "plan," "intends," "estimates," "could," "should," "would," "continue," "seeks," "pro forma" or "anticipates," or other similar words (including their use in the negative), or by discussions of future matters such as the development of new products, technology enhancements, possible changes in legislation and other statements that are not historical. These statements include but are not limited to statements under the captions "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business" as well as other sections in this prospectus. A number of factors could cause results to differ materially from those anticipated by the forward-looking statements, including those discussed under "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." You should be aware that the occurrence of any of the events discussed under "Risk Factors" and elsewhere in this prospectus could substantially harm our business, results of operations and financial condition and that if any of these events occurs, the trading price of our common stock could decline and you could lose all or a part of the value of your shares of our common stock.

The cautionary statements made in this prospectus are intended to be applicable to all related forward-looking statements wherever they may appear in this prospectus. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this prospectus.

USE OF PROCEEDS

Our net proceeds from the sale of shares of common stock offered hereby are estimated to be $92.9 million, based on the assumed public offering price of $33.13 per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Although we do not have any current plans for the application of the offering proceeds other than for working capital and general corporate purposes, in the future we may decide to use the net proceeds for a number of specific 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, none of which are planned or being negotiated as of the date of this prospectus.

The amounts and timing of our actual expenditures will depend significantly upon a number of factors, including future revenue growth, if any, 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 traded 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:

	Price Range of Common Stock	
	High	Low
Year Ended December 31, 1998:		
First Quarter	$10.13	$ 7.56
Second Quarter	9.06	7.38
Third Quarter	8.13	4.00
Fourth Quarter	8.00	4.13
Year Ended December 31, 1999:		
First Quarter	$ 7.50	$ 4.88
Second Quarter	5.88	4.00
Third Quarter	5.94	3.75
Fourth Quarter	29.63	5.38
Year Ended December 31, 2000:		
First Quarter	$47.50	$20.75
Second Quarter	39.70	13.94
Third Quarter	46.00	29.13
Fourth Quarter (through November 21, 2000)	44.88	31.38

On November 21, 2000, the last reported sale price of our common stock on the Nasdaq National Market was $33.13 per share. As of October 31, 2000, there were 130 stockholders of record of our common stock and approximately 6,600 beneficial holders.

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.

CAPITALIZATION

The following table sets forth:

- our capitalization at September 30, 2000; and
- our capitalization as adjusted to give effect to the sale of 3,000,000 shares of common stock offered hereby at an assumed offering price of $33.13 per share and the application of the estimated net proceeds.

	September 30, 2000	
	Actual	As Adjusted
	(dollars in thousands)	
Long-term debt, net of current portion	$ 1,910	$ 1,910
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; 22,066,248 shares issued and outstanding actual; 25,066,248 shares issued and outstanding as adjusted	22	25
Additional paid-in capital	142,798	235,713
Deferred compensation and notes receivable from stockholders	(162)	(162)
Accumulated other comprehensive income/loss	(177)	(177)
Accumulated deficit	(61,046)	(61,046)
Total stockholders' equity	81,435	174,353
Total capitalization	$ 83,345	$ 176,263

This information excludes:

- 3,605,648 shares of common stock reserved for the exercise of options outstanding as of September 30, 2000 at a weighted average exercise price of $10.67 per share;
- 355,504 shares of common stock reserved for the exercise of warrants outstanding as of September 30, 2000 at a weighted average exercise price of $10.50 per share;
- 233,778 shares of common stock reserved for issuance under our employee stock purchase plan; and
- 563,607 shares of common stock reserved for issuance under our other stock incentive plans but not subject to awards as of September 30, 2000.

Subsequent to September 30, 2000, we issued 3,811 shares upon the exercise of options and under the employee stock purchase plan at a weighted average price of $7.44 and 222,125 options at a weighted average exercise price of $38.61.

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, or incorporated by reference into, this prospectus. The selected consolidated statement of operations and balance sheet data for the years ended December 31, 1995, 1996, 1997, 1998 and 1999 are derived from our audited consolidated financial statements. The selected consolidated statement of operations data for the nine months ended September 30, 1999 and 2000 and the selected consolidated balance sheet data as of September 30, 2000 are derived from our unaudited consolidated financial statements. In the opinion of our management, our unaudited consolidated financial statements include all adjustments, consisting of normal recurring adjustments, necessary for a fair presentation of this information. The operating results for the nine months ended September 30, 2000 are not necessarily indicative of results that may be expected for the year ended December 31, 2000 or any other interim period or future year.

	Year Ended December 31,					Nine Months Ended September 30,	
	1995	1996	1997	1998	1999	1999	2000
	(in thousands, except per share data)						
Statement of Operations Data:							
Revenues:							
Sponsored research and development	$ 3,000	$ 9,092	$14,985	$ 8,751	$ 12,171	$ 9,760	$ 4,943
Sponsored research and development from related party	--	--	--	3,610	491	501	--
Milestones and license fees	2,750	9,000	10,250	2,500	3,000	1,500	5,050
Grant income and other revenues	356	1,124	909	1,176	1,129	831	1,050
Total revenues	6,106	19,216	26,144	16,037	16,791	12,592	11,043
Operating expenses:							
Research and development	7,740	12,569	18,758	21,803	29,169	21,893	28,404
General and administrative	2,728	3,697	5,664	6,594	7,476	5,587	6,930
Write-off of acquired in-process research and development and licenses	--	--	--	4,910	--	--	--
Total operating expenses	10,468	16,266	24,422	33,307	36,645	27,480	35,334
Income (loss) from operations	(4,362)	2,950	1,722	(17,270)	(19,854)	(14,888)	(24,291)
Interest income, net	839	2,598	3,931	4,000	2,851	2,040	4,293
Other income	177	574	818	504	1,066	889	973
Equity in NPI net losses and other adjustments, net	--	--	(1,130)	(7,188)	(885)	(1,174)	(47)
Net income (loss) before income taxes	(3,346)	6,122	5,341	(19,954)	(16,822)	(13,133)	(19,072)
Income taxes	--	248	214	1	--	--	302
Net income (loss)	$(3,346)	$ 5,874	$ 5,127	$(19,955)	$(16,822)	$(13,133)	$(19,374)
Earnings (loss) per share:							
Basic	$ (0.29)	$ 0.39	$ 0.30	$ (1.10)	$ (0.88)	$ (0.69)	$ (0.88)
Diluted	$ (0.29)	$ 0.36	$ 0.28	$ (1.10)	$ (0.88)	$ (0.69)	$ (0.88)
Shares used in calculation of earnings (loss) per share:							
Basic	11,684	14,971	16,930	18,141	19,072	18,975	21,900
Diluted	11,684	16,127	18,184	18,141	19,072	18,975	21,900

	December 31,					
	1995	1996	1997	1998	1999	September 30, 2000
	(in thousands)					
Balance Sheet Data:						
Cash, cash equivalents and short-term investments	$ 18,696	$ 69,920	$ 75,092	$ 62,670	$ 91,098	$ 79,448
Working capital	16,989	68,023	69,362	60,064	86,168	72,241
Total assets	24,012	77,957	91,903	80,529	109,222	96,260
Long-term debt and capital lease obligations	1,631	847	722	2,247	2,139	1,910
Accumulated deficit	(15,895)	(10,022)	(4,895)	(24,850)	(41,672)	(61,046)
Total stockholders' equity	19,225	72,767	83,152	71,958	96,354	81,435

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, pertaining generally to the expected continuation of our collaborative agreements, the receipt of research payments thereunder, the future achievement of various milestones in product development and the receipt of payments related thereto, the potential receipt of royalty payments, preclinical testing and clinical trials of potential products, the period of time that our existing capital resources will meet our funding requirements, and our financial results and operations. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth below and those outlined in our 1999 Annual Report on Form 10-K filed with the Securities and Exchange Commission.

Overview

We incorporated in California in 1992 and we reincorporated in Delaware in 1996. Since we were founded, we have been engaged in the discovery and development of novel pharmaceutical products for diseases and disorders of the central nervous and endocrine systems. To date, we have not generated any revenues from the sale of products, and we do not expect to generate any product revenues in the foreseeable future. We have funded our operations primarily through private and public offerings of our common stock and payments 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 products are advanced through the various stages of clinical development. As of September 30, 2000, we have incurred a cumulative deficit of $61.0 million and we expect to incur operating losses in the future, which may be greater than losses in prior years.

Results of Operations

Nine Months ended September 30, 2000 and 1999

Revenues for the nine months ended September 30, 2000 were $11.0 million compared with $12.6 million for the nine months ended September 30, 1999. Although we recorded $5.4 million under the Taisho Pharmaceutical collaboration during the first nine months of 2000, this increase in revenues was offset by the conclusion of the Novartis Pharmaceuticals collaboration in January 2000 and a portion of the Eli Lilly collaboration in October 1999. Under the Novartis and Eli Lilly agreements, we received sponsored research and development revenues in 1999 which did not recur in 2000. We also received $1.5 million in milestone payments from Wyeth-Ayerst Laboratories during 1999.

During the third quarter of 2000, we received a $3.0 million license fee from Taisho, which was recognized as income. In the fourth quarter of 2000, we are required to adopt Staff Accounting Bulletin 101 issued by the SEC. This pronouncement provides guidance on the recognition of up front payments received under research and development arrangements. Under the pronouncement, the $3.0 million license fee will be deferred and recognized as income over the life of the Taisho agreement, estimated at five years.

For the nine months ended September 30, 2000 and 1999, research and development expenses were $28.4 million and $21.9 million, respectively. The increase in expenses reflects higher costs associated with expanding clinical development activities and the addition of scientific personnel. We expect these expenses to rise over the remainder of 2000 as we expand clinical studies on current compounds and new compounds advance to the clinical development stages. Also included in the nine months ended September 30, 2000 were $1.1 million of non-cash charges associated with the employee stock purchase program and options granted to consultants, compared to $118,000 in the nine months ended September 30, 1999.

For the nine months ended September 30, 2000 and 1999, general and administrative expenses totaled $6.9 million and $5.6 million, respectively. This increase resulted primarily from business development

consulting expense and non-cash charges associated with the employee stock purchase program and options granted to consultants. In the nine-month periods ended September 30, 2000 and 1999, business development consulting expense was $580,000 and $8,000, respectively, and non-cash charges associated with the employee stock purchase program and options granted to consultants were $876,000 and $134,000, respectively. We expect these expenses to continue to rise over the remainder of 2000 as we expand clinical studies.

Interest income increased to $4.5 million during the nine months ended September 30, 2000 compared to $2.2 million for the same period last year. The increase was primarily due to higher investment balances generated by our private placement of our common stock. Completed in December 1999, this transaction generated net proceeds of $39.3 million. We anticipate interest earnings for the remainder of the 2000 to decline from quarter-to-quarter as we will need cash reserves to fund progressive clinical trials and hire additional scientific personnel.

Net loss for the first nine months of 2000 was $19.4 million, or $0.88 per share, compared to $13.1 million, or $0.69 per share, for the same period in 1999. The increase in net loss resulted from a decline in revenues of $1.6 million, an increase in operating expenses of $7.9 million and an increase in Japanese income taxes of $300,000 associated with the Taisho collaboration. These factors were partially offset by an increase in interest income of $2.3 million. Also, during the first nine months of 1999, we recorded equity in Neuroscience Pharma (NPI), Inc. losses of $1.2 million. We expect net losses to increase this year due to higher operating costs associated with the advancement of our compounds through progressive clinical development and the addition of scientific personnel.

To date, our revenues have come from funded research and achievements of milestones under corporate collaborations. The nature and amount of these revenues from period-to-period may lead to substantial fluctuations in our results of quarterly revenues and earnings. Accordingly, results and earnings of one period are not predictive of future periods.

Years ended December 31, 1997, 1998 and 1999

Our revenues for the year ended December 31, 1999 were $16.8 million compared with $16.0 million in 1998, and $26.1 million in 1997. Although similar in amount, revenues for 1999 and 1998 had a different composition resulting from several significant events. During 1999, we entered into a collaborative agreement with Wyeth-Ayerst and agreed to a two-year extension of our 1995 collaboration with Janssen Pharmaceutica. Revenues received in 1999 under the new agreements consisted of $5.4 million of sponsored research and development funding and $3.0 million in milestone achievements.

The increase in 1999 revenues generated by the new agreements was offset by a decline in revenues received under the Eli Lilly, Novartis and Neuroscience Pharma (NPI), Inc. collaborations that were concluded during the year. Revenues in 1998 for sponsored research and development funding and milestone achievements under these agreements were $5.0 million and $2.3 million, respectively.

Revenues recorded during 1997 included the initiation of the Eli Lilly collaboration and the final year of sponsored research funding under the 1995 Janssen agreement. Revenues in 1997 for sponsored research and development funding and milestone achievements under these and the Novartis agreements were higher than those recorded in 1999 by $12.2 million and $5.3 million, respectively.

Research and development expenses increased to $29.2 million during 1999 compared with $21.8 million in 1998 and $18.8 million in 1997. Increased expenses reflect advancement of our drug candidates through progressive clinical development phases. We expect to incur significant increases in future periods as later phases of development typically involve an increase in the scope of studies and number of patients treated.

General and administrative expenses increased to $7.5 million during 1999 compared with $6.6 million in 1998 and $5.7 million in 1997. Increased expenses resulted from additional professional services, including

patent and legal services, to support our expanded clinical development efforts. We anticipate similar increases in general and administrative expenses in the future as these efforts continue.

During 1998, we wrote-off acquired in-process research and development costs of $4.9 million. This amount included the acquisition of Northwest NeuroLogic and the in-licensing of drug candidates for our insomnia and malignant glioma programs. Both of the in-licensed programs are currently under clinical development.

Interest income decreased to $3.1 million during 1999 compared with $4.2 million for 1998 and $4.1 million in 1997. The decrease in 1999 compared with 1998 and 1997 primarily resulted from lower investment balances. Management anticipates an increase in interest income during future periods resulting from cash reserves generated by the sale of our common stock in December 1999 and increased revenues from anticipated collaborations.

In December 1999, we sold our investment in Neuroscience Pharma (NPI), Inc. and recorded a gain of $526,000. Our proportionate share of NPI operating losses during 1999, 1998 and 1997 were $764,000, $3.4 million and $1.1 million, respectively. In addition, we recorded a write-down in the investment value of $646,000 during 1999 and $3.8 million during 1998 relating to the decline in cash redemption value of the NPI preferred shares.

