SYNAPTIC PHARMACEUTICAL CORP
Form 10-K
March 23, 2001

SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549
FORM 10-K

Mark One:

[X] ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 (FEE REQUIRED)
For the fiscal year ended December 31, 2000

OR

[ ] TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 (NO FEE REQUIRED)

Commission File Number 0-27324

SYNAPTIC PHARMACEUTICAL CORPORATION
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of incorporation or organization)

215 College Road
Paramus, NJ
(Address of principal executive offices)

22-2859704
(I.R.S. Employer Identification No.)

07652
(Zip Code)

(201) 261-1331
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:
None

Securities registered pursuant to Section 12(g) of the Act:
Common Stock, par value $.01 per share
Rights to Purchase Series A Junior Convertible Preferred Stock, par value $.01 per share
(Title of Class)

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), during the preceding 12 months (or for such shorter period that the registrant was required to file such reports) and (2) has been subject to such filing requirements for the past 90 days.

Yes X No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this

Form 10-K. [ ]

The approximate aggregate market value of the voting and non voting common equity held by non-affiliates of the registrant was approximately $35,400,000 as of February 16, 2001, based upon the closing price of the Common Stock as reported on The Nasdaq Stock Market on such date. For purposes of this calculation, shares of Common Stock held by directors, officers and stockholders whose ownership in the registrant is known by the registrant to exceed five percent have been excluded. This number is provided only for purposes of this report and does not represent an admission by either the registrant or any such person as to the status of such person.

As of February 16, 2001, there were 10,938,497 shares of the registrant's Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Synaptic Pharmaceutical Corporation Proxy Statement, to be filed not later than 120 days after December 31, 2000, in connection with the registrant's 2001 Annual Meeting of Stockholders, referred to herein as the "Proxy Statement," are incorporated by reference into Part III of this Report on Form 10-K.

SYNAPTIC PHARMACEUTICAL CORPORATION

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Part I

Item 1. Business

Overview

Synaptic Pharmaceutical Corporation ("Synaptic" or the "Company") is a drug discovery company utilizing G protein-coupled receptors ("GPCRs") as targets for novel therapeutics. The Company is utilizing its large portfolio of patented GPCR targets as a basis for the creation of improved drugs that act through these targets. The Company and its licensees are first utilizing these receptor targets to discover their function in the body and thus specific physiological disorders with which they may be associated, and secondly, to design compounds that can potentially be developed as drugs.

Since the Company's inception in 1988, it has developed significant expertise in the molecular biology, pharmacology and medicinal chemistry of the GPCR family. The Company selected this receptor family because GPCRs have been shown to be attractive drug targets, as evidenced by the commercial availability of drugs for a wide variety of therapeutic indications that work by means of their interactions with GPCRs. The GPCR family is estimated to include approximately 1,000 distinct receptors. Of these, approximately 500 receptors, mostly from the groupings that include rhodopsin and secretin, are thought to be useful targets for drug discovery. Accordingly, the Company believes that there are substantial opportunities to use many receptors within the GPCR family as targets for novel drugs. Today, the Company has been awarded over 110 patents relating to its GPCR efforts.

For more than 12 years, we have based our drug discovery efforts on a genomics program that discovers the genes that code for GPCRs. At the same time that we initiated our genomics program we initiated a program in functional genomics, a term which describes the technologies that are involved in identifying the physiological function of a given receptor. Synaptic initiated its functional genomics program in order to help prioritize which targets the Company wanted to pursue in its drug discovery programs. Synaptic utilizes the biological method, as opposed to the chemical method, in its functional genomics efforts to identify the physiological functions of receptors. The biological method involves first identifying the specific natural ligand with which the receptor preferentially interacts. We have created a Universal Functional Assay (UFA(TM)) which significantly reduces the time and the cost, compared to traditional methods, for the identification of endogenous ligands. We believe that knowing the endogenous ligand for the receptor provides a wealth of pharmacological insights that are extremely important in determining whether a

given receptor will be a valuable drug discovery target.

We believe that our competitive advantage derives from being the first Company to be involved in genomics and functional genomics, and from our ability to identify endogenous ligands for newly discovered receptors. Being the first Company in these areas has allowed us to accumulate a significant patent estate around the more valuable parts of the GPCR family. Also by being one of the pioneers of functional genomics, Synaptic has been able to discover the function in humans of a number of GPCRs. We call the identification of the function of a receptor in humans "target validation". To date we have validated the function for the Alpha 1a adrenergic receptor and the serotonin 1F receptor in human Phase II trials.

Once a GPCR has been identified as a valuable drug discovery target and the endogenous ligand has been identified, the next step in the drug discovery process is to identify compounds that interact with the chosen GPCR. The Company has created a GPCR-biased chemical library of approximately 40,000 distinct structures that can be used in high throughput screening. The "hits" from this screening process become the

starting points for chemical lead optimization
programs aimed at the discovery of potent, selective tool compounds. These compounds can than be tested in animals in order to attempt to obtain information as to the possible function of the GPCR. We call the step in the process that leads to identification of the role of a GPCR in an animal model, "proof of concept". To date our GPCR-biased chemical library and our licensees libraries have yielded tool compounds that have allowed for proof of concept for six GPCRs.

Gene discovery, functional genomics, high throughput screening and chemical lead optimization are only a few of the steps in the multi-step process of drug discovery. The Company has created and is utilizing a platform of technologies that it calls SNAP Discovery in order to facilitate the creation of new drugs. Synaptic has varying levels of expertise in the many steps of the drug discovery and development process. In order to gain access to expertise required to effect steps where it has limited capabilities, we utilize contract research organizations, academic laboratories and pharmaceutical companies to move our programs forward into the late preclinical, as well as the clinical phases of the drug development process.

Over the first twelve years of the Company's existence we have entered into a number of collaborative or licensing arrangements with pharmaceutical companies. These arrangements include milestone payments and royalties to Synaptic as compounds being developed by the collaborator or licensee move through clinical development and into the market. The Company's business model contemplates a combination of licensed programs being developed by others and a number of internal programs that the Company is developing on its own as the best means of creating value for its shareholders.

Certain discussions in this Report refer to various phases of preclinical testing and clinical trials. For a description of these phases, see "Government Regulation" below.

Business Model

Synaptic's business model involves the discovery and development, together with its collaborative partners and licensees, of a broad array of drugs based upon the Company's proprietary GPCR targets, and the licensing of certain of its technologies to third parties who will use the technology in their drug development efforts. In order to achieve its objectives we employ the following strategies:

Business Strategy: To develop compounds initially through Phase II and eventually take a product to the market.

The Company's business strategy is to integrate complementary drug discovery and development functions into its existing SNAP Discovery platform with the goal of eventually moving drugs through the clinical development process and into the market.

Research Strategy: To discover and design potential drugs utilizing Synaptic's large portfolio of patented GPCR targets and its small molecule chemical library.

The principal research strategy of the Company is to discover and design, or to have collaborative partners and other licensees discover and design, potential drugs through the use of our GPCR technologies and expertise. The Company and its licensees are using these technologies to identify and optimize drug-like chemical series for further development.

Research Strategy: To develop a broad array of functional genomics technologies.

The Company's second research strategy is to attempt to obtain "proof of concept" in animal models of individual GPCRs. We have discovered, and will continue to attempt to discover and integrate, technologies that will facilitate an understanding of the various functions of specific GPCRs in the body.

Financial Strategy: To utilize the Company's patent estate, its developed technologies and the capital markets as the basis for funding the Company's drug discovery and development programs.

The Company's financial strategy is to create revenues from the nonexclusive licensing to others of portions of its broad GPCR patent estate and certain of the drug discovery technologies that it has created. Exclusive licensing of our drug discovery programs or compounds may be used from time to time and is determined on a project-by-project basis. The capital markets will be utilized, when appropriate, in order to provide a greater source of funds to help defray the costs of drug development.

Background

The Role of Receptors in Controlling Cellular Function

Most drugs work by binding to a particular target in the body, thereby altering communications between cells or otherwise regulating cellular activity. Therefore, the traditional path to discovering small molecule drugs typically begins with the identification of a biological target that is believed to regulate cellular communications or activities which could be altered to treat a given disorder. A test or assay is then developed in order to discover compounds with biological activity at this target. Such an assay facilitates the screening

of the target against a library of many compounds that have been synthesized in the laboratory. Compounds that bind to the target protein and alter its activity are referred to as "hits." Medicinal chemists

then optimize these hits until
they have sufficient potency to become lead candidates and then improve their "drug-like" properties, such as absorption, stability, freedom from unwanted activities, etc., with the goal of producing a successful drug development candidate.

Chemists typically try to streamline the process by copying chemical structures from known active compounds. Even taking this approach, however, the number of possible compounds that could be made is too large to actually test against even a single target using any available technology. Generally, the search is further narrowed either by educated guessing or by in silico methodologies. As a result of the uncertainty of this approach, traditional methods can take many years or may fail entirely.

If it were possible to predict in advance which compounds would result in a hit at a novel target, and which chemical changes would help optimize hits into drug candidates, the drug discovery process would be vastly simplified. Unfortunately, the traditional drug discovery process has had to rely on a trial and error approach that has proven extremely expensive, inefficient and unreliable. Further, making all of the trillions upon trillions of possible small organic compounds, much less testing them all against even a single target, would be impossible. Optimization of hits to achieve the delicate balance of properties necessary for a successful drug is still a daunting task. Most hits are never optimized into successful drugs despite years of effort.

Receptor-Based Drug Therapy

Many illnesses arise because of abnormalities in intercellular communication, and the concept of receptor-based drug therapy was developed to address this problem. The goal of receptor-based drug therapy is to develop drugs that will interact with the receptor believed to be associated with the targeted abnormality, thereby inhibiting or enhancing the cascade of events that is mediated by the receptor. A number of receptor-based drugs have been developed and are currently being marketed. During the past several years it has been discovered that a single ligand, for instance serotonin, reacts with not one but several receptors. The members of a group of receptors that interact with the same ligand are called receptor subtypes. A major problem with currently available receptor-based drugs is that they do not differentiate among receptor subtypes and, while they may indeed interact with the targeted receptor subtypes, thereby having some therapeutic effect, they may also interact with other receptor subtypes within the same family as the targeted receptor subtypes. These other receptor subtypes may be associated with other physiological functions, and interactions of these drugs with them often result in undesirable side effects. In addition, many of these drugs have limited therapeutic utility because they must be used in sub-optimal doses in order to minimize these side effects.

The Post-Genomics Era (Functional Genomics)

Over the past decade, most of the major pharmaceutical companies have developed an interest in using cloned receptors in at least some of their drug discovery efforts. This interest coincides with, and may in part be responsible for, the sequencing of the entire human genome. While worldwide genomics efforts have resulted in the development of new technologies which greatly accelerate

the pace at which new receptors are discovered, most of these discoveries to date have been "orphan receptors," i.e., sequences without known natural ligands. Without information regarding the natural ligands for these receptors, it is difficult to hypothesize about their role in specific physiological functions.

Over the next several decades, a principal focus of the biotechnology and pharmaceutical industries will be to utilize the vast body of data being generated with respect to cloned receptors to better understand

these receptors,
their physiological functions and their potential as targets for the design and development of drugs that are safer and more efficacious than existing drugs. We believe that our SNAP Discovery platform will play an important role in (i) the discovery of new GPCRs, (ii) the elucidation of the functions of newly discovered GPCRs and their potential as drug targets, and (iii) the design of compounds that interact with these GPCRs.

Synaptic's GPCR SNAP Discovery Platform

The Company believes that its success in the discovery of GPCRs and subsequently their function in the body, will enable it to further refine the understanding of many disease processes. There is increasing evidence to suggest that some disorders may actually involve the malfunctioning of one or more of a variety of receptors included within different receptor families. For example, in the case of obesity, there is pharmacological data indicating that NPY, MCH, galanin and serotonin receptors are involved in controlling food intake. As a result, more than one drug could be developed to treat obesity, but these drugs would work through different biological mechanisms by exerting their therapeutic effects by interacting with receptors belonging to different families. We believe that our drug discovery and design technologies make it possible to discover two or more separate drugs that could benefit distinct patient populations whose symptoms (for example, obesity), while identical, stem from different physiological disorders and therefore require different treatments.