Net loss for 1999 was $16.8 million, or $0.88 per share, compared to net loss of $20.0 million, or $1.10 per share, for 1998 and net income of $5.1 million or $0.30 per share for 1997. Management expects to incur similar operating losses in the next two to three years as our clinical development efforts continue to grow.

To date, our revenues have come principally from funded research and achievements of milestones under corporate collaborations. The nature and amount of these revenues from period to period may lead to substantial fluctuations in the results of year-to-year revenues and earnings. Accordingly, results and earnings of one period are not predictive of future periods.

Liquidity and Capital Resources

At September 30, 2000, our cash, cash equivalents, and short-term investments totaled $79.4 million compared with $91.1 million and $62.7 million at December 31, 1999 and 1998, respectively. The increase in cash balances at December 31, 1999 resulted from the private placement of our common stock which resulted in net cash proceeds of $39.3 million. The decline in cash balances from December 31, 1999 to September 30, 2000 reflects the funding of progressive clinical development programs and the addition of scientific personnel.

Net cash used in operating activities during the first nine months of 2000 was $12.8 million compared with $12.4 million for the same period last year. The increase in net cash used during 2000 resulted primarily from the addition of scientific personnel and the funding of clinical development programs. We expect cash usage to continue during the year as we expand our clinical trial efforts. Net cash used by operating activities during fiscal year 1999 was $10.3 million compared with $10.7 million in fiscal year 1998 and net cash provided of $11.0 million in fiscal year 1997. The decrease in cash used in operations during 1999 compared with 1998 resulted primarily from increased sponsored research and milestone revenues received under our collaborations during 1999. The increase in cash used during 1998 compared with 1997 resulted primarily from higher sponsored research and milestone revenues received under our collaborations during 1997, which included a $5.0 million lump sum payment from Eli Lilly, in addition to lower operating expenses.

Net cash used in investing activities during the first nine months of 2000 was $53,000 compared with net cash provided of $7.9 million during the same period in 1999. The increase in cash used resulted primarily from the timing differences in the investment purchases, sales, maturities and the fluctuations in our portfolio mix between cash equivalents and short-term holdings. We expect similar fluctuations to continue over the

remainder of the year. Net cash used by investing activities during fiscal year 1999 was $21.2 million compared with net cash provided of $4.7 million in fiscal year 1998 and net cash used of $7.2 million in fiscal year 1997. The fluctuations in cash used resulted primarily from the timing differences in the investment purchases, sales, 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. Capital equipment purchases are expected to be $2.4 million for the fiscal year 2000, of which $2.0 million will be financed through leasing arrangements.

Net cash provided by financing activities during 2000 was $2.8 million compared to $421,000 during 1999. Proceeds from the issuance of common stock upon exercises of employee stock options provided cash during 2000, while proceeds from capital leases and issuances of common stock provided cash in 1999. Management anticipates an increase in proceeds from capital leasing during the last quarter of 2000. Net cash provided by financing activities during fiscal year 1999 was $41.0 million compared with $1.9 million and $659,000 during fiscal years 1998 and 1997, respectively. Cash provided during 1999 resulted from net proceeds received from the private sale of our common stock and exercise of employee stock options. Cash provided during 1998 resulted from capital lease financing of equipment purchases. Cash provided during 1997 resulted from the issuance of our common stock upon the exercises of stock options and warrants and proceeds received from a note payable used to finance the purchase of land.

On July 21, 2000, we signed an exclusive agreement with Taisho Pharmaceutical Co., Ltd. The agreement provides Taisho the exclusive rights to NBI-6024, our altered peptide ligand for diabetes in Europe and Asia. The collaboration includes licensing and option fees, payments for certain development and regulatory milestones, and significant reimbursement of the worldwide development expenses. In addition, we will receive payments based on sales upon commercialization of products in Europe and Japan. We have retained all rights to NBI-6024 in North America, but Taisho has exercised its option to negotiate with respect to these rights and we are in currently in negotiations with Taisho. As of September 30, 2000, we have received $2.0 million in option fees, $3.0 million in license fees and $388,000 in reimbursement for development expenses related to this collaboration.

In September 1999, we signed an amendment to our 1995 agreement with Janssen Pharmaceutica, N.V. The amendment provides for a new sponsored research period designed to identify new corticotropin-releasing factor receptor antagonists which will be subject to the terms of the original agreement signed in 1995. The term of the amendment is from April 1999 through February 2001. Under the agreement, we will receive $5.0 million in sponsored research funding, up to $3.5 million in milestone achievements, $500,000 for research already conducted under this technology and reimbursement of all outside and third-party costs associated with the project. As of September 30, 2000, we have received $3.9 million in sponsored research, $684,000 in reimbursed third-party costs and $500,000 payment for prior research.

In March 1999, we entered into an agreement with Wyeth-Ayerst Laboratories, the pharmaceutical division of American Home Products, on the research, development and commercialization of compounds which modulate excitatory amino acid transporters for the treatment of neurodegenerative and psychiatric diseases.

The Wyeth-Ayerst agreement includes sharing proprietary technologies, funding for research, payments for milestones reached, plus royalties on sales from products resulting from the collaboration. Under the terms of the agreement, we expect to receive three to five years of funding for research and development as well as worldwide royalties on commercial sales of products that result from the collaboration. Wyeth-Ayerst will also provide us with access to chemical libraries for screening within the collaborative field. As of September 30, 2000, we have received $5.3 million in sponsored research payments and $3.0 million for the achievement of four milestones.

During 1998, we expensed acquired in-process research and development of $4.9 million. These charges consisted of $4.2 million for the acquisition of Northwest NeuroLogic, through which we received licenses to

the melanocortin receptor and excitatory amino acid transporters programs, and $710,000 for licenses to an insomnia and brain cancer compounds. We performed scientific due diligence related to the acquired projects and because they were based on narrow scientific hypothesis, we concluded that none of these programs had alternative future uses.

The nature and efforts required to develop the acquired in-process research and development into commercially viable products include research to identify a clinical candidate, preclinical development, clinical testing, FDA approval and commercialization. This process may cost in excess of $100 million and can take as long as 10 years to complete. It is also important to note that if a clinical candidate is identified, the further development of that candidate can be halted or abandoned at any time due to a number of factors. These factors include, but are not limited to, funding constraints, safety or a change in market demand.

Because of our limited financial resources, our strategy to develop some of our programs is to enter into collaborative agreements with major pharmaceutical companies. Through these collaborations, we could partially recover our research costs through contract research and milestone revenues. The collaborators would then be financially responsible for all clinical development and commercialization costs.

In May 1998, when we acquired the in-process research and development programs from Northwest NeuroLogic, we estimated the costs to identify a clinical candidate and provide minimal research support during the clinical development stages for the melanocortin receptor program to be $15.4 million over an 8-year period. Costs to identify a clinical candidate and provide minimal research support during the clinical development stages of the excitatory amino acid transporters program were estimated at $22.4 million. Estimated revenues from the collaborative arrangements were anticipated to reduce our net costs. The clinical development and commercialization costs were to be completely funded by the collaborator.

During fiscal year 2000, we anticipate that our gross costs for continued research on these programs will approximate $5 million. Our research efforts may not result in clinical candidates for either compound. We intend to collaborate on the melanocortin receptor technology. We would expect the collaborator to then be responsible for the clinical development, commercialization and funding. Our excitatory amino acid transporters program is currently under a collaborative agreement with Wyeth-Ayerst. Consequently, we cannot estimate the time or resources they will commit to the development of this program.

Our insomnia and brain cancer compounds are both in the early stages of clinical testing. During 2000, we expect to spend approximately $20 million on additional clinical testing of the brain cancer and insomnia compounds. We expect the clinical testing of both compounds to continue for at least the next two years, but our efforts may not result in commercially viable products. If our efforts were completely successful and we did not collaborate on these compounds, we estimate that each compound could cost an additional $50-$150 million and take up to five years to reach commercial viability.

For each of our programs, we periodically assess the scientific progress and merits of the programs to determine if continued research and development is economically viable. Certain of our programs have been terminated due to the lack of scientific progress and lack of prospects for ultimate commercialization. Because of the uncertainties associated with research and development of these programs, we may not be successful in achieving commercialization. As such, the ultimate timeline and costs to commercialize a product cannot be accurately estimated.

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 assure you that these capital resources and payments will be sufficient to conduct 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 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, potentially including off-balance sheet financing. 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 successfully develop our products under development or that our products, if successfully developed, will generate revenues sufficient to enable us to earn a profit.

Interest Rate Risk

We are exposed to interest rate risk on our short-term investments and on our long-term debt. 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 with maturities of less than 44 months. If a 10% change in interest rates were to have occurred on September 30, 2000, 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.

Interest risk exposure on long-term debt relates to our note payable, which bears a floating interest rate of prime plus one quarter percent (9.50% at September 30, 2000, 8.75% at December 31, 1999 and 8.00% at December 31, 1998). At September 30, 2000, December 31, 1999 and 1998, the note balance was $348,000, $461,000 and $610,000, respectively. This note is payable in equal monthly installments through January 2003. Based on the balance of our long-term debt, we have concluded that we do not have a material financial market risk exposure.

Cautionary Note on Forward-Looking Statements

Our business is subject to significant risks, including but not limited to, the risks inherent in our research and development activities, including the successful continuation of our strategic collaborations, the successful completion of clinical trials, the lengthy, expensive and uncertain process of seeking regulatory approvals, uncertainties associated both with the potential infringement of patents and other intellectual property rights of third parties, and with obtaining and enforcing our own patents and patent rights, uncertainties regarding government reforms and of product pricing and reimbursement levels, technological change and competition, manufacturing uncertainties and dependence on third parties. Even if our product candidates appear promising at an early stage of development, they may not reach the market for numerous reasons. Such reasons include the possibilities that the product will be ineffective or unsafe during clinical trials, will fail to receive necessary regulatory approvals, will be difficult to manufacture on a large scale, will be uneconomical to market or will be precluded from commercialization by proprietary rights of third parties. For more information about the risks we face, see the section "Risk Factors" beginning on page 5.

New Accounting Pronouncements

In December 1999, the SEC issued Staff Accounting Bulletin No. 101, "Revenue Recognition in Financial Statements." SAB 101 provides guidance in applying generally accepted accounting principles to revenue recognition in financial statements, including the recognition of nonrefundable up-front fees received in conjunction with a research and development arrangement.

We are required to adopt this pronouncement effective in the fourth quarter of 2000. As required by the adoption, we reviewed all up-front payments, license fees and milestones received in the current and prior years. Up-front payments have been received for program cost reimbursements incurred during a negotiation period. License fees are received in exchange for a grant to use our proprietary technologies on an as-is basis, for the term of the collaborative agreement. Milestones are received for specific scientific achievements determined at the beginning of the collaboration. These achievements are remote and unpredictable at the onset of the collaboration and are based on the success of scientific efforts.

Based on that review, we determined that the $3.0 million in license fees received from Taisho and recognized as revenue during the third quarter of 2000, will be subject to the adoption of SAB 101. We are continuing to review the impact of the adoption on milestones revenues. Currently, we believe that $3.0 million in milestones payments received from Wyeth-Ayerst during 1999 may also be subject to the accounting provisions of SAB 101. All other fees received relate to agreements under which all performance obligations have been met, or the agreements have been terminated.

In accordance with APB 20, the adoption of SAB 101 will be recognized by including the cumulative effect of the change in accounting principle in the net loss for the fourth quarter of 2000. We estimate that our otherwise reported net loss for the year ended December 31, 2000 will increase by approximately $2.8 million. This change results from the deferral of revenue associated with the Taisho agreement. These deferred revenues will then be amortized as income at $600,000 in each of the years 2001 through 2004 and $350,000 in 2005. We are continuing to review the impact of SAB 101 on milestone payments and will adjust the cumulative effect of the accounting change if appropriate.

The following section contains forward-looking statements which involve risks and uncertainties. These statements are often preceded by words such as "intend," "anticipate," "believe," "expect" and similar words. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of a number of factors, including those set forth under the section "Risk Factors" and elsewhere in this prospectus.

Neurocrine Biosciences, Inc. is a product-based biopharmaceutical company focused on neurologic and endocrine diseases and disorders. Our product candidates address some of the largest pharmaceutical markets in the world including insomnia, anxiety, depression, cancer and diabetes. We currently have 15 programs in various stages of research and development. Of these 15 programs, four programs are in clinical development and four programs are in advanced preclinical development which we expect to progress into human clinical trials in the near future. We believe the other seven research projects will help supply clinical development candidates in the future. While we independently develop the majority of our product candidates, we utilize collaborators in four of our 15 programs, including Janssen Pharmaceutica, a subsidiary of Johnson & Johnson, Wyeth-Ayerst Laboratories, a division of American Home Products, Taisho Pharmaceutical and Eli Lilly. Under these collaborations, we receive funds for current product development, but retain rights to North American commercial participation in addition to receiving milestone payments and royalties on worldwide product sales.

Our Business Strategy

Our goal is to become the leading therapeutic product-based biopharmaceutical company focused on neurologic and endocrine diseases and disorders. There are six key elements to our business strategy:

Build a Large and Diversified Product Portfolio to Mitigate Overall Clinical and Technical Risk. We believe that by building a large and diverse product pipeline, we can mitigate some of the risks associated with drug development. We currently have 15 programs in various stages of research and development with four projects in clinical development, four programs in advanced preclinical development which we expect to progress into the clinic in the near future, and seven research projects to supply clinical compounds for the future. 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 high probabilities of technical and commercial success.

Identify Novel Drug Targets for the Development of Innovative Therapies to Address Large Unmet Market Opportunities. We utilize a multidisciplinary research approach to identify and validate novel drug targets for internal development or collaboration. For example, corticotropin-releasing factor, 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. Gonadotropin-releasing factor antagonists, compounds designed to reduce the secretions of sex steroids, may represent the first novel non-injectible means of treatment of prostate cancer and endometriosis. Melanocortin and hypocretin modulators are compounds which affect proteins in the brain believed to be involved in many activities of the body. We believe these compounds build upon our franchise and expertise in obesity and sleep disorders. The creativity and productivity of our discovery research group will continue to be a critical component for our continued success. Our team of approximately 100 biologists and chemists have a goal of delivering three innovative clinical compounds over the next five years to fuel our research and development pipeline.

Establish 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 commercial or co-promotional rights in North America. We intend to further leverage our resources by continuing to enter into strategic alliances to enhance

our internal development and commercialization capabilities. To date, we have entered into strategic alliances with:

- Janssen, to focus on corticotropin-releasing factor receptor antagonists to treat anxiety and depression;

- Wyeth-Ayerst, to research, develop and commercialize compounds to treat neurodegenerative and psychiatric diseases;

- Taisho, to develop our compound to treat a type of diabetes in which the body does not produce enough insulin; and

- Eli Lilly, to collaborate in the discovery, development and commercialization of treatments of central nervous system disorders, including obesity.

Acquire Rights to Complementary Drug Candidates. We plan to continue to selectively acquire rights to products in various stages of development to take advantage of our drug development capabilities. In May 1998, we licensed from the National Institutes of Health an interleukin 4 fusion toxin which is currently in clinical trials for recurrent malignant glioma. In May 1998, we acquired Northwest NeuroLogic, Inc. 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-Ayerst. We also acquired from Northwest NeuroLogic melanocortin technology and other intellectual property that we are developing. In June 1998, we licensed exclusive worldwide commercial rights for NBI-34060, our compound for the treatment of insomnia, from DOV Pharmaceuticals and have since moved this compound into advanced clinical development.

Supplement Our Internal Research Capabilities by Collaborating with Leading Platform Technology Companies. We believe we can complement our multidisciplinary research process by selectively accessing new technologies from platform technology companies. Through creative collaborations with technology leaders, we believe we can accelerate and expand our internal discovery efforts. We have entered into a number of alliances with other platform technology companies to enhance our drug discovery and development capabilities. These alliances include:

- our alliance with Rigel, Inc. to use Rigel's intellectual property and expertise to discover novel protein targets involved in neural cell and antibody activation;

- our alliance with Arena Pharmaceuticals involving the application of Arena's constitutive activation technology to a family of receptors;

- our alliance with Array Biopharma, Inc. to design and synthesize a focused library of small molecules; and

- our alliance with Caliper Technologies Corp. to utilize Caliper's proprietary microfluidics technology to screen against our targets.

Outsource Capital Intensive and Non-Strategic Activities. We intend to focus our resources on research and development activities by outsourcing our requirements for clinical drug supply and certain preclinical studies and clinical monitoring activities. We believe the availability of skilled contract manufacturers and contractors will allow us to cost-effectively meet these needs and thereby allow us to concentrate our full attention and resources on our core discovery and development programs to generate additional product opportunities.

Our Product Pipeline

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

Program	Compound	Targeted Indication	Status	Commercial Rights
Products Under Development:				
GABA-A Agonist.....	NBI-34060	Insomnia	Phase II	Neurocrine
CRF R\\1\\ Antagonist...		Anxiety, Depression	Preclinical	Janssen/Neurocrine
CRF R\\1\\ Antagonist...		Anxiety, Depression	Preclinical	Neurocrine
IL-4 Fusion Toxin.....	NBI-3001	Malignant Glioma	Phase II	Neurocrine
IL-4 Fusion Toxin.....	NBI-3001	Additional Cancers (kidney, lung)	Preclinical	Neurocrine
Altered Peptide Ligand..	NBI-5788	Multiple Sclerosis	Phase II	Neurocrine
Altered Peptide Ligand..	NBI-6024	Type I Diabetes	Phase I	Taisho/Neurocrine
GnRH Antagonist.....		Endometriosis, Prostate Cancer	Development	Neurocrine
Research:				
Excitatory Amino Acid Transporters.....		Neurodegenerative Diseases	Research	Wyeth-Ayerst/Neurocrine
CRF R\\1\\ Antagonist...		Gastrointestinal Disorders	Research	Neurocrine
CRF R\\2\\ Antagonist...		Eating Disorders	Research	Neurocrine
Urocortin/CRF R\\2\\ Agonist.....		Obesity	Research	Eli Lilly
Melanocortin Receptor Agonist.....		Obesity	Research	Neurocrine
Melanin Concentrating Hormone Antagonist.....		Obesity	Research	Neurocrine
Hypocretin Agonist/Antagonist.....		Sleep Disorders	Research	Neurocrine

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"Phase II" indicates that the 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.

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

"Preclinical" indicates that a drug candidate is being selected or has been selected and is undergoing toxicology studies and manufacturing to allow for Phase I clinical trials.

"Development" indicates that lead compounds have been discovered that meet certain laboratory and preclinical criteria. These compounds may undergo structural modification and more extensive evaluation prior to selection for preclinical development.

"Research" indicates identification and evaluation of compounds in laboratory and preclinical models.

Products Under Development

GABA-A Agonist

Insomnia is a prevalent neurological disorder in the United States, with up to 62% of the adult population reporting trouble sleeping a few nights per week or more, according to the National Sleep Foundation. Despite this widespread prevalence, insomnia remains a disorder with high unmet medical needs, including the ability to maintain sleep throughout the night without next-day residual effects. 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, a class of drugs that targets the GABA-A receptor, known as benzodiazepines, were used as sedatives to treat insomnia. The most well-known of the benzodiazepines is Valium(R). This class of drugs produced several undesirable side effects, including negative interactions with other central nervous system depressants, such as alcohol, the development of tolerance upon repeat dosing, insomnia following discontinuation of dosing, hangover effects the next day, 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 whose cognitive function may already be impaired by the aging process. During the late 1980s, a class of drugs targeting a specific site on the GABA-A receptor, known as non-benzodiazepines, were developed. The non-benzodiazepines reduce the side effects associated with benzodiazepines. The most popular of the non-benzodiazepines are marketed as Ambien(R) and Sonata(R). Ambien(R) is the current leader with U.S. sales of $535 million in 1999.

Our drug candidate for the treatment of insomnia, NBI-34060, a non-benzodiazepine, acts on a specific site on the GABA-A receptor. It is through this mechanism that the currently marketed non-benzodiazepine therapeutics also produce their sleep-promoting effects. However, NBI-34060 is more potent than the currently marketed non-benzodiazepines, including Ambien(R) and Sonata(R), and is more selective for the specific subtype of receptors within the brain believed to be responsible for promoting sleep than the benzodiazepines. We believe that this improved profile and more selective drug targeting will reduce the side effects characteristic of the currently marketed products. We believe that receptor binding studies and preclinical studies on NBI-34060 indicate that it is a highly potent GABA-A receptor activator, or agonist, that acts very specifically on the receptor subtype we are targeting. NBI-34060 also appears to be devoid of next day hangover effects and we expect it to have a considerably reduced amnestic potential. The elderly population, which represents a large portion of the insomnia market, would benefit especially from a novel therapeutic with an improved safety profile, rapidity of onset and decrease in memory impairment.

Researchers designed the first Phase I clinical trial on NBI-34060 to determine the safety and tolerance of NBI-34060 and provide a preliminary evaluation of the sedative potential in 42 normal volunteers as reflected in self-ratings of drowsiness, disruption of memory and impairment of coordination. In this trial, subjects tolerated NBI-34060 well, and reported no serious or unexpected adverse side effects. The subjects consistently reported drowsiness, indicating strong potential for the sedative properties of the compound. Subsequently, in the first quarter of 1999, we completed a second Phase I clinical trial in 30 healthy volunteers to further explore the safety and kinetic profile of NBI-34060. As demonstrated in the first Phase I trial, NBI-34060 demonstrated a very good safety profile.

In 1999, we completed a Phase II placebo-controlled multi-center clinical trial evaluating the efficacy of NBI-34060 in 228 subjects with transient insomnia. Transient insomnia means occasional sleeplessness caused by environmental factors, such as jetlag. The trial was conducted in a sleep laboratory setting employing objective assessments of sleep onset and safety. The results indicated that NBI-34060 is safe and effective in helping subjects with transient insomnia achieve rapid sleep without the next day residual effects associated with most currently marketed sedatives. The results showed that the primary clinical endpoint and the required regulatory endpoint for approval, time to sleep onset, was reached at a statistically significant level. In this trial, those subjects receiving NBI-34060 took a mean time of 16 minutes to progress to sleep onset versus a mean time of 34 minutes in the placebo group. These results were statistically significant at p (less than) 0.001. This means

that applying widely used statistical methods, the chance that these results could have occurred by accident was less than one in 1,000. In addition, the data indicated that a majority of subjects in the treated group fell asleep within 9.5 minutes as indicated by the median time to sleep onset as compared to 23 minutes in the placebo group.

Based on the results from our Phase II trial, we have moved to expand clinical development of NBI-34060. So far this year we have initiated five clinical trials to evaluate various formulations and patient subgroups and we expect to initiate or complete up to nine additional clinical trials involving an additional 300 subjects by year-end. Among other research goals, we intend to determine whether NBI-34060 is effective in treating chronic insomnia, which is sleeplessness not caused by environmental factors. We are developing a formulation of NBI-34060 to treat chronic insomnia. We are also designing a large scale pivotal Phase III program, from which we expect to determine the approvability of the drug candidate. We currently expect to begin this pivotal trial in the second half of 2001.

Another important feature of NBI-34060 is its relatively short half-life, or duration of action of the compound, in the body. The levels of NBI-34060 in the blood stream reach the highest point 30 minutes after the subject takes the tablet. The NBI-34060 is then rapidly removed from the blood stream so it cannot be detected four hours later. This rapid peak of drug results in rapid sleep onset followed by rapid removal of the drug from the body, reducing the risk of next-day effects of the drug. We believe that this short duration of action will allow for bedtime dosing for people who have trouble falling asleep and dosing in the middle of the night for people who have trouble staying asleep without causing the side effects and next day hangover that occurs with the longer acting drugs like Ambien(R) and Sonata(R). We also believe that this short duration of action will allow us to formulate the drug in a modified release form that will effectively provide two doses of drug, a bedtime dose and a middle of the night dose, which will both rapidly induce sleep and maintain sleep through the night. If successful, this would represent the first non-benzodiazepine approved by the FDA for maintaining, rather than simply inducing, sleep.

We face the risk that the side effects and efficacy profile of NBI-34060 seen in our Phase I and II trials may not be confirmed in additional clinical trials or that the results of future trials may not warrant further trials.

Corticotropin-Releasing Factor

According to the Surgeon General's 1999 Report on Mental Health, 6.5% of the U.S. adult population experiences a major depressive episode each year and 16.4% of the U.S. adult population has an anxiety disorder. Existing anti-depressant and anti-anxiety therapeutics sold in excess of $10.6 billion worldwide in 1999, according to market analyst reports from Med Ad News. However, there remain significant unmet medical needs. The leading drug class known as the selective serotonin reuptake inhibitors are not effective 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 anti-depressant with fewer side effects would represent a major advance in the treatment of depression. Corticotropin-releasing factor antagonists may provide such an advance in anti-depressant therapy through a specific mechanism for combating the hormonal abnormalities associated with 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. Corticotropin-releasing factor 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 corticotropin-releasing factor, which induces the physical effects that are associated with stress and which can lead to depression or anxiety.

The novelty and specificity of the corticotropin-releasing factor 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 corticotropin-releasing factor, or CRF, field through our intellectual property portfolio and relationship with experts in the neuropsychiatric field. Wylie Vale, Ph.D., our co-founder and Chief Scientific Advisor, is considered to be a leader in this field of research. We have further characterized the CRF receptor system and have identified additional members of the CRF receptor family. We have received patents 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 Prozac(R), Zoloft(R), Paxil(R) and Celexa(R) 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 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.

In our CRF R\\1\\ antagonist program, our corporate collaborator, Janssen Pharmaceutica, selected a CRF R\\1\\ receptor antagonist drug candidate, NBI-30775, for preclinical studies in 1996. Janssen initiated and completed a number of Phase I clinical trials on the compound in late 1998 and initiated a Phase IIa open label trial in 1999. 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, Janssen administered NBI-30775 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. We were strongly encouraged by these results, which we believe support the hypothesized mechanism of action. While this trial found NBI-30775 to be safe, reversible increases in liver enzymes occurred in two volunteers in an expanded safety study. As a result, Janssen announced its decision to discontinue development of NBI-30775. However, because of the positive efficacy results for NBI-30775, Janssen decided to proceed with a back-up compound identified from its research relationship with us. We expect Janssen to select a back-up compound soon, and to begin preclinical studies thereafter.

In addition to our CRF R\\1\\ program with Janssen, we are conducting an independent CRF R\\1\\ antagonist program focused on a series of chemical compounds that are proprietary to us. We have selected several lead candidates for this program and we expect to enter Phase I clinical trials in late 2000 and early 2001.

We face the risk that CRF R\\1\\ antagonist compounds may not be effective and safe therapeutics for the treatment of depression or any other conditions. In addition, we or Janssen may decide not to initiate Phase I clinical testing or progress to later clinical trials in a timely manner, if at all.

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. The Surgeon General's 1999 Report on Mental Health estimates that anxiety disorders affect 16.4% of the U.S. adult population. Of the pharmaceutical agents that other companies currently market for the treatment of anxiety disorders, benzodiazepines, such as Valium(R) and Xanax(R), 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. Despite these adverse effects, total sales of benzodiazepines were approximately $800 million in 1999. 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.

With our corporate collaborator, Janssen, and in our independent CRF R\\1\\ antagonist program, we are developing small molecule therapeutics to block the effects of overproduction of CRF in anxiety. As a co-examined variable in the Janssen open label Phase IIa clinical trial for depression described above, Janssen analyzed the anti-anxiety effects of the CRF R\\1\\ receptor antagonist NBI-30775 using the Hamilton Anxiety Scores. Janssen observed 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. Despite these early results, we or Janssen may decide not to initiate clinical testing of CRF R\\1\\ antagonist compounds for anxiety. Even if those trials are conducted, the data may not support continuation of the program and additional clinical trials.

IL-4 Fusion Toxin

Interleukin 4, or IL-4, is a natural chemical which 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 cancers. Targeted toxins are a novel form of anticancer therapy under investigation in a variety of clinical settings. Targeted toxin therapeutics carry a bacterial toxin to a target site on the cancer cells 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.

In 1998, we exclusively licensed from the National Institutes of Health a targeted toxin compound, IL-4 fusion toxin, which we call NBI-3001. A collaboration between the FDA and the National Cancer Institute designed the IL-4 fusion toxin. It is a combination protein in which IL-4 is attached to Pseudomonas exotoxin, a bacterial toxin that can kill cells. The IL-4 portion of the fusion toxin preferentially binds to human cancer cells because the cancer cells express elevated levels of receptors for IL-4 on their surface, while IL-4 receptor expression is absent or undetectable in normal brain tissue. Once the IL-4 portion of the IL-4 fusion toxin targets the toxin to the cancer cells, the toxin portion of the molecule preferentially kills the cancer cells.