Overview -- The Three Principal Steps

The Company's GPCR drug discovery and design technologies are employed in three separate steps of the drug discovery process.

(i) Genomics. Genomics is the discovery and cloning of the genes. Our genomics efforts are focused on genes for GPCRs. In this step, we employ molecular biology technologies, such as genetic engineering, automated gene sequencing and bioinformatics to discover and clone receptor genes. Many of the component technologies in this step are proprietary to Synaptic.

(ii) Functional Genomics. The term "functional genomics" refers to the technologies involved in the process of target validation. For example, certain functional genomics technologies facilitate the discovery of the endogenous ligands for receptors and, thus, the biological roles of these receptors in the body. Others involve mapping the distribution of the receptor gene or gene product in the body in both normal and diseased tissues. Others involve assays that facilitate both the search for compounds that are selective for the receptors of interest and the use of selective compounds in various animal models of behavior and physiology in an attempt to provoke a response in an animal model system that might indicate the role of these receptors in the body. Observation of a response in an animal model constitutes a confirmation,

or "proof of concept," of a role of the receptor targeted by the selective compounds and provides an opportunity to develop hypotheses concerning the possible therapeutic utility of drugs that act at the receptors of interest. There is no guarantee, however, that effects seen in animals will also occur in humans. The downstream steps in the process of `target validation' include preclinical testing and Phase I and Phase II clinical trials.

(iii) Chemistry: Compound Design and Optimization. Chemistry, as it relates to Synaptic's GPCR drug discovery and design technology, involves two principal activities: the design and synthesis of compounds that are selective for the receptor of interest and that can thus be used in "proof of concept" studies; and, following "proof of concept", the optimization of selective chemical series to arrive at a

compound which has the desired pharmacological
profile and which can thus proceed through preclinical testing and clinical trials.

Research and Drug Discovery Programs: Focus on G Protein-Coupled Receptor Family

The family of receptors to which we have chosen to apply our drug discovery technologies is the G protein-coupled receptor family, so called because the cascade of events that ensues within the receiving cell following the occurrence of the ligand-receptor interaction is mediated by a class of proteins called "GTP-binding regulatory proteins," or "G proteins," found within the cell.

The Company chose to focus on the GPCR family because it believes that this family provides the optimum opportunity for the exploitation of its drug design technology. First, it is known that G protein-coupled receptors play a major role in intercellular communication and that drugs that block ("antagonists") or enhance ("agonists") their activity have therapeutic utility. Examples of these drugs include: Zantac(R), a histamine receptor antagonist for the treatment of ulcers; Claritin(R), a histamine receptor antagonist for the treatment of allergy; Imitrex(R), a serotonin receptor agonist for the treatment of migraine headache; and Hytrin(R), an adrenergic receptor antagonist for the treatment of hypertension and urinary retention resulting from benign prostatic hyperplasia ("BPH"). Second, there is a large body of knowledge about some of the basic structural elements of drugs that interact with these receptors that has accumulated over the years from which the Company and its collaborative partners and licensees can draw in beginning their drug discovery programs. Third, the GPCR family is extremely large and, based on several estimates, exceeds 1,000 receptor subtypes belonging to more than 45 known families and an unknown number of additional families the natural ligands of which either have not yet been identified or have been identified but have not been publicly disclosed.

The Company's SNAP Discovery platform is being utilized or has been utilized in a number of different research and drug discovery programs. Some of these programs are currently being conducted by the Company independently. Others have been conducted by the Company independently or in collaboration with pharmaceutical companies but are currently inactive and available for licensing by the Company. Finally, some of the programs are being conducted by the Company in joint research programs with its collaborative partners or by the Company's licensees.

Total operating expenses incurred by Synaptic for each of the fiscal years 2000, 1999 and 1998 were $20,212,000, $19,652,000 and $19,576,000,

respectively, of which approximately $1,021,000, $1,759,000 and $7,182,000, respectively, was funded by our collaborative partners during these years.

Current programs in which the Company's human receptor-targeted drug design technology is being utilized include the following:

Summary of Research and Drug Discovery Programs

Company Programs: GPCR Targets	Primary Indications	Status
MCH	Obesity	Preclinical
SUT - 4	Incontinence	Preclinical
SCT - 11	Depression	Preclinical
Trace Amines	CNS Disorders	Discovery
SMT - 3	Diabetes	Discovery

Research and Drug Discovery Programs

The Company is currently focusing its efforts on five drug discovery programs. These drug discovery programs have been chosen because the Company believes it has a competitive advantage in its intellectual property position, its identification of the endogenous ligand or its identification of a novel function for the GPCR target.

MCH

Current research in obesity indicates that the brain controls a person's appetite through a complex network of signals that are exchanged between the body and the brain. For over a decade, scientists at Synaptic have been working with GPCRs, key components involved in this complex network of signals. A number of receptors in the GPCR family have been hypothesized to be potential targets for drug discovery programs. Included within these GPCRs are the serotonin 2C receptor, the neuropeptide Y5 receptor, the galanin GPCR family and the melanin concentrating hormone ("MCH") receptor(s), among others.

The medications most often used in the management of obesity are commonly known as "appetite suppressant" medications. Appetite suppressant medications promote weight loss by decreasing appetite or increasing the feeling of satiety. These medications decrease appetite by increasing serotonin or catecholamines--brain chemicals that affect appetite, as well as mood. Most currently available appetite suppressant medications are approved by the U.S. Food and Drug Administration (FDA) for short-term use, meaning a few weeks or months. Sibutramine(R) is the only appetite suppressant medication approved for longer-term use in significantly obese patients, although its safety and effectiveness have not been established for use beyond one year.

Among the GPCR targets for obesity on which the Company is working is the MCH receptor. The natural ligand, MCH, stimulates feeding in rats, and rats

lacking the MCH gene are lean. Synaptic identified the gene for the MCH receptor by means of its SNAP Discovery platform through which it discovered the

gene and
natural ligand. Synaptic's chemists have designed compounds that have allowed proof of concept in animal feeding models. Preclinical development activities in this program are being carried out.

Incontinence

A recent estimate of the prevalence of incontinence in the United States reveals that it affects approximately 35 percent of women over the age of 50. Of the women who experience incontinence, 40-50 percent have symptoms of urgency and frequency of urination or "urge incontinence." These symptoms are often associated with a condition that is described as "overactive bladder." Drugs that are currently used to treat urge incontinence such as the anticholinergics Ditropan(R) and Detrol(R) are aimed at reducing bladder activity by blocking muscarinic receptors in the bladder. These drugs are associated with side effects such as dry mouth, dry skin, visual blurring, nausea and constipation. The increasing prevalence of urge incontinence, together with the side effect profile and limited efficacy of these drugs has spurred the search for new mechanisms of action that may be useful targets for the treatment of this disorder.

Scientists at Synaptic, utilizing their expertise in GPCRs, have identified a novel receptor, the SUT-4 or Synaptic Urinary Target 4 receptor, that is localized in the central nervous system. Using the Company's UFA(TM) technology, the natural ligand for this receptor was then determined. Next, our scientists were able to identify tool compounds using the SNAP Discovery platform. These tool compounds, when studied in an in vivo rat model, inhibit the sensory signals from the bladder that give rise to bladder contractions. These studies indicate that we have identified a novel mechanism of action that may be useful in the treatment of urge incontinence. Small molecule compounds that act at SUT-4 are now being evaluated in several models of incontinence.

Depression

More than 19 million American adults (9.5% of the population) suffer from depression. Treatment includes medication, short-term psychotherapy, or a combination of both. Untreated depression is costly. A RAND Corporation study found that patients with depressive symptoms spend more days in bed than those with diabetes, arthritis, back problems, lung problems or gastrointestinal disorders. Estimates of the total annual cost of untreated depression in 1990 ranged from $30-$44 billion in the United States alone. Of the $44 billion figure, lost workdays account for close to $12 billion of this cost. Additionally, more than $11 billion in other costs accrue from decreased productivity due to symptoms that sap energy, affect work habits or cause problems with concentration, memory and decision-making.

A number of different pharmacological approaches have been developed to treat depression. The first generation of drugs shown to be effective in the treatment of depression, such as the tricyclic antidepressants, lithium and the monoamine oxidase inhibitors, have side effects that limit their effectiveness. More recently, selective serotonin reuptake inhibitors (SSRIs), such as Prozac(R), Zoloft(R), Paxil(R) and Celexa(R), have been shown to be highly effective in the treatment of many forms of depression. A number of SSRI

compounds are now approved for marketing, and these drugs have captured a significant market share. However, all of these currently available drugs have deleterious side effects that may limit their use in many patients. In addition, these drugs are effective only after a lag period of days to weeks following initial administration. This lag time can be a serious problem, especially in the depressed suicidal patient. Furthermore, there are a significant number of patients who do not adequately respond to any of the currently available drug therapies.

Synaptic, utilizing its genomics and functional genomics expertise, believes that it has identified a function in the body for one of its proprietary GPCRs. Compounds that interact with this receptor, which we call SCT- 11, when tested in vivo show similar effects to the SSRIs. Since this novel approach targets a GPCR, we believe that compounds acting through this mechanism may have a rapid onset of action and may be safer and more efficacious than existing antidepressants. Our lead compound is in preclinical development.

Trace Amines

Scientists at Synaptic have discovered and cloned a new class of receptors that are sensitive to "Trace Amines," a family of chemical messengers thought to play a role in a variety of illnesses including depression, psychosis, migraine, asthma, and hypertension. The Company is expanding its drug discovery efforts to include this new class of GPCRs. Over the last 20 years, several lines of evidence have pointed to trace amines as neurotransmitters and neuromodulators, however, researchers had been unable to find Trace Amine receptors in mammalian systems, until our discovery.

Trace Amines that act on the newly discovered receptors include Tyramine, Tryptamine and (beta)-Phenylamine. Trace Amines are closely related to biogenic amines, which include the classical neurotransmitters serotonin, dopamine and norepinephrine. The receptors and transporters for biogenic amines are the targets for a number of drugs for the treatment of depression, heart disease, migraine headache, ulcers and allergy. We believe that the similarities between Trace Amines and biogenic amines make Trace Amine receptors attractive targets for discovering drugs and developing treatments for a wide variety of disorders.

Using the SNAP Discovery platform, Synaptic has advanced several Trace Amine receptors, and is using the small molecule selective leads it has identified, into proof of concept studies for a variety of disorders.

Diabetes

Diabetes Mellitus is a significant health problem characterized by hyperglycemia resulting from impairment in insulin secretion and/or insulin action. Type II diabetes affects more than 16 million adults in the United States and places these individuals at high risk for serious complications of the eyes, nerves, kidneys and cardiovascular system. As obesity rates worldwide are increasing, so too is the prevalence of diabetes. Points for possible intervention in diabetes include the stimulation of insulin release from the pancreas, either directly or through the central nervous system, inhibition of glucose production in the liver, blockade of cholesterol absorption in the intestines and alterations in the sensitivity of insulin receptors. Current therapies for diabetes include insulin replacement via injections which must be timed and dosed very carefully, insulin sensitizers such as Rezulin(R), which

can cause liver toxicity, and Avandia(R) and Actos(R), which are very new to the market. Sulfonylureas and meglitinides such as Prandin(R) can cause hypoglycemia and are contraindicated in kidney disease. Glucose production blockers such as Glucophage(R) can cause GI irritation and are not recommended if liver, kidney or heart disease are present and alpha glucosidase blockers such as Acarbose(R) can cause GI cramping and flatulence.