Malignant Glioma. Malignant brain tumors are a significant cause of cancer death. Despite current therapeutic options such as surgery, radiation and chemotherapy, according to the American Cancer Society, the median survival rate for malignant glioma, the most common form of malignant brain cancer, is only in the range of nine to 12 months. These tumors arise within the brain and generally remain confined to the brain. The clinical course of malignant glioma is characterized by relentless loss of vital neurological functions and death within approximately 12 months.

In 1999 we initiated a Phase I/II trial of NBI-3001 in patients with malignant glioma in which the primary endpoints were safety and tumor regression. We completed this trial in June 2000. We enrolled a total of 31 patients with recurrent gliomas which were unresponsive to surgery and radiotherapy in the trial. Our researchers treated patients with intratumoral infusions of NBI-3001 for up to four days. This trial found NBI-3001 to be safe and to have an acceptable degree of tolerability in this patient population. While approximately one-third of the patients exhibited side effects during or immediately following therapy, these

effects were consistent with marked tumor cell death and the subsequent inflammatory response to this tumor cell death. The researchers did not observe any significant peripheral drug-related toxicities. The researchers reported that, of the 27 patients who completed therapy:

- seven patients, or 26%, experienced complete remissions, defined as no evidence of viable tumor;

- 10 patients, or 37%, experienced a partial response, defined as greater than 50% reduction in tumor mass; and

- 10 patients, or 37%, continued to suffer from stable or progressive disease.

In addition, the six-month median survival data showed trends toward efficacy. We plan to initiate an additional confirmatory Phase II trial to further establish dosing regiment, safety and efficacy in the fourth quarter of 2000. We also plan to initiate a Phase III trial in mid-2001.

In October 1999, the FDA granted us fast track designation for NBI-3001. Fast track designation allows us to accelerate our clinical program for NBI-3001 and expedite receipt of regulatory approvals. In April 2000, we were awarded orphan drug designation for NBI-3001 for astrocytic glioma. Under FDA rules, drug developers may obtain orphan drug designation for drugs that treat a disease or condition that affects fewer than 200,000 people in the United States per year. Orphan drug designation provides us with seven years of marketing exclusivity following approval, tax incentives and access to grant funding. We face the risk that we will not successfully complete clinical testing or progress to later clinical trials in a timely manner, or at all.

Additional Cancers. In conjunction with our clinical trials of IL-4 fusion toxin in malignant glioma, we entered into a collaborative research and development agreement with the FDA to investigate the safety and efficacy of IL-4 fusion toxin in laboratory models of different cancers and by different routes of administration. Research teams from the FDA and NIH have published results with IL-4 fusion toxin demonstrating a high level of binding and destruction of specific types of cancers. We are conducting preclinical research to support the application of NBI-3001 to peripheral solid tumors and have shown that IL-4 fusion toxin can be safely administered intravenously in preclinical models. We plan to initiate a Phase I clinical trial in the first quarter of 2001 to first investigate the safety and efficacy of NBI-3001 against kidney and non-small-cell lung cancers. We face the risks that the effectiveness of NBI-3001 seen in our laboratory models, or the safety profile of NBI-3001 seen in our preclinical models, may not be confirmed in clinical trials or that the results of future clinical trials may not warrant further development in any of these settings or that the trial results may not support initiating clinical trials in cancers other than malignant glioma.

Altered Peptide Ligands

The American Autoimmune Related Diseases Association estimates that over 50 million people in the United States suffer from autoimmune diseases such as multiple sclerosis, rheumatoid arthritis, Type I 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, certain 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 I 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 an 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, bacterias or other proteins the T cell recognizes as foreign. T cells recognize these antigens 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. Patients develop a slow, steady deterioration of neurologic function over an average duration of approximately 30 years. According to the National Multiple Sclerosis Society, there are an estimated 350,000 cases of multiple sclerosis in the United States and a similar number of patients in Europe with approximately 17,000 new cases diagnosed worldwide each year. 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.

Our co-founder, Dr. Lawrence Steinman, identified one of the dominant destructive T cell types in the brains of patients who had died of multiple sclerosis. Dr. Steinman further identified one of the dominant antigens on the normal cell targeted by the autoreactive T cells, a peptide from a brain protein know as myelin basic protein. 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 application with the FDA and received approval in 1996 to commence clinical trials. We subsequently completed Phase I clinical trials, and initiated two Phase II clinical trials of our altered peptide ligand for the treatment of multiple sclerosis, NBI-5788, in 1999.

The first Phase II trial was a multi-center, placebo controlled, randomized parallel group design involving three doses of the altered peptide ligand in 5, 20, and 50 mg weekly doses for four months in 13 centers in North America and Europe. In July 1999 while the Phase II trials were underway, Novartis exercised its right to terminate the collaboration effective January 2000. Subsequently, the Data and Safety Monitoring Board for the trial recommended, and we agreed, that administration of the trial drug be discontinued based on reports of adverse allergic reactions. We continued to evaluate all of the enrolled patients in the study through December 1999 in accordance with the study protocol. We reacquired all rights to the program from Novartis on January 7, 2000 and initiated data analysis. The final data analysis from the multi-center trial showed no increases in either clinical relapses or in new lesions in all patients, even those with allergic reactions. Of the patients completing the double-blind phase of the study, the total volume of enhancing lesions was reduced in the 5 mg dose group compared to the placebo-control patents ($p<0.029$ Mann Whitney for two treatments). We could not conduct this same secondary analysis in the 20 mg or 50 mg groups, since there were not enough patients with positive scans for us to evaluate their magnetic resonance imaging changes. Moreover, 57% of the patients in the 5 mg group experienced reductions in the volume of new enhancing lesions compared to 25% in the placebo group. Because of these factors, we believe that for this compound, optimal dosing may be at lower levels, and we are currently planning a Phase IIb trial to establish the efficacy profile and optimum dosing regiment for NBI-5788.

The second Phase II trial, which we conducted in collaboration with the National Institutes of Health, involved an open-label, unblinded, non-placebo control trial in eight patients, seven of whom received multiple injections of 50 mg weekly while the final subject received 5 mg. In this trial, published in Nature Medicine, the authors observed a higher incidence of new brain lesions in two patients who received 50 mg doses and the one patient who received 5 mg doses. As a result, the trial was stopped. However, the authors did not provide direct evidence that NBI-5788 triggered the lesions.

Our aim for future trials will be to further establish the benefit of low-dose altered peptide ligand therapy in patients with multiple sclerosis. We face the risks that we may not initiate or complete additional clinical trials or that results of any such studies may not warrant additional clinical development of potential products.

Type I Diabetes. Utilizing our experience in the development of altered peptide ligands for multiple sclerosis, we have extended this approach to Type I or juvenile-onset diabetes, which is a metabolic disease in which the body does not produce enough insulin. Like multiple sclerosis, in Type I diabetes the immune system erroneously targets healthy tissue, in this case the pancreatic cells responsible for the production of insulin. Type I diabetes is one of the most prevalent chronic childhood conditions in North America, afflicting approximately one million patients in 1999. 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 I diabetes consists of daily insulin injections to regulate blood glucose levels.

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 pre-diabetic patients, thus allowing them to delay or avoid chronic insulin therapy. Working with leading diabetologists at the Barbara Davis Center for Childhood Diabetes at the University of Colorado, our scientists have engineered an altered peptide ligand that affects immune cells targeting the pancreas. 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 I diabetes patients indicate that NBI-6024 is recognized by patients' immune cells. This suggests that NBI-6024 may have the potential to intervene in the disease process in humans. We have completed a Phase I safety and dose escalating clinical program in diabetic patients. This trial included 20 Type I diabetic patients. Data from this trial indicates that NBI-6024 is safe and well tolerated. We have initiated an additional Phase I multi-dose trial and we expect to initiate several Phase II trials in 2001 to assess the safety and biological activity of multiple doses of NBI-6024 in adult, adolescent and pediatric patients with Type I diabetes and a Phase II/III trial in the second quarter of 2001.

In January 2000, we entered into an agreement with Taisho Pharmaceutical Co., Ltd. providing Taisho with an exclusive option to obtain European, Asian and North American rights to NBI-6024. In July 2000, Taisho exercised the option as to European and Asian rights, and we granted Taisho exclusive rights to NBI-6024 in those regions. Under the collaboration agreement, we will receive licensing and option fees, payments for certain development and regulatory milestones, significant reimbursement of worldwide development expenses and payments based on sales upon commercialization. We currently retain all rights to NBI-6024 in North America, but in July 2000, Taisho exercised its option to acquire these rights and we are currently negotiating the terms of the acquisition with Taisho.

We face the risk that large-scale studies of our drug in Type I diabetes patients may show different results than our preclinical studies in animals and in cells derived from Type I diabetes patients or our Phase I trials.

Gonadotropin-Releasing Hormone Receptor

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 prostate cancer and endometriosis. Other companies have developed several peptide drugs on this principle, such as Lupron(R) and Zoladex(R), and according to market analyst reports by Euromonitor and Epicom Business Intelligence, these drugs now have an estimated market size in excess of $2.0 billion annually worldwide. 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 market potential for an orally delivered gonadotropin-releasing hormone antagonist that does not have the tendency to initially exacerbate the patient's condition. We have screened our small molecule library and conducted structure activity studies to produce small molecule orally-active gonadotropin-releasing hormone antagonists. We have identified several series of small molecule compounds and are conducting additional studies to select a final clinical candidate. We hope to select a lead clinical

candidate by year end and expect to initiate Phase I clinical trials in the second half of 2001. We hope that the results of these Phase I studies will be predictive of efficacy in all potential indications. We face the risk that our work in this area may not lead to clinical candidates or that, even if we select a candidate, clinical trials may show it is not safe and effective.

We plan to focus our clinical efforts on prostate cancer and in the area of women's health, including endometriosis, uterine fibroids and infertility. According to a 1993 article in Contemporary OB/GYN, researchers believe that more than five million women in the U.S. alone are affected by chronic endometriosis, representing approximately 10% prevalence in reproductive age women. Of those afflicted, more than 200,000 patients are treated in a hospital setting, and an additional 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 encourage a higher treatment rate. We also hope our drug will be effective against prostate cancer, which has over 180,000 new cases per year in the U.S., according to the American Cancer Society.

Research

Excitatory Amino Acid Transporters

Some of the most successful central nervous system drugs, including selective serotonin reuptake inhibitors such as Prozac(R), selectively target brain amino acid transporters. Similarly, we are targeting a set of proteins generally located in the brain which transport brain chemicals in and out of cells, called excitatory amino acid transporters, to selectively control the levels of a brain chemical called glutamate in order 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 are collaborating with Wyeth-Ayerst Laboratories, a division of American Home Products Corporation, to control glutamate transporter function as a novel strategy for the treatment of neurodegenerative and psychiatric disorders. Our collaboration includes basic research to understand the function and regulation of the transporters, along with the identification and characterization of chemical and biological leads. We face the risks that we may be unable to demonstrate that these excitatory amino acid transporters are therapeutic targets or that we may fail to identify any product candidates for preclinical or subsequent clinical development.

In 2000 we expanded our excitatory amino acid transporter research and initiated a research program focused on retinal cell death associated with damage from low blood flow. The National Institutes of Health awarded us a research grant to fund our work to identify novel compounds for the alleviation of neuronal cell death in response to a wide range of conditions including diabetic induced nerve damage, glaucoma and other circulatory conditions of the eye. This work is independent of our collaboration with Wyeth-Ayerst.

CRF R\\1\\ Peripheral Uses

Recent reports have suggested that corticotropin-releasing factor, or 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 up to 15% of American adults, mostly women, according to the International Foundation for Gastrointestinal Disorders. Irritable bowel syndrome can be a lifelong, intermittent disease, involving chronic or recurrent abdominal pain and frequent diarrhea or constipation, or both. 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, 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. 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. We

are evaluating our proprietary CRF R\\1\\ antagonists for treatment of irritable bowel syndrome. We face the risks that preclinical studies may not warrant initiating clinical testing of these candidates or that any initial clinical data may not support continuation of the program and additional clinical trials.

CRF R\\2\\ Antagonists

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 evaluating our proprietary CRF R\\2\\ antagonist for treatment of a variety of eating disorders. We have screened our small molecule library and conducted exploratory chemistry to identify a new series of compounds to undergo further study. We face the risks that our work in this area will not lead to clinical candidates or that clinical trials will not find our candidates to be safe and effective.

CRF R\\2\\ Agonists/Urocortin Agonist

CRF R\\2\\ agonists may represent a therapeutic strategy to elevate CRF and a related neuropeptide called urocortin. Preliminary data indicate that CRF and urocortin may act as central regulators of both appetite and metabolism. We have evaluated CRF R\\2\\ agonists in various models of obesity and have observed reduced food intake and weight loss. In 1996, in collaboration with Eli Lilly, we initiated a three-year research collaboration 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. We face the risks that Eli Lilly may not initiate further research and that, if they do, the research may not identify suitable candidate compounds for development in a timely manner, or at all.

Melanocortin Receptor Agonists/Antagonists

Melanocortin receptors are proteins on the surface of cells which help regulate some body functions such as eating and skin color. To date, researchers have identified a family of five melanocortin receptor subtypes. Recently, researchers discovered that one of the melanocortin receptor subtypes, subtype 4, plays an important role in the mechanism regulating appetite, body weight and insulin secretion. The subtype 4 receptor is activated by melanocyte stimulating hormone. When melanocyte stimulating hormone is injected, 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 or diabetes. We hope to identify an orally active subtype 4 agonist compound. However, we may fail to do so and we face the risk that our melanocortin research will not lead to product candidates.

Melanin Concentrating Hormone Antagonists

Recent studies suggest that melanin concentrating hormone plays a role in regulating eating behavior. Based on these findings, we believe that blocking the effect of melanin concentrating hormone with a small molecule antagonist may represent a novel approach to the treatment of obesity. Thus, we have identified the melanin concentrating hormone receptor as a compelling drug target that may be complementary to other obesity/anorexia drug targets in our drug discovery pipeline. We face the risk that our research in this area will not lead to product candidates.

Hypocretin

Hypocretins are peptides that researchers have linked to a variety of activities, including the control of eating, cardiovascular regulation and water intake. Recent publications have also reported that hypocretins appear to have a critical role as regulators of sleep. Some studies point to a lack of hypocretin as being

instrumental in the development of narcolepsy and suggest that a small molecule agonist may be able to offset the lack of hypocretin and provide therapy for narcolepsy. It is possible that the hypocretin system also contributes to the regulation of other sleeping disorders such as insomnia, particularly since administration of excess hypocretin into animals promotes wakefulness. We have screened our small molecule library to identify agonists and antagonists for the hypocretin receptors and are in the process of optimizing the compounds that resulted from these screens. We will be using these compounds to further characterize the hypocretin system. We face the risk that our research in this area will not lead to product candidates.

Our Discovery Technology

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

Our Multi-Channel Technology. Our multi-channel technology approach integrates an array of medicinal chemistry, computational and combinatorial tools to facilitate the drug discovery process. At the start of a new project, when we know relatively little about the selected molecular target, we analyze screening data using two-dimensional descriptors of molecular properties. Through a proprietary method, our chemists can search large virtual libraries of novel, readily synthesizable compounds and select for parallel synthesis only those which match the collective properties of the screening hits. Later in the project, once more robust data becomes available, we combine our proprietary filter with more intensive three-dimensional searches. We use these tools, together with the cumulative knowledge and experience of our medicinal chemists and detailed pharmacodynamic and pharmacokinetic measurements, to select compounds that are most likely to proceed through the drug development process.

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 robotics 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 10,000-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.

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 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:

Janssen Pharmaceutica, N.V. In January 1995, we entered into the first of two research and development agreements with Janssen Pharmaceutica, N.V., an indirect wholly-owned subsidiary of Johnson & Johnson, to collaborate in the discovery, development and commercialization of small molecule CRF R\\1\\ antagonists for the treatment of anxiety, depression and substance abuse. These collaborations utilize our expertise in cloning and characterizing CRF R\\1\\ subtypes, CRF pharmacology and medicinal chemistry. Under the January 1995 agreement, Janssen funded three years of research at Neurocrine and received exclusive licenses to all CRF R\\1\\ antagonist compounds developed during the term of the funded research or during the year thereafter. The term of the licenses are for the term of the patents licensed under the agreement. Pursuant to this agreement, we have received $2.0 million in license payments and will receive royalties on product sales for the term of the patents covering the compounds subject to reduction for payments to third parties. We will also receive royalties for products not covered by issued patents and agreed minimum annual royalties. In addition, we have the option of co-promoting the first marketed product from the collaboration in North America for five years. The 1995 agreement will terminate upon the expiration of the patents covering the collaboration products but may also be terminated for failure by either party to meet its obligations, bankruptcy or in some circumstances upon assignment of the agreement by either us or Janssen. In 1996 Janssen selected a clinical candidate from the compounds discovered in connection with the first Janssen agreement and commenced clinical trials in Europe. The collaborative research portion of the first Janssen agreement was completed as scheduled in 1997. In September 1999, together with Janssen, we entered into an amended agreement to expand the collaborative research and development efforts to identify additional small molecule CRF antagonists for the treatment of psychiatric disorders. In connection with the amended Janssen agreement, we received an initial payment and will receive two years of additional research funding for our scientists working in collaboration with Janssen. All collaboration products identified under the 1999 agreement are subject to the same terms and conditions as the products arising under the 1995 agreement.

Under the Janssen agreements, we are entitled to receive up to $39.2 million for sponsored research, milestones and license fees, plus additional amounts for potential royalties and reimbursement of outside costs. The amount we are entitled to receive includes $14.7 million for sponsored research and $2.0 million in license fees, plus up to $13.5 million in milestone payments for the indications of anxiety, depression and substance abuse, in each case upon achievement of development and regulatory goals. As of September 30, 2000, we have received a total of $19.8 million, including $13.6 million in sponsored research, $3.5 million in milestones, $2.0 million in license fees and $684,000 for reimbursement of outside costs. Janssen is responsible for funding all clinical development and marketing activities, including reimbursement to us for our promotional efforts, if any. In connection with the 1995 agreement, Johnson & Johnson Development Corporation purchased $5.0 million of our common stock.

Taisho Pharmaceutical Co., Ltd. In December 1999, we entered into an agreement with Taisho Pharmaceutical Co., Ltd. providing to Taisho an exclusive option to obtain European, Asian and North American development and commercialization rights for our altered peptide ligand product, NBI-6024, for Type I Diabetes. In June 2000, Taisho exercised its option as to Europe and Asia, and we and Taisho formed a steering committee to oversee the worldwide development of NBI-6024. We will receive option fees, license fees, milestone payments and reimbursement of 50% of worldwide development expenses. In addition, we will receive payments on product sales in Europe and Japan for the term of the patents covering NBI-6024 subject to adjustment for payments to third parties. We have retained all rights to NBI-6024 in North America, but Taisho has exercised its option to acquire these rights and we are currently negotiating the terms of the acquisition with Taisho. We received $2 million for the option, and another $3 million for the European and Asian commercialization rights when Taisho initially exercised the option. We are also entitled to receive up to $21.0 million for milestones, plus additional amounts for reimbursement of development costs and potential sublicense fees. As of September 30, 2000, we have received a total of $388,000 in reimbursement of development costs.

Wyeth-Ayerst Laboratories. Effective January 1999, we entered into a Collaboration and License Agreement with Wyeth-Ayerst Laboratories, a division of American Home Products Corporation, relating to the research, development and commercialization of compounds that control excitatory amino acid transporters for the treatment of neurodegenerative and psychiatric diseases. Pursuant to the agreement, we are entitled to receive up to $80.2 million for sponsored research and milestones, plus additional amounts for potential royalties. The amount we are entitled to receive consists of $11.0 million for sponsored research over a three- year period, plus up to $69.2 million in milestone payments upon achievement of certain research, development and regulatory events. We have granted Wyeth-Ayerst exclusive and non-exclusive rights to our excitatory amino acid transporters technology as well as exclusive rights to any products development during the collaboration. These licenses are for the term of the patents licensed. We will receive royalties on 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. We also have the option to co-promote collaboration products in Canada and the United States under some conditions. Wyeth-Ayerst may terminate the agreement if they decide that the research is not successful, if they decide to stop the program or if we are acquired by another company. The agreement may also be terminated by either party for the other party's failure to meet its obligations under the agreement or bankruptcy. As of September 30, 2000, we have received a total of $8.3 million from Wyeth-Ayerst under the agreement, consisting of $5.3 million in sponsored research and $3.0 million in milestone payments.

Eli Lilly and Company. In October 1996, we entered into a research and license agreement with Eli Lilly and Company 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 R\\2\\ agonists for central nervous system diseases and disorders. Under the agreement, we were entitled to receive three years of funded research payments. 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. Through October 1999, we received a total of $17.2 million in research and development payments under the agreement. We have granted Lilly an exclusive worldwide license to manufacture and market CRF binding protein ligand antagonists and CRF R\\2\\ agonist products. The licenses granted under the agreement are for the term of the patents licensed and we are entitled to receive a royalty on product sales for the term of those patents. We have the option to elect to co-promote products for the treatment of dementia in the United States, and receive a portion of the profits resulting from sales subject to our obligation to pay a portion of the development costs for such product rather than royalties. The agreement may be terminated for failure by either party to meet its obligations or if blocking patents prevent the development of products.

Risks Related to Our Strategic Alliances. We face the risks that we or any of the above collaborators may not be successful in research and drug discovery, that any preclinical and clinical drug candidates arising from the collaborations may not generate commercial product candidates that have viable clinical, regulatory and intellectual property profiles or that any commercial products arising from any of these collaborations may not enjoy market acceptance. Therefore, we may never receive any milestone payments or royalty income under any of our collaboration agreements.

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 five issued U.S. patents, approximately 60 pending U.S. patent applications and another approximately 105 issued and pending foreign patents and applications. We have licensed, from institutions such as The Salk Institute, Stanford University, Oregon Health Sciences University, DOV Pharmaceuticals and others, the rights to an additional 30 issued U.S. patents, 20 pending U.S. patent applications, and 50 issued and pending foreign filings. Two of our European patents are subject to opposition proceedings. These proceedings relate to the CRF R\\2\\ patent and our

broad patent covering immune therapeutics in diabetes. If successful, these opposition proceedings could reduce the breadth of some of our proprietary rights, but we believe they would not materially impede our commercialization strategy. 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 unintentionally 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 pending and issued patent claims to melanin concentrating hormone ligand and receptor, the hypocretin ligand and receptor and certain 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. In addition, we are aware of two U.S. 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.

NBI-34060, our leading gamma amino-butyric acid agonist compound for the treatment of insomnia, is covered generically in an issued U.S. patent, which we licensed from DOV Pharmaceuticals. It is not currently covered by any foreign patents of which we are aware. The term of the U.S. patent is due to expire in June 2003. We intend to seek additional protection of this compound in three ways. First, patent term extension under the Hatch/Waxman Patent Term Extension Act may add patent life in the U.S. beyond the June 2003 expiration, depending on the length of clinical trials and other factors involved in the filing of a new drug application. Second, we have filed seven U.S. and foreign patent applications on NBI-34060, its synthesis and formulations, which could extend patent protection to the year 2020. We face the risk that these patents may not issue, or may subsequently be challenged successfully. Third, in addition to this 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 10 years in the European Union, measured from the date of FDA, or corresponding foreign, approval.

In-Licensed Technology

We have in-licensed the following technologies to complement our ongoing clinical and research programs. Most of these licenses extend for the term of the related patent and contain customary royalty, termination and other provisions.

- In August 1999, we licensed nonexclusive rights to the human gonadotropin-releasing hormone receptor from Mount Sinai School of Medicine.

- In January 1999, we licensed exclusive worldwide rights to patents relating to excitatory amino acid transporters and melanocortin 1-5 from Oregon Health Sciences University.

- In December 1998, we licensed nonexclusive rights to technology covering melanocortin subtype 4 from the University of Michigan.

- In June 1998, we licensed exclusive worldwide rights to our sedative compound, NBI-34060, from DOV Pharmaceuticals, Inc.

- In May 1998, we licensed exclusive worldwide rights to patents covering NBI-3001, our IL-4 fusion toxin, from the National Institutes of Health and inventors Ira Pastan and David Fitzgerald.

- In November 1996, we licensed exclusive worldwide rights to technology directed to peptide therapeutics for the treatment of autoimmune disease from Trustees of Dartmouth College.

- In October 1997, we licensed co-exclusive rights to technology relating to the prevention of diabetes from University Technology Corporation.

- In November 1994, we licensed exclusive worldwide rights to technology relating to treatment of multiple sclerosis using peptide analogs of myelin basic protein from Stanford University.

- In November 1993, we licensed exclusive worldwide rights to CRF R\\1\\ from the Salk Institute for Biological Studies.

Manufacturing

We currently rely, and will continue to rely for at least the next few years, on contract manufacturers to produce sufficient quantities of our product candidates for use in our preclinical and anticipated clinical trials. Manufacturers of our NBI-34060 clinical trial material include Organichem Corporation and Pharmaceutics International Inc. Polypeptide Laboratories and Prima Pharm Inc. manufacture our altered peptide ligands NB1-6024 and NB1-5788. Cedarburg Pharmaceuticals and Albany Molecular Research manufacture our CRF antagonist compounds. We also rely, and intend to continue to rely, on third parties to provide the components of these product candidates, such as proteins, peptides, phospholipids, small molecules and bulk chemical materials.

There is currently a limited supply of some of these components. Furthermore, 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.

If we are unable to establish and maintain relationships with third parties for manufacturing sufficient quantities of our product candidates and their components that meet our planned time and cost parameters, it could delay the development and timing of our clinical trials.

Marketing and Sales

We currently have no sales, marketing or distribution capabilities. In order to commercialize any of our product candidates, we must either internally develop sales, marketing and distribution capabilities or make arrangements with third parties to perform these services. We intend to sell, market and distribute some products directly and intend to rely on relationships with third parties to sell, market and distribute other products. Under our collaboration agreements with Janssen, Wyeth-Ayerst and Eli Lilly, we may have the opportunity to co-promote our products in the United States. To market any of our products directly, we must develop a marketing and sales force with technical expertise and with supporting distribution capabilities, none of which we currently have.

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 substantial compliance with appropriate federal and state statutes and regulations require the expenditure of substantial time and financial resources.

Preclinical studies are generally 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 investigative new drug application which must be approved before we can begin clinical trials 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 subjects to determine the early safety profile, maximum tolerated dose and pharmacokinetics 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 trials are conducted with patients afflicted with a target disease in order to provide enough data to demonstrate with substantial evidence the efficacy and safety required by the FDA.

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 conducted many 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 a new drug application, 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. Similar regulatory procedures must also be complied with in countries outside the United States.

If the FDA approves the new drug application, 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.

Orphan Drug Designation

The FDA may grant orphan drug designation to drugs intended to treat a "rare disease or condition," which is generally a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting a new drug application. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. If a product that has orphan drug designation subsequently receives FDA approval for the indication for which it has orphan drug designation, the product is entitled to orphan exclusivity, which means the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years. Our IL-4 fusion toxin product candidate has received orphan drug designation from the FDA for astrocytic glioma.

Approvals Outside the United States

We will 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 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.

Fast Track Designation

Congress enacted the Food and Drug Administration Modernization Act of 1997, in part, to ensure the timely availability of safe and effective drugs, biologics and medical devices by expediting the FDA review process for new products. The Food and Drug Administration Modernization Act establishes a statutory program for the approval of so-called fast track products. The new law defines a fast track product as a new drug or biologic intended for the treatment of a serious or life-threatening condition that demonstrates the potential to address unmet medical needs for such a condition. Under the new fast track program, the sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a fast track product at any time during clinical development of the product. Fast-track designation provides an expedited review of a product, which accelerates FDA review.

We may seek fast track designation to secure expedited review of appropriate product candidates. We can never be sure that we will obtain fast track designation. We cannot predict the ultimate impact, if any, of the new fast track process on the timing or likelihood of FDA approval of any of our potential products. We received fast track designation for our IL-4 fusion toxin.

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 anxiety, depression, insomnia, malignant glioma, other forms of cancer and multiple sclerosis.