Scientists at Synaptic, utilizing their expertise in GPCRs, have identified a novel receptor that is localized predominantly in the human pancreas. Using the Company's UFA(TM) technology, the natural ligand for this receptor was identified. Taken together, the localization of this GPCR in the human pancreas, as well

as the biology that is known about the endogenous ligand, make this receptor a candidate for the discovery and development of a drug that will stimulate glucose-dependent insulin release. Preliminary studies at Synaptic have verified that the ligand for this receptor stimulates the secretion of insulin from isolated rat pancreatic islets. We are currently applying our SNAP Discovery platform to perform high throughput screening of the Company's GPCR-biased compound library to identify small molecule tools that will be useful in exploiting this novel mechanism of action.

Summary of Joint Research Programs

Company	Program	Primary Indication
Grunenthal	Drug Discovery	Pain
Kissei	Gene Discovery, Cloning and Proof of Concept	Undisclosed

Joint Research Programs

A key element of Synaptic's business strategy is to leverage resources and to attempt to generate royalty-based revenues through collaborative and licensing arrangements with pharmaceutical companies. The Company is currently collaborating with two pharmaceutical companies pursuant to: (i) the Cooperation Agreement dated January 12, 1998, as amended (the "Grunenthal Agreement"), with Grunenthal GmbH ("Grunenthal") and (ii) the Collaborative Research and License Agreement dated January 24, 2000 (the "Kissei Agreement"), with Kissei Pharmaceutical Co., Ltd. ("Kissei"). Concurrently with the establishment of these collaborative arrangements, Synaptic granted certain rights with respect to its technology and patent rights to Grunenthal and Kissei. Set forth below is a brief summary of these collaborative arrangements.

Grunenthal Collaboration

In January 1998, the Company and Grunenthal entered into the Grunenthal Agreement pursuant to which they agreed to collaborate in the identification and development of drugs for the alleviation of pain. The basis of the collaboration has been the complementary technologies of the two companies. Synaptic has cloned the genes for many receptors whose biological functions are not known. Grunenthal has a broad expertise in various animal models of pain. The work of

the collaboration involves the coupling of the Company's human receptor-targeted drug design technology with Grunenthal's expertise in pain-related technology in an attempt first to identify receptors that could be targets of drugs that alleviate pain and then to design and develop drugs targeted to these receptors.

Under the terms of the Grunenthal Agreement, Synaptic agreed to make available to Grunenthal for evaluation all receptors (to the extent not already licensed exclusively to a third party) cloned by Synaptic for which there is evidence of a role in the mediation of pain or whose function has not yet been elucidated but which were first cloned by Synaptic from tissues known to be so implicated. Synaptic further agreed not to pursue these receptors, independently or with any third party, as targets of potential drugs for the alleviation of pain during the evaluation period applicable to the receptors or during the period over which activities involving any such receptor are being jointly conducted with Grunenthal.

The terms of the Grunenthal Agreement provide that the companies are responsible for their own expenses incurred during the research stage of any project undertaken as part of the collaboration but will each be responsible for 50% of all development costs incurred as part of the project with respect to any resulting drug candidates up to the commencement of Phase III clinical trials. Synaptic will retain manufacturing and marketing rights in the United States, Canada and Mexico with respect to any drug candidates resulting from the collaboration, while Grunenthal will retain manufacturing and marketing rights in Europe, Central America (other than Mexico) and South America with respect to any of these drug candidates. The two companies will share these rights in all other countries. With respect to each country in its own territories and in the shared territories in which it desires to market a drug candidate, each of Synaptic and Grunenthal will be responsible for conducting Phase III clinical trials, if required, for obtaining any necessary regulatory approval, and for all associated costs.

Kissei Collaboration

In January 2000, the Company and Kissei entered into the Kissei Agreement. Under the agreement Synaptic will conduct both a genomics and functional genomics program on behalf of Kissei. As part of this program, scientists at Synaptic are attempting to clone genes that code for G protein-coupled receptors from tissues selected by Kissei and to identify the ligands for these receptors. Kissei will attempt to discover and develop compounds that act at these receptors. The term of the collaboration is three years.

Under the terms of the Kissei Agreement, Kissei will provide the Company with funding to support Synaptic's research. Kissei will have the opportunity to select up to a specified number of receptors that are discovered by Synaptic during the course of the collaboration and to receive an exclusive worldwide license to use the selected receptors to develop, manufacture and market drugs that act through those receptors. Kissei's license will convert to a nonexclusive license in all countries except Japan following its achievement of certain milestones. In consideration for this license, Kissei will be required to pay the Company license fees, milestone payments and royalty payments on any drug that reaches the marketplace.

Kissei has the right to terminate the Kissei Agreement effective in January 2001, 2002 or 2003 upon at least three months' prior written notice. In the event of this kind of termination, Kissei will not be required to provide

the Company with research funding that has not come due prior to termination.

Summary of Other Licensees' Programs

Licensee	Program	Primary Indications	Types and Numbers of Synaptic's Issued U.S. and Foreign Patents
Lilly	Serotonin	Various	Receptor 41 Functional Use 1
Novartis	NPY	Obesity and Cardiovascular Disorders	Receptor 23
Glaxo (1)	Alpha 1a, 1b, 1d	Unknown	Receptor 7
PRI	Alpha 1a, 1b, 1d	BPH	Receptor 7 Functional Use 9

(1) Glaxo has a nonexclusive license to use Synaptic's alpha 1 receptors for certain purposes, but is not required to provide Synaptic with any information regarding such use unless it files an NDA for a royalty-bearing compound under its agreement with Synaptic. Glaxo has not notified Synaptic of an NDA filing.

Other Licensees' Programs

In addition to the licenses granted in connection with the Company's ongoing collaborative arrangements, licenses to certain of the Company's technology and patent rights have been granted to three other pharmaceutical companies pursuant to: (A) the Research, Option and License Agreement dated January 25, 1991, as amended (the "Lilly Agreement"), with Eli Lilly and Company ("Lilly"); (B) the Research and License Agreement dated August 4, 1994, as amended (the "First Novartis Agreement") and the Research and License Agreement dated May 31, 1996 (the "Second Novartis Agreement," and together with the First Novartis Agreement, the "Novartis Agreements"), with Novartis Pharma AG ("Novartis"); and (C) the Option and License Agreement dated March 2, 1998 (the "Glaxo Agreement"), with Glaxo Group Limited ("Glaxo"). The Lilly and Novartis licenses were granted concurrently with the establishment by Synaptic of collaborative arrangements with these companies. While the Novartis collaboration and the Lilly collaboration ended in August 1998 and July 1999, respectively, the associated licenses continue for the respective periods provided in the Novartis Agreements and the Lilly Agreement.

Lilly Programs

Serotonin is one of the major neurotransmitters of the body. It affects mood, sleep rhythms, sexual functions, appetite, temperature control, gastro-intestinal movement and the cardiovascular, pulmonary and genito-urinary systems. Drugs that inhibit or enhance the actions of serotonin have proven to be effective in the treatment of an array of disorders, such as migraine

headache, depression and anxiety. However, many of the serotonergic drugs currently available were designed without the use of cloned serotonin receptor subtype genes and some of these drugs have unacceptable side effect profiles. It is generally believed that the poor

side effect profiles stem from the interaction of these drugs with multiple serotonin receptor subtypes. The serotonin family is extremely large, comprising at least 14 receptor subtypes. While each of these receptor subtypes may be implicated in a physiological function distinct from the other subtypes, all of the receptor subtypes respond to the neurotransmitter serotonin--and may be responding to nonsubtype-selective drugs. As a consequence, a nonsubtype-selective drug intended to exert its effects on one physiological function may in fact have the unintended consequence of exerting its effects on other physiological functions, thereby causing the undesirable side effects.

During the course of the collaboration, one of the serotonin receptors, the serotonin 1F receptor, was validated as a target for the treatment of migraine headaches. In addition to migraine headache, there are a wide variety of additional applications for serotonin-based drugs, including potential therapies for the treatment of obesity and novel receptor-based therapies for the treatment of depression. Although many years of research have been committed to the serotonin receptor system by dozens of research teams around the world, the understanding of the biological role of most of the serotonin receptors is still in a very early stage. Considerable work must be done in order to validate many of the serotonin receptors as drug targets.

Under the terms of the Lilly Agreement, Lilly received an exclusive worldwide license to use all but two of the Company's existing serotonin drug discovery systems for the development and commercialization of drugs that affect serotonergic transmission. The Company retained the unlimited right to use two of its existing serotonin drug discovery systems and a limited right to use all of its other serotonin drug discovery systems for cross-reactivity screening of compounds in nonserotonin drug discovery programs.

The terms of the Lilly Agreement provide that Lilly is responsible for all development, manufacturing, marketing and sales of drugs resulting from the use of Synaptic's technology. The Company will be entitled to receive from Lilly payments upon the achievement of certain drug development milestones and royalties on sales of any drugs developed through the use of the Company's technology. Royalties will be payable in respect of sales in any country over the period commencing with the date of the first commercial sale of a drug and ending with the expiration of related patent rights in that country. Lilly's milestone and royalty payment obligations under the Lilly Agreement continue, notwithstanding the expiration of the term of the collaboration.

Novartis Programs

From August 1994 to August 1998, the Company and Novartis engaged in a collaboration directed primarily to the identification and development of NPY drugs for the treatment of obesity and eating disorders. As part of its collaboration with the Company, Novartis received an exclusive worldwide license to use the Company's NPY receptor subtype drug discovery systems for the limited purpose of developing and commercializing Y5 antagonists, as well as any other NPY drugs, for the treatment of obesity and eating disorders, as well as cardiovascular disorders. Novartis also received rights under several of the Company's patents and patent applications. The license and rights remain

exclusive until August 2001, following which time they become nonexclusive.

The Y5 receptor was initially isolated by the Company's scientists from rat hypothalamus. In laboratory tests, the activity of NPY and related peptides on the Y5 receptor correlates with the ability of these peptides to stimulate feeding in animals. As part of its collaboration with the Company, Novartis then showed in proof of concept studies that several peptides that activated the Y5 receptor preferentially over other known NPY receptors increased food intake in rats. Additional proof of concept studies by Synaptic and Novartis showed that small molecules that selectively block the Y5 receptor significantly reduce food

intake in rats and reduce body weight after chronic administration. The Company's collaboration with Novartis focused on discovering and developing a potent and selective Y5 antagonist for the treatment of obesity. To our knowledge Novartis is continuing its efforts to identify a Y5 antagonist as a development candidate for this obesity program.

Under the license agreement Novartis will be required to make payments to the Company upon the achievement by Novartis of certain drug development milestones and, subject to certain limitations, to pay the Company royalties on the sale of any drugs developed through the use of the Company's technology.

Glaxo Agreement

In March 1998, the Company and Glaxo entered into the Glaxo Agreement pursuant to which the Company granted Glaxo a nonexclusive license under the Company's alpha 1 adrenergic receptor patents to develop and sell alpha-1a selective compounds for therapeutic applications other than the treatment of BPH. Synaptic will be entitled to receive royalties on sales of any alpha-1a selective drugs sold by Glaxo so long as Synaptic has an issued patent relating to an alpha 1 adrenergic receptor subtype in at least one major market country at that time.

The R.W. Johnson Pharmaceutical Research Institute

In September 2000, Synaptic and The R.W. Johnson Pharmaceutical Research Institute, a Division of Ortho-McNeil Pharmaceutical, Inc. (PRI), entered into an agreement in which Synaptic granted nonexclusive licenses covering Synaptic's alpha-1 adrenergic receptors and benign prostatic hypertrophy (BPH) patents. The license agreement between Synaptic and PRI provides PRI the freedom to operate under Synaptic's functional use patents for BPH and Synaptic's alpha-1 adrenergic receptor patents for all therapeutic indications. In exchange for the nonexclusive licenses, PRI paid provide and up-front licensing fee. PRI is required to make payments to Synaptic upon the achievement of certain drug development milestones and to pay royalties on the sales of any drugs developed, if any.

Other Agreements

It is the Company's practice to meet with pharmaceutical and biotechnology companies on an on-going basis to discuss possible collaborations on projects of mutual interest and/or out-licensing of Synaptic's technology on a non-collaborative basis. At present, the Company is in the early stages of discussing a number of possible arrangements. There can be no assurance, however, that these discussions will result in the consummation of collaborative

or licensing arrangements.