In the area of anxiety disorders, our product candidates will compete with well-established products such as Valium(R), marketed by Hoffman-La Roche, Xanax(R), marketed by Pharmacia Upjohn, Buspar(R), marketed by Bristol-Myers-Squibb, and others.

We are also developing products for depression, which will compete with well-established products in the antidepressant class, including Prozac(R), marketed by Eli Lilly, Zoloft(R) marketed by Pfizer, and Paxil(R), marketed by Smith Kline Beecham. Certain technologies under development by other pharmaceutical companies could result in additional commercial treatments for depression and anxiety. In addition, a number of companies are also conducting research on molecules to block CRF, which is the same mechanism of action employed by our compounds.

We are also developing a gamma amino-butyric acid receptor agonist, NBI-34060, for the treatment of insomnia. Ambien(R) and Sonata(R) are already marketed for the treatment of insomnia by Searle/Synthelabo and American Home Products, respectively.

Guilford Pharmaceuticals' Gliadel(R), approved for use in a subset of brain cancers known as malignant glioma, would potentially compete with our IL-4 fusion toxin product, NBI-3001, if our product is approved by the FDA. Temozolomide, marketed by Schering Plough, is approved in Europe only for recurrent malignant glioma, where it may also compete with our IL-4 fusion toxin product.

We are also pursuing development of NBI-3001 for the treatment of peripheral solid tumors, such as kidney cancer and non-small-cell lung cancer. Proleukin(R) is marketed by Chiron for the treatment of kidney cancer, and drug treatments for non-small-cell lung cancer include Platinol(R) and Taxol(R), which are marketed by Bristol-Myers Squibb, and Gemzar(R), which is marketed by Eli Lilly.

Products that may compete with NBI-5788, our altered peptide ligand for multiple sclerosis, include Betaseron(R) and Avonex(R), similar forms of beta-interferon marketed by Berlex BioSciences and Biogen, respectively. Copaxone(R), a peptide polymer marketed by Teva, has also been approved for the marketing in the United States and certain other countries for the treatment of multiple sclerosis.

There are a number of competitors to products in our research pipeline. Lupron Depot(R), marketed by Takeda-Abbott Pharmaceuticals, Zoladex(R), marketed by and AstraZeneca, and Synarel(R), marketed by Pharmacia Upjohn, are gonadotropin-releasing hormone peptide agonists that have been approved for the treatment of prostate cancer, endometriosis, infertility, breast cancer and central precocious puberty. In addition, peptide antagonists, including Abarelix(R) and Antagon Injection(R), are under development by Amgen and Organon, respectively, for these indications. These drugs may compete with any small molecule gonadotropin-releasing hormone antagonists we develop for these indications. Anti-obesity therapeutics currently available include Xenical(R) from Roche Laboratories and Meridia(R) from Knoll Pharmaceuticals. 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 impact our stock price.

Employees

As of October 31, 2000 we had 179 employees, consisting of 169 full-time and 10 part-time employees. Of the full-time employees, approximately 60 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. We are highly dependent on the principal members of our management and scientific staff. If we were to lose the services of any of these personnel, we might not be able to achieve our development objectives. 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 strategy.

Properties

We lease 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. This facility was constructed in 1998 and is under lease through August 2013. Our lease payments are $208,000 per month with annual increases of 4% on September 1st of each year. We have sublet approximately 14,500 square feet of this building to two separate tenants through February 1, 2001 and September 30, 2001, respectively.

We believe that our property and equipment are generally well maintained, in good operating condition and adequate for our current needs.

Legal Proceedings

We are currently not subject to any material legal proceedings.

Our Scientific Advisory Board

We have assembled a Scientific Advisory Board that currently consists of 12 individuals. Members of our Scientific Advisory Board are leaders in the fields of neurobiology, immunology, endocrinology, psychiatry and medicinal chemistry. Our Scientific Advisory Board members meet at least yearly to advise us in the selection, implementation and prioritization of our research programs. Some members meet more frequently to advise us with regard to our specific programs.

Our Scientific Advisory Board presently consists of the following individuals:

Susan G. Amara, Ph.D., a Senior Scientist and Professor at the Vollum Institute for Advanced Biomedical Research, is an expert on the cellular and molecular biology of neurotransmitter transporters, excitatory amino acid transporter structure and regulation and signaling roles of neurotransmitter transporters.

Floyd E. Bloom, M.D., is Chairman of the Department of Neuropharmacology at The Scripps Research Institute. Dr. Bloom is an internationally recognized expert in the fields of neuropharmacology and neurobiology.

Michael Brownstein, M.D., Ph.D., is Chief of the Laboratory of Cell Biology at the National Institute of Mental Health. He is a recognized expert in molecular pharmacology as it applies to the field of neuroendocrinology, where he has defined many of the pharmaceutically important neurotransmitter receptors and transporter systems.

Roger D. Cone, Ph.D., a senior scientist at the Vollum Institute for Advanced Biomedical Research, is an international expert on the neuroendocrine system, with particular expertise on the melanocortin system and the hypothalamic control of energy homeostasis. Dr. Cone is an editor of the journal Endocrinology.

Stephen M. Hedrick, Ph.D., is Professor and Chairman of Cell Biology at the University of California, San Diego. Dr. Hedrick is an expert in T cell immunology and co-discovered the first T cell receptor genes and identified the regions responsible for antigen binding. He is an editor for the Journal of Immunology.

Florian Holsboer, M.D., Ph.D., is Director at the Max Planck Institute fur Psychiatrie. Dr. Holsboer is an international expert on the role of glucocorticoids and neuropeptides, particularly CRF, in neuropsychiatric disorders. He coordinates the efforts of several hundred scientists and clinicians at the Max Planck Institute, a major European neuropsychiatric institute.

George F. Koob, Ph.D., is a Member of the Department of Neuropharmacology at The Scripps Research Institute and an Adjunct Professor in the Departments of Psychology and Psychiatry at the University of California, San Diego. Dr. Koob is an internationally recognized behavioral pharmacology expert on the role of peptides in the central nervous system, the neurochemical basis of addiction and in the development of preclinical behavioral procedures for the screening of anxiolytic and antidepressant drugs and memory enhancers.

Charles B. Nemeroff, M.D., Ph.D., is Chairman and Professor of the Department of Psychiatry and Behavioral Sciences at Emory University School of Medicine. Dr. Nemeroff is an internationally recognized expert on the effects of neuropeptides on behavior and their relevance in clinically important conditions such as depression, anxiety and schizophrenia, and has published over 400 articles on this subject.

Thomas Roth, Ph.D., is the Head of the Division of Sleep Disorder Research at the Henry Ford Hospital Research Institute. Dr. Roth is an internationally recognized expert in the field of sleep research. His areas of specialization are sleep homeostasis and neuropharmacology of sleep.

Lawrence J. Steinman, M.D., is our Chief Scientific Advisor, Neuroimmunology and a member of our Founding Board of Scientific and Medical Advisors and our Executive Committee.

Wylie W. Vale, Ph.D., is our Chief Scientific Advisor, Neuroendocrinology and a member of our Founding Board of Scientific and Medical Advisors and our Executive Committee.

Stanley J. Watson, Jr., M.D., Ph.D., is Professor and Associate Chair for Research in the Department of Psychiatry and Co-Director of the Mental Health Research Institute at the University of Michigan. Dr. Watson is a recognized expert in neuropeptides and their receptors and their role in psychiatric diseases and behavior. Dr. Watson is also a member of the Institute of Medicine of the National Academy of Sciences.

Each of the members of our Scientific Advisory Board has signed a consulting agreement that contains confidentiality provisions and restricts him or her from competing with us for the term of the agreement. Each member of our Scientific Advisory Board receives either a per diem consulting fee or a retainer fee. Each member also has received Neurocrine stock or stock options, which vest over time. All members of our Scientific Advisory Board are full-time employees of a university or research institute that has regulations and policies which limit their ability to act as part-time consultants or in other capacities for any commercial enterprise, including Neurocrine. A change in these regulations or policies could adversely affect our relationship with any of our Scientific Advisory Board members.

MANAGEMENT

Executive Officers and Directors

Our Executive Officers and Directors are as follows:

Name	Age	Position
Gary A. Lyons.....	49	President, Chief Executive Officer and Director
Paul W. Hawran.....	48	Executive Vice President and Chief Financial Officer
D. Bruce Campbell, Ph.D.	55	Senior Vice President, Development
Margaret E. Valeur-Jensen, J.D., Ph.D. ...	43	Senior Vice President, General Counsel and Corporate Secretary
Joseph A. Mollica, Ph.D. (1)(2).....	59	Chairman of the Board of Directors
Richard F. Pops (1).....	38	Director
Stephen A. Sherwin, M.D.(2).....	52	Director
Wylie W. Vale, Ph.D. ...	59	Director

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(1) Member of the Audit Committee

(2) Member of the Compensation Committee

Gary A. Lyons has served as our President, Chief Executive Officer and a Director 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 Vice President of Business Development, Mr. Lyons was responsible for international licensing, acquisitions and partnering. He was also responsible for Genentech's Corporate Venture Program, which participated in early financing and/or formation of a number of biotechnology companies. In addition, Mr. Lyons had operating responsibility for Genentech's two subsidiaries, Genentech Canada, Inc. and Genentech Limited (Japan). As Vice President of Sales, Mr. Lyons 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 for 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 2000 after having served as our Senior Vice President and Chief Financial Officer since February 1996 and our Vice President and Chief Financial Officer from 1993 to 1996. Mr. Hawran directs strategic planning, finance, 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 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 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, California and Pennsylvania Institute of Certified Public Accountants and the Financial Executives Institute.

D. Bruce Campbell, Ph.D., became our Senior Vice President, Development in January 2000 after having joined us as Vice President, Development in February 1998. In his capacity, Dr. Campbell is responsible for directing our selection and advancement of drug candidates from research into clinical development. He joined us after 27 years at Servier United Kingdom (U.K.), 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 since 1991 and was involved in the development and registration of a wide range of drugs and vaccines for the treatment of sleep disorders, depression, diabetes, cancer, obesity, neurodegenerative diseases, hypertension, hyperlipidaemia, respiratory disease, peripheral vascular disease,

osteoporosis, flu and tetanus, and blood products such as Factor VIII and albulmin. Dr. Campbell is a past Chairman and Board Member of the Drug Information Association (DIA) and member of the ICH/EFPIA Safety Working Party and is a visiting Professor in Pharmacology at Guys and Kings College London UK. He is recognized as one of the experts on the regulatory aspects of kinetics and toxicology in new drug development and has written standard texts on the subject. Dr. Campbell is also on the editorial board of international journals and a member of many scientific societies and has published more than 100 papers. He is a Fellow of the Royal Society of Chemistry and received 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. Dr. Valeur-Jensen has recognized experience in legal transactions for licensing, corporate partnerships and product commercialization as well as in building intellectual property portfolios. She is responsible for all of our corporate and patent law practices and is a member of our senior management committee. From 1995 to 1998, Dr. Valeur-Jensen 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. She earned a J.D. degree with honors from Stanford University, a Ph.D. in Biochemistry and Molecular Biology from Syracuse University, and was Post-Doctoral Fellow at Massachusetts General Hospital and Harvard Medical School.

Joseph A. Mollica, Ph.D., has served as one of our Directors since June 1997 and became Chairman of the Board in April 1998. Since February 1994, Dr. Mollica 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, Dr. Mollica served as Vice President, Medical Products of DuPont Company and then as President and CEO of DuPont Merck Pharmaceutical Company from 1991 to 1993. At Ciba-Geigy, where he was employed from 1966 to 1986, Dr. Mollica served in a variety of positions of increasing responsibility, rising to Senior Vice President of Ciba-Geigy's Pharmaceutical Division. Dr. Mollica is currently on the Boards of Pharmacopeia, Inc., Impath, Inc. and Nexell Therapeutics, Inc. He received his B.S. from the University of Rhode Island and his M.S. and Ph.D. from the University of Wisconsin.

Richard F. Pops became one of our Directors in April 1998. Since 1991, he has served as Chief Executive Officer of Alkermes, Inc., a publicly traded company involved in the development of pharmaceutical products based on advanced drug delivery systems. Mr. Pops currently serves on the board of directors of Alkermes, Genomics Collaborative, Inc., the Biotechnology Industry Organization, the Massachusetts Biotechnology Council and The Brain Tumor Society, and is Chairman of the Advisory Board of the Department of Biological Chemistry and Molecular Pharmacology at Harvard Medical School. He received a B.A. degree in Economics from Stanford University in 1983.

Stephen A. Sherwin, M.D., was elected to our Board of Directors on April 22, 1999. Since March 1990, Dr. Sherwin has served as Chief Executive Officer and Director of Cell Genesys, Inc. 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, Inc., most recently as Vice President of Clinical Research. Prior to 1983, Dr. Sherwin held various positions on the staff of the National Cancer Institute. He also serves as a Director of Abgenix, Inc., Calyx Therapeutic, Inc. and Rigel Pharmaceuticals, Inc. Dr. Sherwin holds a B.A. from Yale and an M.D. from Harvard Medical School.

Wylie W. Vale, Ph.D., is a Founder and Chairman of our Board of Scientific and Medical Advisors. Dr. Vale was elected a Director in September 1992. He is a Professor and former Chairman of the Faculty at The Salk Institute for Biological Studies and is the Senior Investigator and Head of The Clayton Foundation Laboratories for Peptide Biology at The Salk Institute, where he has been employed for 29 years. He is also an Adjunct Professor of Medicine at the University of California at San Diego and was recently elected to the Institute of Medicine. Dr. Vale is recognized for his work on the molecular, pharmacological and biomedical characterization of neuroendocrine factors including somatostatin, growth hormone releasing factor,

gonadotropin-releasing hormone activin and the activin receptor (the first receptor serine kinase), corticotropin-releasing factor, CRF-binding protein, the CRF R\\1\\ receptor and urocortin, the native ligand for the CRF R\\2\\ receptor. In recognition of his discoveries, he has received numerous awards and is a member of the National Academy of Arts and Sciences 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.

PRINCIPAL STOCKHOLDERS

The following table sets forth the beneficial ownership of our common stock as of October 31, 2000 by (i) each of our executive officers, (ii) each of our directors, (iii) all of our directors and executive officers as a group and (iv) all persons known to us to be the beneficial owners of more than 5% of our common stock. A total of 22,066,248 shares of our common stock were issued and outstanding as of October 31, 2000.