Patents, Proprietary Technology and Trade Secrets

The Company's success depends, in part, on its ability to establish, protect and enforce its proprietary rights relating to its technology. The Company's policy is to seek, when appropriate, protection for its gene discoveries, compound discoveries and other proprietary technology by filing patent applications in the United States and other countries. The Company has filed numerous patent applications both in the United States and in other countries covering its inventions.

As of February 28, 2001, the Company had been issued a total of 76 patents worldwide relating to the genes that code for various G protein-coupled receptors. These patents expire between 2008 and 2019. In addition, as of that date additional patent applications relating to the Company's receptor gene discoveries had been filed in the United States and in other countries.

In April 1995, the Company was issued its first functional use patent in the United States. This patent covers the use of selective alpha-1a antagonists for the treatment of BPH. As of February 28, 2001, the Company had been issued a total of nine patents relating to the same subject matter in the United States and in other countries. These patents expire between 2012 and 2015. Additional related or corresponding patent applications of the Company are on file in the United States and in other countries.

In August 1999, the Company received a functional use patent in the United States covering the use of selective serotonin 1D agonists for the treatment of migraine headache. Additional patent applications relating to the same subject matter have been filed in other countries.

The Company has also filed patent applications in the United States and in other countries covering its neurotransmitter transporter discoveries. Whereas receptors are protein molecules that bind to and are activated by certain ligands, transporters are protein molecules that serve to terminate the action of certain ligands by carrying them back into the cells from which they are released. As of February 28, 2001, the Company had been issued nine patents relating to six of these transporter discoveries in the United States and in another country. Additional related or corresponding applications have been filed by the Company in the United States and abroad. The Company is no longer actively working on its transporter program. However, the Company is seeking to license its transporter technology to others.

Additional patent applications covering the Company's compound discoveries and other inventions have been filed in the United States and in other countries and the Company expects to file additional patent applications in the future.

The Company has granted certain rights under several of its patents and patent applications to Lilly, Novartis, Grunenthal, Glaxo and Kissei.

Patent law as it relates to inventions in the biotechnology field is still evolving, and involves complex legal and factual questions for which legal principles are not firmly established. Accordingly, there can be no assurance that patents will be granted with respect to any of the Company's patent applications currently pending in the United States or in other countries, or with respect to applications filed by the Company in the future. The failure by

the Company to receive patents pursuant to the applications referred to herein and any future applications could have a material adverse effect on the Company.

There is no clear policy involving the breadth of claims allowed in patents or the degree of protection afforded thereunder. Accordingly, no firm predictions can be made regarding the breadth or enforceability of claims allowed in the patents that have been issued to the Company or in patents that may be issued to the Company in the future, and there can be no assurance that claims in the Company's patents, either as initially allowed by the United States Patent and Trademark Office or any of its non-United States counterparts or as subsequently interpreted by courts inside or outside the United States, will be sufficiently broad to protect the Company's proprietary rights.

On June 5, 2000, the Company filed suit in the United States District Court for the District of New Jersey against M.D.S. Panlabs, Inc., a Washington corporation, and Panlabs Taiwan Ltd., a Taiwanese corporation (collectively, "Panlabs"). The suit alleges that Panlabs has infringed several issued U.S. Patents

owned by the Company that relate to cloned human receptors and their use in binding assays. The suit also alleges that Panlabs has been importing, selling and offering to sell products of the Company's patented binding assay processes to pharmaceutical companies and others in the United States and particularly in New Jersey. See "Legal Proceedings" in PART I, Item 3, hereof.

Also, there can be no assurance that the Company's patents or patent applications will not be challenged by way of interference proceedings or opposed by third parties or that the Company will not be required to participate in interference proceedings or oppose the patents or patent applications of third parties in order to protect its rights. Interference and opposition proceedings can be expensive to prosecute and defend. As of February 28, 2001, the Company was seeking to provoke an interference by the United States Patent and Trademark Office between one of its patent applications and an issued patent of a third party. There can be no assurance that the outcome of the anticipated interference proceeding will be favorable to the Company. In the event that the outcome of the interference proceeding were unfavorable to the Company, the Company might not be able to practice the subject matter of the relevant patent application in the United States. Accordingly, an unfavorable outcome in an interference proceeding would have an adverse effect on the Company. Even if the ultimate outcome of the interference proceeding is favorable to the Company, the Company's participation could result in substantial cost.

Further, no assurance can be given that patents issued to the Company will not be infringed, invalidated or circumvented by others, or that the rights granted thereunder will be commercially valuable or will provide competitive advantages to the Company and its present or future collaborative partners or licensees. Moreover, because patent applications in the United States are maintained in secrecy until patents issue, because patent applications in certain other countries generally are not published until more than eighteen months after they are filed and because publication of technological developments in the scientific or patent literature often lags behind the date of these developments, the Company cannot be certain that it was the first to invent the subject matter covered by its patents or patent applications or that it was the first to file patent applications for these inventions.

The commercial success of the Company depends in part on the Company's ability to operate without infringing patents and proprietary rights of third parties. The Company is aware of a large number of patents and patent

applications of third parties that contain claims to genes that code for G protein-coupled receptors, and/or compounds that interact with GPCRs. Patents issued to others may preclude the Company from using or licensing certain of its receptor discoveries or may preclude the Company or its collaborative partners and other licensees from commercializing drugs developed with the use of the Company's technology. The Company has acquired a license to use certain technologies covered by a patent owned by Columbia University. The Columbia University license is a worldwide nonexclusive license to manufacture, use, sell and sublicense drugs derived from the use of certain recombinant DNA technology. In consideration for this license, the Company has agreed to pay royalties on sales of drugs developed through the use of the license. The term of the license extends until the expiration of the last to expire of the patent rights covered by the license. The Company has procured licenses to several technologies that are used in several of its programs. The Company may be required to obtain additional licenses to patents or other proprietary rights of other parties in order to pursue its own technologies. No assurance can be given that any additional licenses would be made available on terms acceptable to the Company, if at all. The failure to obtain licenses could result in delays in the Company's or its collaborative partners' or licensees' activities, including the development, manufacture or sale of drugs requiring these licenses, or preclude their development, manufacture or sale.

In some cases, litigation or other proceedings may be necessary to assert infringement claims against others, to defend against claims of infringement, to enforce patents issued to the Company, to protect trade secrets, know-how or other intellectual property rights owned by the Company, or to determine the scope and validity of the proprietary rights of third parties. Such litigation could result in substantial costs to and diversion of resources by the Company and could have a material adverse effect on the Company. There can be no assurance that any of the Company's patents would ultimately be held valid or that efforts to defend any of its patents, trade secrets, know-how or other intellectual property rights would be successful. An adverse outcome in litigation or in a proceeding could subject the Company to significant liabilities, require the Company to cease using the subject technology or require the Company to license the subject technology from the third party, all of which could have a material adverse effect on the Company's business.

In addition to patent protection, the Company relies upon trade secrets, proprietary know-how and continuing technological advances to develop and maintain its competitive position. To maintain the confidentiality of its trade secrets and proprietary information, the Company requires its employees, consultants and collaborative partners to execute confidentiality agreements upon the commencement of their relationships with the Company. In the case of employees, the agreements also provide that all inventions resulting from work performed by them while in the employ of the Company will be the exclusive property of the Company. There can be no assurance, however, that these agreements will not be breached, that the Company would have adequate remedies in the event of a breach or that the Company's trade secrets or proprietary information will not otherwise become known or developed independently by others.

Competition

Synaptic and its collaborators and licensees are pursuing areas of drug discovery and development in which we believe there is a potential for extensive technological innovation in relatively short periods of time. We operate in a field in which new discoveries occur at a rapid pace. Competitors may succeed in

developing technologies or products that are more effective than ours or in obtaining regulatory approvals for their drugs more rapidly than we are able to, which could render our products obsolete or noncompetitive. Competition in the pharmaceutical industry is intense and is expected to continue to increase. Many competitors, including biotechnology and pharmaceutical companies, are actively engaged in research and development in the areas of obesity, depression, urology and CNS disorders. Many of our competitors have substantially greater financial, technical, marketing, and personnel resources. In addition, some of them have considerable experience in preclinical testing, human clinical trials, and other regulatory approval procedures. Moreover, certain academic institutions, governmental agencies, and other research organizations are conducting research in the same areas in which we are working. These institutions are becoming increasingly aware of the commercial value of their findings and are more actively seeking patent protection and licensing arrangements to collect royalties for the technology that they have developed. These institutions may also market competitive commercial products on their own or through joint ventures and will compete with us in recruiting highly qualified scientific personnel. There can be no assurance that a pharmacological method of treatment for certain disorders, such as obesity or depression, will prove to be superior to existing or newly discovered approaches to the treatment of those disorders.

Government Regulation

The development, manufacturing and marketing of drugs developed through the use of the Company's technology are subject to regulation by numerous Federal, state and local governmental authorities in the United States, the principal one of which is the FDA, and by similar agencies in other

countries
(each of such Federal, state, local and other authorities and agencies, a "Regulatory Agency"). Regulatory Agencies impose mandatory procedures and standards for the conduct of certain preclinical testing and clinical trials and the production and marketing of drugs for human therapeutic use. Product development and approval of a new drug are likely to take many years and involve the expenditure of substantial resources.

The steps required by the FDA before new drugs may be marketed in the United States include: (i) preclinical studies; (ii) the submission to the FDA of a request for authorization to conduct clinical trials on an investigational new drug (an "IND"); (iii) adequate and well-controlled clinical trials to establish the safety and efficacy of the drug for its intended use; (iv) submission to the FDA of a new drug application (an "NDA"); and (v) review and approval of the NDA by the FDA.

In the United States, preclinical testing includes both in vitro and in vivo laboratory evaluation and characterization of the safety and efficacy of a drug and its formulation. Laboratories involved in preclinical testing must comply with FDA regulations regarding Good Laboratory Practices. Preclinical testing results are submitted to the FDA as part of the IND and are reviewed by the FDA prior to the commencement of human clinical trials. Unless the FDA objects to an IND, the IND will become effective 30 days following its receipt by the FDA. There can be no assurance that submission of an IND will result in the commencement of human clinical trials.

Clinical trials, which involve the administration of the investigational drug to healthy volunteers or to patients under the supervision of a qualified principal investigator, are typically conducted in three

sequential phases, although the phases may overlap with one another. Clinical trials must be conducted in accordance with Good Clinical Practices under protocols that detail the objectives of the study, the parameters to be used to monitor safety and the efficacy criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND. Further, each clinical study must be conducted under the auspices of an independent Institutional Review Board (the "IRB") at the institution where the study will be conducted. The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution. Compounds must be formulated according to the FDA's Good Manufacturing Practices ("GMP").

Phase I clinical trials represent the initial administration of the investigational drug to a small group of healthy human subjects or, more rarely, to a group of selected patients with the targeted disease or disorder. The goal of Phase I clinical trials is typically to test for safety (adverse effects), dose tolerance, absorption, bio-distribution, metabolism, excretion and clinical pharmacology and, if possible, to gain early evidence regarding efficacy.

Phase II clinical trials involve a small sample of the actual intended patient population and may seek to assess the efficacy of the drug for specific targeted indications, to determine dose tolerance and the optimal dose range and/or to gather additional information relating to safety and potential adverse effects.

Once an investigational drug is found to have some efficacy and an acceptable safety profile in the targeted patient population, Phase III clinical trials are initiated to establish further clinical safety and efficacy of the investigational drug in a broader sample of the general patient population at geographically dispersed study sites in order to determine the overall risk-benefit ratio of the drug and to provide an adequate basis for all package labeling. The results of the research and product development, manufacturing, preclinical testing, clinical trials and related information are submitted to the FDA in the form of an NDA for approval of the marketing and shipment of the drug.

Timetables for the various phases of clinical trials and NDA approval cannot be predicted with any certainty. The Company, its collaborative partners or other licensees or the FDA may suspend clinical trials at any time if it is believed that individuals participating in trials are being exposed to unacceptable health risks. Even assuming that clinical trials are completed and that an NDA is submitted to the FDA, there can be no assurance that the NDA will be reviewed by the FDA in a timely manner or that once reviewed, the NDA will be approved. The approval process is affected by a number of factors, including the severity of the targeted indications, the availability of alternative treatments and the risks and benefits demonstrated in clinical trials. The FDA may deny an NDA if applicable regulatory criteria are not satisfied, or may require additional testing or information with respect to the investigational drug. Data obtained from preclinical and clinical activities are susceptible to varying interpretations that could also delay, limit or prevent Regulatory Agency approval. Even if initial FDA approval is obtained, further studies, including post-market studies, may be required in order to provide additional data on safety and will be required in order to gain approval for the use of a product as a treatment for clinical indications other than those for which the product was initially tested. The FDA will also require post-market reporting and may require surveillance programs to monitor the side effects of the drug. Results of post-marketing programs may limit or expand the further marketing of the drug. Further, if there are any modifications to the drug, including changes in

indication, manufacturing process or labeling, an NDA supplement may be required to be submitted to the FDA. Finally, delays or rejections may be encountered based upon changes in Regulatory Agency policy during the period of drug development and/or the period of review of any application for Regulatory Agency approval for a compound. Moreover, because most of the Company's collaborative partners and other licensees are generally responsible for preclinical testing, clinical trials, regulatory approvals, manufacturing and commercialization of drugs, the ability to obtain and the timing of regulatory approvals are not within the control of the Company. There can be no assurance that the regulatory framework described above will not change or that additional regulations will not arise that may affect approval of a potential drug.

Each manufacturing establishment for new drugs is required to receive some form of approval by the FDA. Among the conditions for approval is the requirement that the prospective manufacturer's quality control and manufacturing procedures conform to GMP, which must be followed at all times. In complying with standards set forth in these regulations, manufacturers must continue to expend time, monies and effort in the area of production and quality control to ensure full technical compliance. Manufacturing establishments, both foreign and domestic, are also subject to inspections by or under the authority of the FDA and may be subject to inspections by foreign and other Federal, state or local agencies.

Prior to the commencement of marketing a product in other countries, approval by the regulatory agencies is required, regardless of whether FDA approval has been obtained for such product. The requirements governing the conduct of clinical trials and product approvals vary widely from country to country, and the time required for approval may be longer or shorter than the time required for FDA approval. Although there are some procedures for unified filings for certain European countries, in general, each country has its own procedures and requirements.

Delays in obtaining Regulatory Agency approvals could adversely affect the marketing of any drugs developed by the Company or its collaborative partners or other licensees, impose costly procedures upon the Company's or its collaborative partners' or other licensees' activities, diminish any competitive advantages that the Company or its collaborative partners or other licensees may attain and adversely affect the Company's ability to receive revenues or royalties. There can be no assurance that, even after these delays and expenditures, Regulatory Agency approvals will be obtained for any compounds developed by, in collaboration with or pursuant to licenses from the Company. Moreover, even if Regulatory Agency approval for a compound is granted, this approval may entail limitations on the indicated uses for which it may be marketed. Further, approved drugs and their manufacturers are subject to continual review, and discovery of

previously unknown problems with a drug or
its manufacturer may result in restrictions on such drug or manufacturer, including withdrawal of the drug from the market. Regulatory Agency approval of prices is required in many countries and may be required for the marketing of any drug developed by the Company or its collaborative partners or other licensees.

As with many biotechnology and pharmaceutical companies, the Company's activities involve the use of radioactive compounds and hazardous materials. The Company is subject to local, state and Federal laws and regulations relating to occupational safety, laboratory practices, the use, handling and disposition of radioactive materials, environmental protection and hazardous substance control.

Although the Company believes that its safety procedures for handling and disposing of radioactive compounds and other hazardous materials used in its research and development activities comply with the standards prescribed by Federal, state and local regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of an accident, the Company could be held liable for any damages that result and any such liability could exceed the resources of the Company.

Employees

As of February 28, 2001, the Company had 97 full-time employees, 25 of who hold Ph.D. or M.D. degrees. Of the Company's full-time employees, 80 were engaged directly in scientific research and 17 were engaged in general and administrative functions. The Company's scientific staff members have diversified experience and expertise in molecular and cell biology, biochemistry, molecular pharmacology, medicinal, structural, combinatorial and computer-assisted chemistry and information systems.

All employees have entered into agreements with the Company pursuant to which they are prohibited from disclosing to third parties the Company's proprietary information and assign to the Company all rights to inventions made by them during their employment with the Company.

The Company's employees are not covered by a collective bargaining agreement, and the Company believes that its relationship with its employees is good.

Item 2. Properties

The Company leases laboratory and office space in a facility at 215 College Road in Paramus, New Jersey. The total square footage currently leased by the Company is 83,843. The lease will expire on December 31, 2015. The Company is subleasing 5,000 square feet and 23,008 square feet of its premises to two non-affiliated third parties under agreements expiring in 2001 and 2010, respectively. The Company believes that the 55,835 square feet of space that it currently occupies is adequate to accommodate the anticipated research and administrative needs of the Company for the foreseeable future.

Item 3. Legal Proceedings

On June 5, 2000, the Company filed suit in the United States District Court for the District of New Jersey against M.D.S. Panlabs, Inc., a Washington corporation, and Panlabs Taiwan Ltd., a Taiwanese corporation (collectively, "Panlabs"). The suit alleges that Panlabs has infringed several issued U.S. Patents owned by the Company which relate to cloned human receptors and their use in binding assays. The suit also alleges that Panlabs has been importing, selling and offering to sell products of the Company's patented

binding assay
processes to pharmaceutical companies and others in the United States and particularly in New Jersey.

In the suit, the Company seeks an injunction against Panlabs' infringing activities, an award of damages for the Company's lost profits, the destruction of data obtained by the infringement of its patents, and other

relief.

Company management believes that its complaint against Panlabs is well founded and necessary to protect the value of its intellectual property portfolio.

Management believes that the ultimate resolution of the above matter could have a material impact on the Company's financial position, results of operations and cash flows.

Item 4. Submission of Matters to a Vote of Securityholders

None

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Part II

Item 5. Market For Registrant's Common Equity and Related Stockholder Matters

The Common Stock of the Company trades on The Nasdaq Stock Market under the symbol SNAP. As of February 20, 2001, there were approximately 2,850 holders of record of the Company's Common Stock. No dividends have been paid on the Common Stock to date, and the Company does not currently intend to declare or pay dividends for the foreseeable future.

The following tables set forth the high and low last trade prices for the Common Stock as reported by The Nasdaq Stock Market for the periods indicated below.

2000 Fiscal Year

	High	Low
1st Quarter 2000	16 1/2	5 13/16
2nd Quarter 2000	8	4 1/2
3rd Quarter 2000	7 3/8	5 3/32
4th Quarter 2000	7 3/8	5

1999 Fiscal Year

	High	Low
1st Quarter 1999	19 1/4	6 1/16
2nd Quarter 1999	7 1/2	4 1/2
3rd Quarter 1999	9	4 1/2
4th Quarter 1999	7 1/4	4

Item 6. Selected Financial Data

The following table presents selected information relating to the financial condition and results of operations of the Company for the past five years. The following data should be read in conjunction with the Company's financial statements.

(In thousands, except per share information)

	2000	1999	1998	1997	1996
Total revenues	$ 3,836	$ 1,855	$ 9,352	$ 10,307	$ 9,481
Total expenses	$ 20,212	$ 19,652	$ 19,576	$ 17,853	$ 14,319
Other income, net	$ 2,110	$ 2,676	$ 3,731	$ 2,200	$ 2,205
Net loss	$(13,859)	$(15,121)	$ (6,493)	$ (5,346)	$ (2,633)
Basic and diluted net loss per share	$ (1.28)	$ (1.41)	$ (0.61)	$ (0.66)	$ (0.35)
Total assets	$ 37,571	$ 48,750	$ 64,696	$ 69,402	$ 40,355
Accumulated deficit	$(64,789)	$(50,930)	$(35,809)	$(29,316)	$(23,970)
Stockholders' equity	$ 34,529	$ 47,106	$ 62,676	$ 67,704	$ 39,040

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

Overview

Synaptic Pharmaceutical Corporation ("Synaptic" or the "Company") is a drug discovery company utilizing G protein-coupled receptors ("GPCRs") as targets for novel therapeutics. The Company is utilizing its large portfolio of patented GPCR targets as a basis for the creation of improved drugs that act through these targets. The Company and its licensees are first utilizing these receptor targets to discover their function in the body and thus specific physiological disorders with which they may be associated, and secondly, to design compounds that can potentially be developed as drugs.

The Company is currently collaborating with Grunenthal GmbH ("Grunenthal") and Kissei Pharmaceutical Co., Ltd. ("Kissei"). Concurrently with the establishment of the collaborative arrangement, Synaptic granted Grunenthal a license to certain of its technology and patent rights.

In addition to its ongoing collaborative arrangements, other pharmaceutical companies have licenses to certain of our technology and patent rights. For convenience of reference, the agreements pursuant to which the licenses referred to in this paragraph and the preceding paragraph have been granted are collectively referred to as the "License Agreements."

Since inception, the Company has financed its operations primarily through the sale of its stock, through contract and license revenue under certain of its License Agreements, and through interest income and capital gains resulting from its investments. We also have received monies through government grants under the Small Business Innovative Research ("SBIR") program of the National Institutes of Health and through the sale of a portion of New Jersey State net operating losses carryforwards.

Under the License Agreements, the Company may receive one or more of the following types of revenue: license revenue, contract revenue, royalty revenue or revenue from the sales of drugs. License revenue represents non-refundable payments for a license to one or more of our patents and/or a license to our technology. Payments for licenses are recognized as they are received or, if earlier, when they become guaranteed, provided they are independent of any continuing research activity, otherwise, they are recognized pro-rata during the term of the related research agreement in accordance with Staff Accounting Bulletin No. 101 "Revenue Recognition in Financial Statements". Contract revenue includes research funding to support a specified number of Synaptic's scientists and payments upon the achievement of specified research and development milestones. Research funding revenue is recognized ratably over the period of the collaboration to which it relates and is based upon predetermined funding requirements. Research and development milestone payment revenue is recognized when the related research or development milestone is achieved. Under each of the License Agreements (other than the Grunenthal Agreement), we are entitled to receive royalty payments based upon the sales of drugs that may be developed using our technology or that may be covered by our patents. Under the Grunenthal Agreement, Synaptic has development and marketing rights in certain geographical areas with respect to drugs, if any, that are jointly identified as part of the collaboration with Grunenthal. Accordingly, we may receive revenue from sales in our geographical areas (as defined) of drugs if we market them independently, or we may receive royalty payments if we license our marketing rights to a third party. To date, we have not received

either royalty revenue or revenue from the sales of drugs and we do not expect to receive such revenues for a number of years, if at all.

To date, the Company's expenditures have been for research and development related expenses, general and administrative related expenses, fixed asset purchases and various patent related expenditures incurred in protecting our technologies. Synaptic has been historically unprofitable and had an accumulated deficit of $64,789,000 at December 31, 2000. We expect to continue to incur operating losses for a number of years and may not become profitable, unless and until we receive royalty revenue or revenue from sales of drugs that may be developed with the use of our technology or patent rights.

Results of Operations

Comparison of Fiscal Years Ended December 31, 2000, 1999 and 1998

Revenues. The Company recognized revenue of $3,836,000, $1,855,000 and $9,352,000 for the fiscal years of 2000, 1999 and 1998, respectively. The increase of $1,981,000 from 1999 to 2000 was attributable to an increase in license revenue of $2,750,000 resulting primarily from the grant of a non-exclusive license to certain of Synaptic's technology and patent rights, offset by a reduction in contract revenue of $769,000 resulting from the net reduction in the number of scientists being funded under collaborative arrangements.