Name and Address of Beneficial Owner(1)	Shares Beneficially Owned(2)	Percent of Outstanding Shares	Percent of Outstanding Shares After This Offering
T. Rowe Price Associates 100 East Pratt Street, Baltimore, MD 21202	1,687,800	7.65%	6.73%
D. Bruce Campbell(3)	117,584	*	*
Paul W. Hawran(4)	369,657	1.66%	1.46%
Gary A. Lyons(5)	957,998	4.24%	3.74%
Margaret E. Valeur-Jensen(6)	71,097	*	*
Joseph A. Mollica(7)	42,773	*	*
Richard F. Pops(8)	16,498	*	*
Stephen A. Sherwin(9)	13,304	*	*
Wylie W. Vale(10)	442,183	1.99%	1.75%
All executive officers and Directors as a group (8 persons)(11)	2,031,094	8.74%	7.74%

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* Represents beneficial ownership of less than one percent (1%) of the 22,066,248 outstanding shares of our common stock as of October 31, 2000.

(1) The address of each individual named is Neurocrine Biosciences, Inc., 10555 Science Center Drive, San Diego, CA 92121, unless otherwise indicated.

(2) Beneficial ownership is determined in accordance with the rules of the Securities and Exchange Commission and generally includes voting or investment power with respect to securities. Shares of common stock subject to stock options and warrants currently exercisable or exercisable within 60 days of October 31, 2000 are deemed to be outstanding for computing the percentage ownership of the person holding such options and the percentage ownership of any group of which the holder is a member, but are not deemed outstanding for computing the percentage of any other person. Except as indicated by footnote, and subject to community property laws where applicable, the persons named in the table have sole voting and investment power with respect to all shares of common stock shown beneficially owned by them.

(3) Includes 117,087 shares issuable pursuant to options exercisable within 60 days of October 31, 2000.

(4) Includes 255,359 shares issuable pursuant to options exercisable within 60 days of October 31, 2000.

(5) Includes 535,642 shares issuable pursuant to options exercisable within 60 days of October 31, 2000.

(6) Includes 64,279 shares issuable pursuant to options exercisable within 60 days of October 31, 2000.

(7) Includes 42,773 shares issuable pursuant to options exercisable within 60 days of October 31, 2000.

(8) Includes 16,498 shares issuable pursuant to options exercisable within 60 days of October 31, 2000.

(9) Includes 13,304 shares issuable pursuant to options exercisable within 60 days of October 31, 2000.

(10) Includes 133,053 shares issuable pursuant to options exercisable within 60 days of October 31, 2000.

(11) Includes an aggregate of 1,177,995 shares issuable pursuant to options exercisable within 60 days of October 31, 2000.

UNITED STATES TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following is a general discussion of the principal United States federal income and estate tax consequences of the acquisition, ownership and disposition of our common stock by a Non-U.S. Holder. As used in this prospectus, the term "Non-U.S. Holder" is a person who holds our common stock other than:

- a citizen or resident of the United States,
- a corporation or other entity taxable as a corporation created or organized in or under the laws of the United States or of any political subdivision of the United States,
- an estate the income of which is includable in gross income for United States federal income tax purposes regardless of its source, or
- a trust subject to the primary supervision of a United States court and the control of one or more United States persons, or a trust (other than a wholly-owned grantor trust) that was treated as a domestic trust despite not meeting the requirements described above.

This discussion does not consider:

- state, local or foreign tax consequences,
- specific facts and circumstances that may be relevant to a particular Non-U.S. Holder's tax position in light of their particular circumstances,
- the tax consequences for the stockholders or beneficiaries of a Non-U.S. holder,
- special tax rules that may apply to certain Non-U.S. Holders, including without limitation, partnerships, banks, insurance companies, dealers in securities and traders in securities, or
- special tax rules that may apply to a Non-U.S. Holder that holds our common stock as part of a "straddle," "hedge" or "conversion transaction."

The following discussion is based on provisions of the United States Internal Revenue Code of 1986, as amended, also known as the Code, applicable Treasury regulations and administrative and judicial interpretations, all as of the date of this prospectus, and all of which are subject to change, retroactively or prospectively. The following discussion assumes that our common stock is held as a capital asset. The following summary is for general information. Accordingly, each Non-U.S. Holder should consult a tax advisor regarding the United States federal, state, local and foreign income and other tax consequences of acquiring, holding and disposing of shares of our common stock.

Dividends

We do not anticipate paying cash dividends on our common tock in the foreseeable future. See "Dividend Policy." In the event, however, that dividends are paid on shares of our common stock, dividends paid to a Non-U.S. Holder of our common stock generally will be subject to withholding of United States federal income tax at a 30% rate, or such lower rate as may be provided by an applicable income tax treaty.

Dividends that are effectively connected with a Non-U.S. Holder's conduct of a trade or business in the United States or, if an income tax treaty applies, attributable to a permanent establishment in the United States, known as "United States trade or business income," are generally subject to United States federal income tax on a net income basis at regular graduated rates, but are not generally subject to the 30% withholding tax if the Non-U.S. Holder files the appropriate United States Internal Revenue Service form with the payor. Any United States trade or business income received by a Non-U.S Holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as specified by an applicable income tax treaty.

Dividends paid prior to 2001 to an address in a foreign country are presumed, absent actual knowledge to the contrary, to be paid to a resident of such country for purposes of the withholding discussed above and for purposes of determining the applicability of a tax treaty rate. For dividends paid after 2000, a Non-U.S. Holder of our common stock who claims the benefit of an applicable income tax treaty rate generally will be required to satisfy applicable certification and other requirements. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A Non-U.S. Holder of our common stock that is eligible for a reduced rate of United States withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by filing an appropriate claim for a refund with the United States Internal Revenue Service.

Gain on Disposition of Common Stock

A Non-U.S. Holder generally will not be subject to United States federal income tax in respect of gain recognized on a disposition of our common stock unless:

- the gain is United States trade or business income, in which case the branch profits tax described above may apply to a corporate Non-U.S. Holder,

- the Non-U.S. Holder is an individual who holds our common stock as a capital asset within the meaning of Section 1221 of the Code, is present in the United States for more than 182 days in the taxable year of the disposition and meets certain other requirements,

- the Non-U.S. Holder is subject to tax pursuant to the provisions of the United States tax law applicable to certain United States expatriates, or

- we are or have been a "United States real property holding corporation" for United States federal income tax purposes at any time during the shorter of the five-year period ending on the date of disposition or the period that the Non-U.S. Holder held our common stock.

Generally, a corporation is a "United States real property holding corporation" if the fair market value of its "United States real property interest" equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. We believe we have never been, are not currently and are not likely to become a United States real property holding corporation for United States federal income tax purposes.

Federal Estate Tax

Common stock owned or treated as owned by an individual who is a Non-U.S. Holder at the time of death will be included in the individual's gross estate for United States federal estate tax purposes, unless an applicable estate tax or other treaty provides otherwise.

Information Reporting and Backup Withholding Tax

We must report annually to the United States Internal Revenue Service and to each Non-U.S. Holder the amount of dividends paid to that holder and the tax withheld with respect to those dividends. Copies of the information returns reporting those dividends and withholding may also be made available to the tax authorities in the country in which the Non-U.S. Holder is a resident under the provisions of an applicable income tax treaty or agreement.

Under certain circumstances, United States Treasury Regulations require information reporting and backup withholding at a rate of 31% on certain payments on our common stock. Under currently applicable law, Non-U.S. Holders of our common stock, generally will be exempt from backup withholding on dividends paid prior to 2001 to an address outside the United States. For dividends paid after 2000, however, a Non-U.S. Holder of our common stock that fails to certify its Non-U.S. holder status in accordance with applicable United States Treasury Regulations may be subject to backup withholding at a rate of 31% of dividends.

The payment of the proceeds of the disposition of our common stock by a holder to or through the United States office of a broker generally will be subject to information reporting and backup withholding at a rate of 31% unless the holder either certifies its status as a Non-U.S. Holder under penalties of perjury or otherwise establishes an exemption. The payment of the proceeds of the disposition by a Non-U.S. Holder of our common stock to or through a foreign office of a foreign broker will not be subject to backup withholding or information reporting unless the foreign broker is a "United States related person." In the case of the payment of proceeds from the disposition of our common stock by or through a foreign office of a broker that is a United States person or a "United States related person," information reporting, but currently not backup withholding, on the payment applies unless the broker receives a statement from the owner, signed under penalty of perjury, certifying its foreign status or the broker has documentary evidence in its files that the holder is a Non-U.S. Holder and the broker has no actual knowledge to the contrary. For this purpose, a "United States related person" is:

- a "controlled foreign corporation" for United States federal income tax purposes,

- a foreign person 50% or more of whose gross income from all sources for the three-year period ending with the close of its taxable year preceding the payment, or for such part of the period that the broker has been in existence, is derived from activities that are effectively connected with the conduct of a United State trade or business,

- effective after 2000, a foreign partnership if, at any time during the taxable year, (A) at least 50% of the capital or profits interest in the partnership is owned by United States persons, or (B) the partnership is engaged in a United States trade or business, or

- certain U.S. branches of foreign banks or insurance companies.

Effective after 2000, backup withholding may apply to the payment of disposition proceeds by or through a foreign office or a broker that is a United States person or a United States related person unless certain certification requirements are satisfied or an exemption is otherwise established and the broker has no actual knowledge that the holder is a United States person. Non-U.S. Holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them, including changes to these rules that will become effective after 2000.

Any amounts withheld under the backup withholding rules from a payment to a Non-U.S. Holder will be refunded, or credited against the holder's United States federal income tax liability, if any, provided that the required information is furnished to the United States Internal Revenue Service.

UNDERWRITING

We are offering the shares of common stock described in this prospectus through a number of underwriters. Robertson Stephens, Inc. and Salomon Smith Barney Inc. are the representatives of the underwriters. We will enter into an underwriting agreement with the representatives. Subject to the terms and conditions of the underwriting agreement, we will sell to the underwriters, and each underwriter will separately purchase from us, the number of shares of common stock listed next to its name below at the public offering price, less the underwriting discount described on the cover page of this prospectus:

Underwriter	Number of Shares
Robertson Stephens, Inc.	
Salomon Smith Barney Inc.	
International Underwriter	
Robertson Stephens International, Ltd.	
Salomon Smith Barney Inc.	
Total	3,000,000

The underwriting agreement will provide that the underwriters must buy all of these shares from us if they buy any of them. The underwriters will sell these shares to the public when and if the underwriters buy them from us. The underwriters are offering the common stock subject to a number of conditions, including:

- the underwriters' receipt and acceptance of the common stock from us; and
- the underwriters' right to reject orders in whole or in part.

The underwriters expect to deliver the shares of common stock to purchasers on , 2000.

Over-Allotment Option. We will grant the underwriters an option to buy up to 450,000 additional shares of our common stock at the same price per share as they are paying for the shares shown in the table above. The underwriters may exercise this option only to the extent that they sell more than the total number of shares shown in the table above. The underwriters may exercise this option at any time within 30 days after the date of this prospectus. To the extent that the underwriters exercise this option, the underwriters will be obligated to purchase additional shares from us in the same proportions as they purchased the shares shown in the table above. If purchased, these additional shares will be sold by the underwriters on the same terms as those on which the other shares are sold.

Stock Market Listing. Our common stock is quoted on the Nasdaq National Market under the symbol "NBIX."

Underwriting Discounts and Commissions. The underwriting discount is the difference between the price the underwriters pay to us and the price at which the underwriters initially offer the shares to the public. The size of the underwriting discount is determined through an arms-length negotiation between us and the representatives. The following table shows the per share and total underwriting discount we will allow to the underwriters. These amounts are shown assuming no exercise and full exercise of the underwriters' over-allotment option described above:

		Total	
	Per Share	No Exercise of Option	Full Exercise of Option
Public offering price	$	$	$
Underwriting discount	$	$	$

Proceeds, before expenses, to us.....	$	$	$

The expenses of this offering, not including the underwriting discount, are estimated to be approximately $495,000 and will be paid by us. Expenses include the SEC filing fee, the NASD filing fee, Nasdaq listing fees, printing expenses, legal and accounting fees, transfer agent and registrar fees and other miscellaneous fees and expenses.

Lock-Up Agreements. We and our executive officers and directors have agreed, with exceptions, not to sell or transfer any shares of our common stock for 90 days after the date of this prospectus without first obtaining the written consent of Robertson Stephens, Inc. Specifically, we and these other individuals have agreed not to, directly or indirectly:

- offer to sell, contract to sell, or otherwise sell or dispose of any shares of our common stock;
- loan, pledge or grant any rights with respect to any shares of our common stock;
- engage in any hedging or other transaction that might result in a disposition of shares of our common stock by anyone;
- execute any short sale, whether or not against the box; or
- purchase, sell or grant any put or call option or other right with respect to our common stock or with respect to any security other than a broad-based market basket or index that includes, relates to or derives any significant part of its value from our common stock.

These lock-up agreements do not prohibit bona fide gifts, or transfers in connection with bona fide estate planning, provided the transferees agree in writing to be bound by the lock-up agreement. These lock-up agreements apply to shares of our common stock and also to any options or warrants to purchase any shares of our common stock or any securities convertible into or exchangeable for shares of our common stock. These lock-up agreements apply to all such securities that are owned or later acquired by the persons executing the agreements, except for securities acquired on the open market after signing the lock-up agreement. In addition, we have agreed with Robertson Stephens, Inc. that, to the extent that we have separate market stand-off agreements with our officers and directors, we will not consent to the stockholders' disposition of any shares subject to those separate market stand-off agreements prior to the expiration of the lock-up period. However, Robertson Stephens, Inc. may release any of us from these agreements at any time during the 90-day period, in its sole discretion and without notice, as to some or all of the shares covered by these agreements. Robertson Stephens will consider each lock-up release request on a case by case basis. Among the factors that may be relevant to its consideration are the number of shares proposed to be transferred as compared to the recent average daily trading volume of the stock, the recent strength of the stock price, Robertson Stephens's sense of how the market would react to the announcement of a sale by the particular insider and whether Robertson Stephens, on behalf of the underwriting syndicate, is still engaged in stabilization activity as permitted by Regulation M. Currently, there are no agreements between the representatives and us or any of our stockholders to release any of us from the lock-up agreements during this 90-day period.