The decrease of $7,497,000 from 1999 to 1998 was attributable primarily to the following: a net decrease in contract revenue of $5,347,000 resulting from the contractual termination of three of our collaborative arrangements and the receipt in 1998 of $2,000,000 of non-recurring license revenue under the Glaxo Agreement.

Research and Development Expenses. The Company incurred research and development expenses of $14,360,000, $14,592,000 and $15,274,000 for the fiscal years of 2000, 1999 and 1998, respectively. The decrease of $232,000, or 2%, from 1999 to 2000 was attributable primarily to a net decrease in headcount and a corresponding decrease in supplies which were partially offset by an increase in preclinical testing costs.

The decrease of $682,000, or 4%, from 1998 to 1999 was attributable primarily to a reduction in compensation and fringe benefit expenses due to a net decrease in headcount as well as corresponding reductions in travel and supply costs, which were partially offset by increased rent expense for facilities resulting from previously contracted increases in square footage.

General and Administrative Expenses. The Company incurred general and administrative expenses of $5,852,000, $5,060,000 and $4,302,000 for the fiscal years of 2000, 1999 and 1998, respectively. The increase of $792,000, or 16%, from 1999 to 2000 was attributable primarily to the following: an increase in rent expense; an increase in consulting and finder's fees associated with business development activities; and an increase in legal and patent costs.

The increase of $758,000, or 18%, from 1998 to 1999 was attributable primarily to increases in rent expense resulting from previously contracted increases in square footage and compensation and fringe benefit expenses.

Other Income, Net. The Company recorded other income of $2,110,000,

$2,676,000 and $3,731,000 for the fiscal years of 2000, 1999 and 1998, respectively. The decrease of $566,000 from 1999 to 2000 in other income was primarily due to lower average cash, cash equivalent and marketable securities balances during 2000 as a result of the utilization of these resources to fund Synaptic's operations.

The decrease of $1,055,000 from 1998 to 1999 in other income was primarily due to lower interest income as a result of lower average cash, cash equivalent and marketable securities balances during 1999.

Income Tax Benefit. In November 2000, the Company recognized $407,000 from the sale of a portion of its state net operating loss carryforwards.

Net Loss and Basic and Diluted Net Loss Per Share. The net loss incurred by the Company was $13,859,000 ($1.28 per share), $15,121,000 ($1.41 per share) and $6,493,000 ($0.61 per share) for the fiscal years of 2000, 1999 and 1998, respectively. The decrease in net loss per share of $0.13 resulted primarily from higher revenues and an income tax benefit, which were partially offset by higher total operating expenses and lower other income during the year ended December 31, 2000, as described above.

The increase in net loss per share of $0.80 from 1998 to 1999 resulted primarily from the recognition of lower total revenue and of higher total expenses.

Operating Trends. Revenues may vary from period to period depending on numerous factors including the timing of revenue earned under the License Agreements and revenue that may be earned under future collaborative and/or license agreements. Synaptic will recognize revenue under its research and licensing agreement with Kissei Pharmaceutical Co., Ltd. during 2001 and expects to recognize additional revenues under this agreement during 2002. Under the terms of certain of the License Agreements, revenues may be recognized if certain milestones are achieved. We continue to assess the opportunity for obtaining additional funding under new collaborative and/or license agreements as well as obtaining financing through equity transactions. We continue to monitor our spending level in order to insure that we have enough cash to last through the year 2002.

Preclinical expenses are expected to increase as Synaptic moves its own drug discovery projects forward.

Legal expenses are expected to increase as a result of a suit filed by the Company. See "Legal Proceedings" in PART I, Item 3, hereof.

Other income, net is expected to decline in 2001 and 2002 as existing funds are utilized to support the Company's operations. This decline will be partially offset by rental income that we expect to recognize under our sublease agreements.

The Company is pursuing further sales of its State net operating loss ("NOL") carryforwards and its State research and development credits under the State of New Jersey's Technology Business Tax Certificate Transfer Program (the "Program"). No assurance can be given, however, as to the amount of NOL carryforwards that may be sold under the Program in any one year. External factors that may have an effect on future NOL sales are such items as: limitations imposed by State law, the availability of buyers and related demand.

Property and equipment spending may vary from period to period

depending on numerous factors, including the number of collaborations in which we are involved at any given time and replacement due to normal wear and obsolescence. Equipment spending in 2001 is expected to increase from that of 2000.

At December 31, 2000, Synaptic held marketable securities with an estimated fair value of $29,565,000. Synaptic's primary interest rate exposure results from changes in short-term interest rates. We do not purchase financial instruments for trading or speculative purposes. All of the marketable securities held by Synaptic are classified as available-for-sale securities. The following table provides information about marketable securities held by Synaptic at December 31, 2000:

	Principal Amount and Weighted Average Stated Rate by Expected Maturity				Estimated Fair Value
(000's)	2001	2002	2003	Total	(000's)
Principal	$20,440	$2,500	$6,500	$29,440	$29,565
Weighted Average Stated Rates	7.91%	6.50%	5.77%	7.31%	--

The stated rates of interest expressed in the above table may not approximate the actual yield of the securities which Synaptic currently holds since we have purchased some marketable securities at other than face value. Additionally, some of the securities represented in the above table may be called or redeemed, at the option of the issuer, prior to their expected due dates. If early redemptions occur, we may reinvest the proceeds realized on such calls or redemptions in marketable securities with stated rates of interest or yields that are lower than those of current holdings, affecting both future cash interest streams and future earnings.

In addition to investments in marketable securities, the Company places some of its cash in money market funds in order to keep cash available to fund operations and to hold cash pending investments in marketable securities. Fluctuations in short term interest rates will affect the yield on monies invested in money market funds. These fluctuations can have an impact on future cash interest streams and future earnings of the Company, but the impact of such fluctuations are not expected to be material.

The Company does not believe that inflation has had a material impact on its results of operations.

Liquidity and Capital Resources

At December 31, 2000 and December 31, 1999, cash, cash equivalents and marketable securities aggregated $31,602,000 and $42,143,000, respectively. This decrease was a result of the utilization of these resources to fund the Company's operations.

To date, Synaptic has met its cash requirements through the sale of its stock, through contract and license revenue, through interest income and gains resulting from its investments, through SBIR grants and through the sale of a portion of its State NOL carryforwards. If the current biotechnology financing

environment remains unfavorable, raising additional capital may be difficult.

Synaptic leases laboratory and office facilities under an agreement expiring on December 31, 2015. The minimum annual payment under the lease is currently $2,074,000. The lease provides for fixed escalations in rent payments in the years 2005 and 2010.

At December 31, 2000, the Company had $31,602,000 in cash, cash equivalents and marketable securities. The Company currently intends to utilize these funds primarily to conduct certain of its research programs, for patent related expenditures, for general corporate purposes, to make leasehold improvements to its facilities and to purchase property and equipment. We expect to continue to incur operating losses for a number of years. We believe that cash on hand and cash that we expect to receive through interest payments on investments, will be sufficient to fund operations, as well as our share of certain development costs under the Grunenthal Agreement, through the year 2002.

As of December 31, 2000, the Company had NOL carryforwards of approximately $57,000,000 for Federal income tax purposes that will expire principally in the years 2002 through 2020. In addition, the Company had research and development credit carryforwards of approximately $1,610,000, which will expire principally in 2002 through 2018. Also at December 31, 2000, Synaptic had NOL carryforwards of approximately $41,637,000 for State income tax purposes and State research and development credit carryforwards of $475,000. For financial reporting purposes, a valuation allowance has been recognized to offset the deferred tax assets related to these carryforwards. Due to the limitations imposed by the Tax Reform Act of 1986, and as a result of significant changes in the Company's ownership in 1993 and 1997, the utilization of $25,000,000 of Federal NOL carryforwards is subject to annual limitation. The utilization of the research and development credits is similarly limited.

Recent Accounting Pronouncements

In June 1998, the Financial Accounting Standards Board issued Statement of Financial Accounting Standards No. 133, "Accounting for Derivatives and Hedging Activities" ("SFAS 133"), which establishes accounting and reporting standards for derivative instruments, including certain derivative instruments embedded in other contracts (collectively referred to as derivatives) and for hedging activities. SFAS 133, as amended, is effective for all fiscal quarters of fiscal years beginning after June 15, 2000. As we do not currently intend to engage in derivatives or in hedging transactions, we do not anticipate any effect on Synaptic's results of operations, financial position or cash flows upon the adoption of SFAS 133.

Disclosure Regarding Forward-Looking Statements

This Report includes "forward-looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. These forward-looking statements include, but are not

limited to, those relating to
future cash and spending plans, amounts of future research funding, patent-related plans, additional drug discovery programs, the effectiveness, efficacy, or other results of any of Synaptic's technology or drugs, any other statements regarding future growth, future cash needs, future operations, business plans and financial results, and any other statements which are not historical facts. When used in this document, the words "anticipate," "estimate," "expect," "may," "project," and similar expressions are intended to be among the statements that identify forward-looking statements. These

statements involve risks and uncertainties, including, but not limited to, those risks and uncertainties relating to those described below, as well as other factors detailed elsewhere in this Report, including in Item 1 of this Report under the captions "Patents, Proprietary Technology and Trade Secrets," "Competition" and "Government Regulation" ("Cautionary Statements"). These Cautionary Statements qualify the forward-looking statements included in this Report. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual outcomes may vary materially from those indicated. All subsequent written and oral forward-looking statements attributable to Synaptic or persons acting on its behalf are expressly qualified in their entirety by the Cautionary Statements.

Early Stage of Product Development; Technological Uncertainty

Since its inception in January 1987, Synaptic has focused its activities on the discovery and cloning of receptor genes and the use of these genes as tools in the design of precisely targeted compounds for a broad range of therapeutic applications. To date, neither Synaptic nor any of its collaborative partners or any of its other licensees has completed the development of drugs designed with the use of Company technology and we do not expect that any drugs resulting from our or our collaborative partners' or other licensees' research and development efforts will be commercially available for a number of years, if at all. All compounds discovered by Synaptic and its collaborative partners and other licensees will require extensive preclinical and clinical testing prior to submission of any regulatory application for commercial use. Extensive preclinical and clinical testing required to establish safety and efficacy will take several years, and the time required to commercialize new drugs cannot be predicted with accuracy. Moreover, potential products that appear to be promising at early stages of development may never reach the market for a number of reasons. These reasons include, but are not limited to, the possibilities that potential products are found during preclinical testing or clinical trials to be ineffective or to cause harmful side effects, that they fail to receive necessary regulatory approvals, that they are difficult or uneconomical to manufacture on a large scale, that they fail to achieve market acceptance or that they are precluded from commercialization by proprietary rights of third parties. There can be no assurance that the Company's approach to drug discovery, its research and development efforts or the efforts of Grunenthal, Kissei, Lilly, Novartis or Glaxo, or any future collaborative partner or other licensee of the Company, will result in the development of any drugs, or that any drugs, if successfully developed, will be proven to be safe and effective in clinical trials, receive required regulatory approvals, be capable of being manufactured in commercial quantities at reasonable costs or be successfully commercialized. Product development of new pharmaceuticals is highly uncertain, and unanticipated developments, including clinical or regulatory delays, unexpected adverse effects and inadequate therapeutic efficacy, would slow or prevent product development efforts of the Company and its collaborative partners and other licensees and have a material adverse effect on the Company's operations.

Dependence on Collaborative Partners and Licensees for Development, Regulatory Approvals, Manufacturing, Marketing and Other Resources

A key element of Synaptic's business strategy is to leverage resources by entering into collaborative and licensing arrangements with pharmaceutical companies. Under the agreements with Kissei, Lilly and

Novartis, the Company's

collaborative partners and licensees are each responsible for conducting preclinical testing and clinical trials of compounds developed through the use of the Company's technology, obtaining regulatory approvals and manufacturing and commercializing any resulting drugs. Under the Grunenthal Agreement, Grunenthal is responsible for conducting certain preclinical testing and clinical trials of compounds developed through the use of the Company's technology. Synaptic has no involvement in the research and development activities of Glaxo under the Glaxo Agreement. As a result, the Company's receipt of revenues (whether in the form of drug development milestones, royalties on sales or net sales proceeds) in respect of drugs resulting from its collaborative and licensing arrangements is dependent upon the activities of its collaborative partners and other licensees. The amount and timing of resources dedicated by our collaborative partners and other licensees to the development of drugs that would be subject to royalties payable to Synaptic are not within our control. Moreover, there can be no assurance that the interests of Synaptic will continue to coincide with those of its collaborative partners or other licensees, that one or more of Synaptic's collaborative partners or other licensees will not develop independently or with third parties drugs that could compete with drugs of the types covered by their arrangements with Synaptic, or that disagreements over rights or technology or other proprietary interests will not occur.

If any of Synaptic's collaborative partners or other licensees breaches its agreement with the Company, or fails to devote adequate resources to or conduct in a timely manner its collaborative or licensed activities, the related research programs or the development and commercialization of drug candidates subject to such arrangement could be materially adversely affected. There can be no assurance that the Company's collaborative or licensing arrangements will be successful. Further, there can be no assurance that Synaptic will be able to enter into acceptable collaborative or licensing arrangements with other pharmaceutical companies in the future, or that, if negotiated, such arrangements will be successful.

History of Operating Losses and Accumulated Deficit

The Company has incurred significant operating losses since its inception in January 1987. At December 31, 2000, Synaptic's accumulated deficit was $64,789,000. Losses have resulted principally from costs incurred in connection with the Company's research and development activities and from general and administrative costs associated with operations. We expect to continue to incur substantial operating losses at least over the next several years and expect losses to increase as research funding under collaborative arrangements diminish. As of December 31, 2000, the only revenues generated by the Company had resulted from payments under collaborative and license agreements, and government grants under the SBIR program of the National Institutes of Health. The Company's revenues, expenses and losses may fluctuate from quarter to quarter and year to year. Research payments under the Novartis Agreements expired in 1998, research payments under the Merck Agreement expired in February 1999, and research payments under the Lilly Agreement expired in July 1999. We anticipate that there will initially be little, if any, biological knowledge regarding many of Synaptic's future gene discoveries and, as a result, Synaptic may have fewer opportunities to enter into collaborative arrangements focused on these discoveries. We do not expect to achieve revenues or royalties from sales of drugs for a number of years, if at all. The Company will not achieve revenues or royalties from drug sales unless it or one of its collaborative partners or other licensees successfully completes clinical trials with respect to a drug candidate, obtains regulatory approvals for that drug candidate and commercializes the resulting drug. Failure to achieve significant revenue or profitable operations could impair the Company's ability to sustain operations and there can be no assurance that the Company will ever achieve significant revenues or profitable operations.

Future Capital Needs; Uncertainty of Additional Funding

The operation of Synaptic's business requires substantial capital resources and this requirement is likely to increase in the future. The Company's future financial requirements will depend on many factors, including the continued progress of its research and development programs, the timing and results of preclinical testing and clinical trials, if any, of its or its collaborative partners' or other licensees' drug candidates, the timing of regulatory approvals, if any, technological advances, determinations as to the commercial potential of its or its collaborative partners' or other licensees' proposed products and the status of competitive products. Synaptic's capital requirements will also depend on its ability to establish and maintain collaborative or licensing arrangements with others and on whether its future collaborative partners provide research funding and are responsible for all development activities, preclinical testing and regulatory approvals and, if these approvals are obtained, the manufacturing and marketing of products. In addition, these capital requirements will depend on the time and expense associated with filing and, if necessary, prosecuting and enforcing patent claims.

The Company entered into the Grunenthal Agreement in January 1998. Under this agreement, Synaptic will retain certain ownership rights to products that result from the collaboration. In addition, Synaptic will be significantly involved in the development of any potential products but may also be required to contribute substantial financial resources towards such development. Accordingly, the cost to Synaptic of this arrangement may be significantly greater than the cost to it of participating in a royalty-based collaboration.

No assurance can be given that the Company's existing cash on hand and marketable securities and funds it will receive under its collaborative and license agreements, together with interest income, will be sufficient. We expect that Synaptic will, in the future, seek to raise additional funding from other sources, including other collaborative partners and licensees, and through public or private financings, including sales of equity or debt securities. Any collaborative or licensing arrangement could result in limitations on the Company's ability to control the research and development of potential drugs and the commercialization of resulting drugs, if any, as well as its profits therefrom. Any equity financing could result in dilution to Synaptic's then existing stockholders. There can be no assurance that additional funds will be available on favorable terms or at all, or that these funds, if raised, would be sufficient to permit the Company to continue to conduct its operations. If adequate funds are not available, Synaptic may be required to curtail significantly or eliminate one or more of its receptor or drug discovery programs.

Uncertainties Related to Clinical Trials

Before obtaining required regulatory approvals for the commercial sale of each product under development, the Company or its collaborators and other licensees must demonstrate through preclinical studies and clinical trials that such product is safe and efficacious for use. The results of preclinical studies and initial clinical trials are not necessarily predictive of results that will be obtained from large-scale clinical trials, and there can be no assurance that clinical trials of any product under development will demonstrate the safety and efficacy of such product or will result in a marketable product. The safety and

efficacy of a therapeutic product under development by Synaptic or its collaborative partners or other licensees must be supported by extensive data from clinical trials. A number of companies have suffered significant setbacks in advanced clinical trials, despite promising results in earlier trials. The failure to demonstrate adequately the safety and efficacy of a therapeutic drug under development would delay or prevent regulatory approval of the product that could have a material adverse effect on the Company. In addition, the FDA or other

regulatory agency may require additional clinical trials, which could result in increased costs and significant development delays.

The rate of completion of clinical trials of the Company's or its collaborative partners' and other licensees' products is dependent upon, among other factors, obtaining adequate clinical supplies and the rate of patient accrual. Patient accrual is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites and the eligibility criteria for the trial. Delays in planned patient enrollment in clinical trials may result in increased costs, program delays or both, which could have a material adverse effect on the Company. In addition, Synaptic's collaborative partners and other licensees generally have the right to control the planning and execution of product development and clinical programs, and there can be no assurance that partners and licensees will conduct programs in accordance with schedules that are satisfactory to the Company. There can be no assurance that, if clinical trials are completed, Synaptic or its collaborative partners and other licensees will submit NDAs with respect to any potential products or that any application will be reviewed and approved by the FDA in a timely manner, if at all.

Lack of Manufacturing Experience; Reliance on Contract Manufacturers

The Company currently has no manufacturing facilities and relies on its collaborative partners and other licensees or other manufacturers to produce its compounds for research and development, preclinical and clinical purposes. The products under development by Synaptic and its collaborative partners and other licensees have never been manufactured on a commercial scale and there can be no assurance that products can be manufactured at a cost or in quantities necessary to make them commercially viable. If Synaptic were unable to contract for a sufficient supply of its compounds on acceptable terms, or if it should encounter delays or difficulties in its relationships with manufacturers, any preclinical or clinical testing schedule of the Company would be delayed, resulting in delay in the submission of products for regulatory approval or the market introduction and subsequent sales of products, which could have a material adverse effect on the Company. Moreover, manufacturers that Synaptic may use must adhere to current GMP regulations enforced by the FDA through its facilities inspection program. If these facilities cannot pass a pre-approval plant inspection, the FDA pre-market approval of the products will not be granted.

Lack of Sales and Marketing Capability

The creation of infrastructure to commercialize pharmaceutical products is a difficult, expensive and time-consuming process. Synaptic currently has no sales or marketing capability. To market directly any product it may develop, the Company would need to establish a marketing and sales force with technical expertise and distribution capability or contract with other pharmaceutical

and/or health care companies with distribution systems and direct sales forces. There can be no assurance that the Company would be able to establish direct or indirect sales and distribution capabilities or be successful in gaining market acceptance for licensing arrangements. To the extent that the Company enters into co-promotion or licensing arrangements, any revenues received by the Company will be dependent on the efforts of third parties, and there can be no assurance that these efforts will be successful.

Dependence on Key Personnel

The Company is highly dependent on its management and scientific staff. Loss of the services of any key individual could have an adverse effect on the Company. We believe that our future success will depend,

in part, on our ability
to attract and retain highly talented managerial, scientific, software and bioinformatics personnel and consultants. Synaptic faces intense competition for personnel from, among others, biotechnology and pharmaceutical companies, as well as academic and other research institutions. There can be no assurance that it will be able to attract and retain the personnel it requires on acceptable terms. Failure to attract and retain such personnel could have a material adverse effect on the Company.

External Environment

Over the past several years, there has been a significant reduction in the number of investors who are willing to commit capital to the biotechnology industry. With over 300 public biotechnology companies and over 1,000 private biotechnology companies, the lack of capital is severely impairing the ability of many of these companies to carry out their research. Additionally, many pharmaceutical companies are now routinely performing many of the types of research and services that have historically been performed by biotechnology companies. As a consequence, many pharmaceutical companies are less interested than in the past both in engaging in collaborations with biotechnology companies in a number of areas and in providing them with research funding and other sources of revenue.

Over time, Synaptic could be materially and adversely affected by a lack of available capital and/or a lack of interest on the part of the pharmaceutical industry in its services or products. This unfavorable external environment could result in the Company's inability to complete certain of its research projects and/or in the need for Synaptic to downsize until it begins to receive royalty income pursuant to outstanding licensing arrangements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Quantitative and qualitative disclosures about market risk (i.e., interest rate risk) are included in Item 7 of this Report.

Item 8. Financial Statements

SYNAPTIC PHARMACEUTICAL CORPORATION

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REPORT OF INDEPENDENT AUDITORS

The Board of Directors and Shareholders
SYNAPTIC PHARMACEUTICAL CORPORATION

We have audited the accompanying balance sheets of Synaptic Pharmaceutical Corporation as of December 31, 2000 and 1999, and the related statements of operations and comprehensive income (loss), stockholders' equity and cash flows for each of the three years in the period ended December 31, 2000. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Synaptic Pharmaceutical Corporation at December 31, 2000 and 1999, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2000, in conformity with accounting principles generally accepted in the United States.

ERNST & YOUNG LLP

MetroPark, New Jersey
February 2, 2001

SYNAPTIC PHARMACEUTICAL CORPORATION

BALANCE SHEETS

(in thousands, except share and per share information)

December 31, 2000 and 1999 Assets	2000	1999
Current assets:		
Cash and cash equivalents	$ 2,037	$ 6,236
Marketable securities--current maturities	20,627	6,471
Other current assets	814	847
Total current assets	23,478	13,554
Property and equipment, net	4,781	5,186
Marketable securities	8,938	29,436

Patent and patent application costs, net of accumulated amortization (2000--$2,148; 1999--$1,801)	227	574
Other assets	147	-
	$ 37,571	$ 48,750

Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,128	$ 486
Accrued liabilities	648	525
Accrued compensation	348	386
Deferred revenue	354	-
Total current liabilities	2,478	1,397
Deferred rent obligation	564	247
Stockholders' equity:		
Preferred Stock, $.01 par value; authorized--1,000,000 shares	-	-
Common Stock, $.01 par value; authorized--25,000,000 shares issued and outstanding--10,935,772 shares in 2000 and 10,764,661 shares in 1999	109	108
Additional paid-in capital	99,392	98,719
Accumulated other comprehensive income--net unrealized losses on securities	(183)	(791)
Accumulated deficit	(64,789)	(50,930)
Total stockholders' equity	34,529	47,106
	$ 37,571	$ 48,750

See notes to financial statements.