Indemnification of the Underwriters. We will indemnify the underwriters against some civil liabilities, including liabilities under the Securities Act and liabilities arising from breaches of our representations and warranties contained in the underwriting agreement. If we are unable to provide this indemnification, we will contribute to payments the underwriters may be required to make in respect of those liabilities.

Dealers' Compensation. The underwriters initially will offer our shares to the public at the price specified on the cover page of this prospectus. The underwriters may allow to selected dealers a concession of not more than $ per share. The underwriters may also allow, and any other dealers may reallow, a concession of not more than $ per share to some other dealers. If all the shares are not sold at the public offering price, the underwriters may change the public offering price and the other selling terms. A change in the public offering price will not affect the amount of proceeds that we receive.

Online Activities. A prospectus in electronic format may be made available on the internet sites or through other online services maintained by one or more of the underwriters of this offering, or by their

affiliates. In those cases, prospective investors may view offering terms online and, depending upon the particular underwriter, prospective investors may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares for sale to online brokerage account holders. Any such allocation for online distributions will be made by the representatives on the same basis as other allocations. Other than the prospectus in electronic format, information on these web sites is not a part of this prospectus and you should not rely on other information on these web sites in making a decision to invest in our shares. Neither of the representatives intends to confirm sales through electronic delivery or by any means other than by hand or the mails. Neither of the representatives intends to confirm sales with an electronic prospectus or with any form of prospectus other than a printed prospectus.

Stabilization and Other Transactions. The rules of the SEC generally prohibit the underwriters from trading in our common stock on the open market during this offering. However, the underwriters are allowed to engage in some open market transactions and other activities during this offering that may cause the market price of our common stock to be above or below that which would otherwise prevail in the open market. These activities may include stabilization, short sales and over-allotments, syndicate covering transactions and penalty bids.

- Stabilizing transactions consist of bids or purchases made by the lead representative for the purpose of preventing or slowing a decline in the market price of our common stock while this offering is in progress.

- Short sales and over-allotments occur when the representatives, on behalf of the underwriting syndicate, sell more of our shares than they purchase from us in this offering. "Covered" shorts are short sales made in an amount not greater than the underwriters' option to purchase additional shares from us in the offering. The underwriters may close out any covered short position either by exercising that option to purchase shares from us or by purchasing shares in the open market. In determining the source of shares to close out a covered short position, the underwriters will consider, among other things, the prevailing market price per share compared to the exercise price per share of their option. "Naked" shorts are any short sales by the underwriters in excess of their option. The underwriters must close out any naked short position by purchasing shares in the open market, potentially including purchases made as stabilizing transactions. For this reason, 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.

- Syndicate covering transactions are bids for or purchases of our common stock on the open market by the representatives on behalf of the underwriters in order to reduce a short position incurred by the representatives on behalf of the underwriters. Similar to other purchase transactions, syndicate covering transactions may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market.

- A penalty bid is an arrangement permitting the representatives to reclaim the selling concession that would otherwise accrue to an underwriter if the common stock originally sold by that underwriter was later repurchased by the representatives and therefore was not effectively sold to the public by such underwriter.

If the underwriters commence these activities, they may discontinue them at any time without notice. The underwriters may carry out these transactions on the Nasdaq National Market, in the over-the-counter market or otherwise.

Passive Market Making. Prior to the pricing of this offering, and until the commencement of any stabilizing bid, underwriters and dealers who are qualified market makers on the Nasdaq National Market may engage in passive market making transactions. Passive market making is allowed during the period when the SEC's rules would otherwise prohibit market activity by the underwriters and dealers who are participating in

this offering. Passive market makers must comply with applicable volume and price limitations and must be identified as such. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for our common stock; but if all independent bids are lowered below the passive market maker's bid, the passive market maker must also lower its bid once it exceeds specified purchase limits. Net purchases by a passive market maker on each day are limited to a specified percentage of the passive market maker's average daily trading volume in our common stock during a specified period and must be discontinued when such limit is reached. Underwriters and dealers are not required to engage in passive market making and may end passive market making activities at any time.

Some of the underwriters have in the past and may in the future perform financial advisory services for us.

LEGAL MATTERS

The validity of the shares of our common stock offered hereby will be passed upon by Latham & Watkins, San Francisco, California, counsel to the Company. Certain legal matters will be passed upon for the underwriters by O'Melveny & Myers LLP, San Francisco, California, counsel to the underwriters.

EXPERTS

Our financial statements appearing in our Annual Report on Form 10-K for the year ended December 31, 1999 have been audited by Ernst & Young LLP, independent auditors, as set forth in their report thereon included therein and incorporated herein by reference. Such financial statements are incorporated herein by reference in reliance upon such report given upon the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the informational requirements of the Securities Exchange Act of 1934, as amended. Accordingly, we file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission. You may read and copy any document that we have filed at the SEC's public reference rooms in Washington, D.C., New York, New York, and Chicago, Illinois. Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms. You can obtain copies of our SEC filings at prescribed rates from the SEC Public Reference Section at 450 Fifth Street, N.W., Washington, D.C. 20549. Our SEC filings are also available to you free of charge at the SEC's web site at http://www.sec.gov. Information contained in our web site is not part of this prospectus.

Shares of our common stock are traded as "National Market Securities" on the Nasdaq National Market. Documents we have filed can be inspected at the offices of the National Association of Securities Dealers, Inc., Reports Section, 1735 K Street, N.W., Washington, D.C. 20006.

This prospectus is a part of a registration statement on Form S-3 filed by us with the SEC under the Securities Act of 1933, as amended. This prospectus does not contain all of the information set forth in the registration statement, certain parts of which are omitted in accordance with the rules and regulations of the SEC. For further information with respect to us and the shares of common stock we are offering hereby, please refer to the registration statement. The registration statement may be inspected at the public reference facilities maintained by the SEC at the addresses set forth above. Statements in this prospectus about any document filed as an exhibit are not necessarily complete and, in each instance, you should refer to the copy of such document filed with the SEC. Each such statement is qualified in its entirety by such reference.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" the information filed with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and information that we have filed later with the SEC will automatically update and supersede previously filed information, including information contained in this prospectus.

We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act until this offering has been completed:

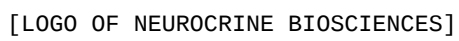
- Our Annual Report on Form 10-K for the fiscal year ended December 31, 1999 (File No. 000-22705) (including information specifically incorporated by reference into our Form 10-K from our 2000 Annual Report to Stockholders and Proxy Statement for our 2000 Annual Meeting of Stockholders), filed with the SEC on March 30, 2000, as amended by our Amended Annual Report on Form 10-K/A;

- Our Current Report on Form 8-K, filed with the SEC on April 6, 2000;
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2000, filed with the SEC on May 15, 2000;
- Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2000, filed with the SEC on August 11, 2000;
- Our Quarterly Report on Form 10-Q for the quarter ended September 30, 2000, filed with the SEC on November 8, 2000;
- The description of our common stock contained in our registration statement on Form 8-A (Registration No. 000-28150), as amended, filed with the SEC on April 3, 1996; and
- The description of the preferred share purchase rights contained in our registration statement on Form 8-A (Registration No. 000-22705), as amended, filed with the SEC on June 16, 1997.

You may request a free copy of these documents by writing to Investor Relations, Neurocrine Biosciences, Inc., 10555 Science Center Drive, San Diego, California 92121, or by calling our Investor Relations department at (858) 658-7600.

"Neurocrine Biosciences" is our trademark. This prospectus also contains trademarks and tradenames of other companies.

You should rely only on the information incorporated by reference or provided in this prospectus or a prospectus supplement or amendment. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. Also, this prospectus does not offer to sell any securities other than the securities covered by this prospectus. You should not assume that the information in this prospectus or a prospectus supplement or amendment is accurate as of any date other than the date on the front of the document.


[LOGO OF NEUROCRINE BIOSCIENCES]

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

SUBJECT TO COMPLETION, DATED NOVEMBER 22, 2000

[LOGO OF NEUROCRINE BIOSCIENCES]

3,000,000 Shares
Common Stock

Neurocrine Biosciences, Inc. is offering 3,000,000 shares of its common stock. Neurocrine Biosciences, Inc.'s common stock is traded on the Nasdaq National Market under the symbol "NBIX." The last reported sale price of the common stock on the Nasdaq National Market on November 21, 2000 was $33.13 per share.

Investing in our common stock involves risks.
See "Risk Factors" beginning on page 5.

	Per Share	Total
Public Offering Price	$	$
Underwriting Discounts and Commissions	$	$
Proceeds to Neurocrine Biosciences, Inc.	$	$

The United States Securities and Exchange Commission has not approved or disapproved these securities, or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Neurocrine Biosciences, Inc. has granted the underwriters a 30-day option to purchase up to an additional 450,000 shares of common stock to cover over-allotments.

Robertson Stephens International | Salomon Smith Barney Inc.

The date of this prospectus is , 2000.

PART II

INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The Company will pay all expenses incident to the offering and sale to the public of the shares being registered other than any commissions and discounts of underwriters, dealers or agents and any transfer taxes. Such expenses are set forth in the following table. All of the amounts shown are estimates except the SEC registration fee, the NASD filing fee and the Nasdaq National Market listing fee.

SEC registration fee	$ 38,226
Nasdaq listing fee	17,500
NASD filing fee	14,990
Printing and engraving expenses	100,000
Legal fees and expenses	250,000
Accounting fees and expenses	60,000
Miscellaneous expenses	14,500
Total	$495,216

Item 15. Indemnification of Directors and Officers.

Section 145 of the General Corporation Law of the State of Delaware provides that a corporation has the power to indemnify a director, officer, employee or agent of the corporation and certain other persons serving at the request of the corporation in related capacities against amounts paid and expenses incurred in connection with an action or proceeding to which he or she is or is threatened to be made a party by reason of such position, if such person has acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal proceeding, if such person had no reasonable cause to believe his or her conduct was unlawful; provided that, in the case of actions brought by or in the right of the corporation, no indemnification may be made with respect to any matter as to which such person has been adjudged to be liable to the corporation unless and only to the extent that the adjudicating court determines that such indemnification is proper under the circumstances. The termination of any action, suit or proceeding by judgment, order, settlement, conviction, or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that the person did not act in good faith and in a manner which the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that his or her conduct was unlawful.

The Registrant's Certificate of Incorporation provides that to the fullest extent permitted by the General Corporation Law of the State of Delaware as the same now exists or as may hereafter be amended, no director shall be personally liable to the Registrant or its stockholders for monetary damages for breach of fiduciary duty as a director, except for liability (i) for any breach of the director's duty of loyalty to the Registrant or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) for authorizing the payment of a dividend or repurchase of stock or (iv) for any transaction in which the director derived an improper personal benefit.

The Registrant's bylaws provide that the Registrant shall, to the maximum extent and in the manner permitted by the General Corporation Law of the State of Delaware as the same now exists or may hereafter be amended, indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending, or completed action, suit or proceeding by reason of the fact that (i) he or she is or was a director or officer of the Registrant, (ii) he or she is or was serving at the request of the Registrant as a director or officer of another corporation, partnership, joint venture, trust or other enterprise, or (iii) he or she was a director or officer of a corporation which was a predecessor corporation of the Registrant or of another enterprise at the request of such predecessor corporation, against expenses (including attorney's fees), judgments, fines and

amounts paid in settlement actually and reasonably incurred by him or her in connection with such action, suit or proceeding.

The Registrant's bylaws provide further that the Registrant, to the maximum extent and in the manner permitted by the General Corporation Law of the State of Delaware as the same now exists or may hereafter be amended, has the power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending, or completed action, suit or proceeding by reason of the fact that (i) he or she is or was an employee or agent (other than a director or officer) of the Registrant, (ii) he or she is or was serving at the request of the Registrant as an employee or agent (other than a director or officer) of another corporation, partnership, joint venture, trust or other enterprise, or (iii) he or she was an employee or agent (other than a director or officer) of a corporation which was a predecessor corporation of the Registrant or of another enterprise at the request of such predecessor corporation, against expenses (including attorney's fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by him or her in connection with such action, suit or proceeding.

Pursuant to its bylaws, the Registrant has the power to purchase and maintain a directors and officers liability policy to insure its directors and officers against certain liabilities.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers or persons controlling the Registrant pursuant to the foregoing provisions, the Registrant has been informed that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is therefore unenforceable.

Item 16. Exhibits.

Exhibit Number	Description
1.1*	Form of Underwriting Agreement.
5.1*	Opinion of Latham & Watkins.
23.1	Consent of Ernst & Young LLP.
23.2	Consent of Counsel (included in Exhibit 5.1).
24.1+	Power of Attorney.
24.2+	Power of Attorney for Joseph A. Mollica and Stephen A. Sherwin.

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* To be filed by amendment.
\+ Previously filed.

Item 17. Undertakings.

(i) The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the Registration Statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(ii) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the

Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

(iii) The undersigned registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this amendment to this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of San Diego, California, on this 22nd day of November, 2000.

NEUROCRINE BIOSCIENCES, INC.

By: /s/ Paul W. Hawran
Paul W. Hawran,
Executive Vice President and Chief Financial Officer

Pursuant to the requirements of the Securities Act of 1933, this amendment to this registration statement has been signed below by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
*	President, Chief Executive Officer and Director (Principal Executive Officer)	November 22, 2000
Gary A. Lyons		
/s/ Paul W. Hawran	Executive Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	November 22, 2000
Paul W. Hawran		
*	Chairman of the Board of Directors	November 22, 2000
Joseph A. Mollica		
*	Director	November 22, 2000
Stephen A. Sherwin		
*	Director	November 22, 2000
Richard F. Pops		
*	Director	November 22, 2000
Wylie W. Vale		

*By: /s/ Paul W. Hawran
Paul W. Hawran
Attorney-in-Fact

INDEX OF EXHIBITS

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23.2	Consent of Counsel (included in Exhibit 5.1).
24.1+	Power of Attorney.
24.2+	Power of Attorney for Joseph A. Mollica and Stephen A. Sherwin.

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* To be filed by amendment.
+ Previously filed.

EXHIBIT 23.1

CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the reference to our firm under the caption "Experts" in this Amendment No. 2 to the Registration Statement on Form S-3 and related Prospectus of Neurocrine Biosciences, Inc. for the registration of 3,450,000 shares of its common stock and to the incorporation by reference therein of our report dated January 27, 2000, with respect to the consolidated financial statements of Neurocrine Biosciences, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 1999, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

San Diego, California

November 22, 2000