SYNAPTIC PHARMACEUTICAL CORPORATION

STATEMENTS OF OPERATIONS AND COMPREHENSIVE INCOME (LOSS)

(in thousands, except share and per share information)

For the Years Ended December 31, 2000, 1999 and 1998

	2000	1999	1998
Revenues:			
Contract revenue	$ 1,086	$ 1,855	$ 7,202
License revenue	2,750	-	2,000
Grant revenue	-	-	150
Total revenues	3,836	1,855	9,352

Expenses:			
Research and development	14,360	14,592	15,274
General and administrative	5,852	5,060	4,302
Total expenses	20,212	19,652	19,576
Loss from operations	(16,376)	(17,797)	(10,224)
Other income, net:			
Interest income	2,106	2,674	3,603
Gain on sale of securities	-	2	128
Other	4	-	-
Other income, net	2,110	2,676	3,731
Net loss before benefit from income taxes	(14,266)	(15,121)	(6,493)
Income tax benefit	407	-	-
Net loss	$(13,859)	$(15,121)	$ (6,493)
Comprehensive loss:			
Net loss	$(13,859)	$(15,121)	$ (6,493)
Unrealized gains (losses) arising during period	608	(702)	(82)
Less: reclassification adjustment for gains included in net income	-	(12)	(21)
Comprehensive loss	$ (13,251)	$(15,835)	$ (6,596)
Basic and diluted net loss per share	$ (1.28)	$ (1.41)	$ (0.61)
Shares used in computation of net loss per share	10,850,262	10,742,296	10,684,892

See notes to financial statements.

SYNAPTIC PHARMACEUTICAL CORPORATION

STATEMENTS OF STOCKHOLDERS' EQUITY

(in thousands, except share information)

	Common Stock Shares	Common Stock Amount	Additional Paid-In Capital	Net Unrealized Gains (Losses) on Securities	Deferred Compen-sation	Accumu-lated Deficit
Balance at January 1, 1998	10,526,585	$ 105	$ 97,049	$ 26	$ (160)	$ (29,316
Purchase of 375 shares of Treasury Stock at cost	--	--	--	--	--	--
Forfeiture of Deferred Compensation related to Stock Incentive Plan	--	--	(20)	--	20	--
Amortization of Deferred Compensation	--	--	--	--	79	--
Issuance of 47,516, shares of common stock pursuant to exercise of stock options	47,141	1	127	--	--	--
Issuance of 137,648 shares of common stock pursuant to exercise of stock warrants	137,648	1	1,307	--	--	--
Adjustment to reflect net unrealized loss on securities	--	--	--	(103)	--	--
Adjustment to reflect recognition of short-swing profits realized on sale of stock by stockholder	--	--	53	--	--	--
Net loss for the year ended December 31, 1998	--	--	--	--	--	(6,493
Balance at December 31, 1998	10,711,374	$ 107	$ 98,516	$ (77)	$ (61)	$ (35,809
Forfeiture of Deferred Compensation related to Stock Incentive Plan	--	--	(11)	--	11	
Amortization of Deferred Compensation	--	--	--	--	50	
Issuance of 53,287, shares of common stock pursuant to exercise of stock options	53,287	1	214	--	--	
Adjustment to reflect net unrealized loss on securities	--	--	--	(714)	--	
Net loss for the year ended December 31, 1999	--	--	--	--	--	(15,1
Balance at December 31, 1999	10,764,661	$ 108	$ 98,719	$ (791)	$ (--)	$ (50,9
Issuance of 171,111, shares of common stock pursuant to exercise of stock options	171,111	1	673	--	--	
Adjustment to reflect net unrealized gain on securities	--	--	--	608	--	
Net loss for the year ended December 31, 2000	--	--	--	--	--	(13,8
Balance at December 31, 2000	10,935,772	$ 109	$ 99,392	$ (183)	$ (--)	$ (64,7

See notes to financial statements.

SYNAPTIC PHARMACEUTICAL CORPORATION

STATEMENTS OF CASH FLOWS

(in thousands)

For the Years Ended December 31, 2000, 1999 and 1998

	2000	1999	1998
Operating activities:			
Net loss	$ (13,859)	$ (15,121)	$ (6,493)
Adjustments to reconcile net loss to net cash (used in) operating activities:			
Depreciation and patent amortization	1,626	1,609	1,505
Amortization of premiums (discounts) on securities	463	479	226
Amortization of deferred compensation	-	50	79
Gains on sales of securities	-	(2)	(128)
Loss on sale of equipment	100	32	-
Deferred rent, net	270	247	-
Changes in operating assets and liabilties:			
Decrease (increase) in other current assets	33	817	(390)
Increase (decrease) in accounts payable, accrued liabilities and accrued compensation	727	(540)	239
Decrease in license agreement revenue receivable	-	-	40
Increase in other assets	(100)	-	-
Increase (decrease) in deferred revenue	354	(83)	83
Net cash (used in) operating activities	(10,386)	(12,512)	(4,839)
Investing activities:			
Proceeds from sale or maturity of investments	6,487	19,039	70,797
Purchases of investments	-	(16,349)	(71,799)
Proceeds from sales of equipment	70	80	-
Reimbursement for leasehold improvements	129	-	-
Purchases of property and equipment	(1,173)	(827)	(2,171)
Net cash provided by (used in) investing activities	5,513	1,943	(3,173)
Financing activities:			
Issuance of common stock, net of purchases	674	215	1,436
Short-swing profits realized on sale of stock by stockholder	-	-	53
Net cash provided by financing activities	674	215	1,489
Net decrease in cash and cash equivalents	(4,199)	(10,354)	(6,523)
Cash and cash equivalents at beginning of period	6,236	16,590	23,113
Cash and cash equivalents at end of period	$ 2,037	$ 6,236	$ 16,590

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See notes to financial statements.

SYNAPTIC PHARMACEUTICAL CORPORATION
NOTES TO FINANCIAL STATEMENTS
December 31, 2000

Note 1 -- Summary of Significant Accounting Policies

Organization. Synaptic Pharmaceutical Corporation ("Synaptic" or the "Company") is a drug discovery company utilizing G protein-coupled receptors ("GPCRs") as targets for novel therapeutics. The Company is utilizing its large portfolio of patented GPCR targets as a basis for the creation of improved drugs that act through these targets. The Company and its licensees are first utilizing these receptor targets to discover their function in the body and thus specific physiological disorders with which they may be associated, and secondly, to design compounds that can potentially be developed as drugs.

Basic and Diluted Net Loss Per Share. Net loss per share is computed using the weighted average number of shares of common stock outstanding. As a result of the Company's operating losses and the anti-dilutive effect from stock options and warrants, these instruments are excluded from the computation of diluted net loss per share.

Revenue Recognition. License revenue represents non-refundable payments for a license to one or more of the Company's patents and/or a license to the Company's technology. Payments for licenses are recognized as they are received or, if earlier, when they become guaranteed, provided they are independent of any continuing research activity, otherwise, they are recognized pro-rata during the term of the related research agreement. Contract revenue includes research funding to support a specified number of the Company's scientists and payments upon the achievement of specified research and development milestones. Research funding revenue is recognized ratably over the period of the collaboration to which it relates. Payments received in advance under the related contracts are recorded as deferred revenue until the research is performed. Research milestone payment revenue is recognized at the time the related research milestone is achieved. Government grant receipts are recorded as revenue in the period in which the related research is performed.

Cash Equivalents. Cash equivalents consist of highly liquid investments with maturities of three months or less when purchased. Included in cash equivalents at December 31, 2000, is approximately $1,651,000 related to investments in money market funds. At December 31, 1999, this amount totaled $6,234,000.

Marketable Securities. All of Synaptic's marketable securities are classified as available-for-sale securities and are carried at fair value, with the unrealized gains and losses reported as a separate component of stockholders' equity. The cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. This amortization is included in interest income. Realized gains and losses and declines in value judged to be other than temporary, if any, are included in other income. The cost of securities sold is based on the specific identification method. Investments held as of December 31, 2000 consist primarily of U.S. Government

and Federal Agency obligations, U.S. corporate debt securities and mortgage-backed securities. The maturities range from January 15, 2001, through November 17, 2003.

The Company has established guidelines relative to diversification, credit ratings and maturities to maintain safety and liquidity. The guidelines are periodically reviewed and modified to take advantage of trends in yields and interest rates.

Property and Equipment. Property and equipment are stated at cost. Depreciation is computed using the straight-line method over the estimated useful lives of the assets. Scientific equipment, office equipment and

furniture
and fixtures are depreciated over a life of 7 years. Leasehold improvements are depreciated principally over the life of the facility lease, which is currently 15 years. Software is depreciated over a life of 3 years.

Patents. Prior to October 1, 1996, patent and patent application costs were capitalized and amortized over 7 years or the estimated life of the patent, if less, using the straight-line method. Capitalized costs through October 1, 1996 will continue to be amortized over the remaining portions of their seven-year lives. Effective October 1, 1996, patent and patent application costs are expensed as incurred. The Company periodically reviews capitalized costs to assess ongoing recoverability.

Accrued Liabilities. Included in accrued liabilities at December 31, 2000 and 1999 are accrued professional fees totaling $340,000 and $270,000, respectively.

Stock-Based Compensation. The Company has elected to follow Accounting Principles Board Opinion No. 25, "Accounting for Stock Issued to Employees" ("APB No. 25"), in accounting for its employee stock options. Under APB No. 25, compensation expense is recognized only when the exercise price of options is below the market price of the underlying stock on the date of grant. This expense is recognized ratably over the vesting period.

Use of Estimates. The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements. Estimates also affect the reported amounts of revenues and expenses during the reporting period. Actual results could differ from these estimates.

Comprehensive Income (Loss). Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period resulting from transactions and other events and circumstances from nonowner sources. Comprehensive loss for Synaptic, in addition to net loss, includes unrealized gains and losses on marketable securities held for sale, currently recorded in stockholders' equity.

Recent Accounting Pronouncements. In June 1998, the Financial Accounting Standards Board issued Statement of Financial Accounting Standards No. 133, "Accounting for Derivatives and Hedging Activities" ("SFAS 133"), which establishes accounting and reporting standards for derivative instruments, including certain derivative instruments embedded in other contracts (collectively referred to as derivatives) and for hedging activities. SFAS 133,

as amended, is effective for all fiscal quarters of fiscal years beginning after June 15, 2000. As the Company does not currently intend to engage in derivatives or in hedging transactions, the Company does not anticipate any effect on its results of operations, financial position or cash flows upon the adoption of SFAS 133.

Reclassifications. Certain prior year amounts have been reclassified to conform with the current year presentation.

Note 2 -- Marketable Securities

The following is a summary of all of Synaptic's marketable securities. All of these securities are classified as available-for-sale securities. Determination of estimated fair value is based on quoted market prices:

	Cost	Gross Unrealized Gains	Gross Unrealized (Losses)	Estimated Fair Value
December 31, 2000:				
U.S. Treasury obligations and obligations of U.S. government agencies	$ 8,000,000	$ --	$ (57,000)	$ 7,943,000
U.S. corporate debt securities	21,748,000	--	(126,000)	21,622,000
	$29,748,000	$ --	$(183,000)	$29,565,000
December 31, 1999:				
U.S. Treasury obligations and obligations of U.S. government agencies	$ 8,000,000	$ --	$(279,000)	$ 7,721,000
U.S. corporate debt securities	28,698,000	--	(512,000)	28,186,000
	$36,698,000	$ --	$(791,000)	$35,907,000

The gross realized gains on sale of available-for-sale securities for the years ending December 31, 2000, 1999 and 1998 totaled $0, $2,000 and $128,000, respectively. There were no gross realized losses during 2000, 1999 and 1998. The net adjustment to unrealized gains (losses) on available-for-sale securities included as a separate component of stockholders' equity totaled $608,000 in 2000, $(714,000) in 1999 and $(103,000) in 1998.

Note 3 -- Collaborative and Licensing Arrangements

At December 31, 2000, Synaptic was engaged in collaborations with Kissei Pharmaceutical Co., Ltd. ("Kissei") and Grunenthal GmbH ("Grunenthal"). In addition to these ongoing collaborative arrangements, at December 31, 2000, four other pharmaceutical companies have licenses to certain of the Company's technology and patent rights. Details of these arrangements are set forth below:

Kissei Pharmaceutical Co., Ltd. Synaptic and Kissei are parties to a research and licensing agreement to identify novel receptors, which will be identified utilizing the Company's genomics and functional genomics discovery

technologies. Under the term of the three-year agreement, Kissei will provide funding to Synaptic to support research that is aimed at discovering novel receptors through the use of the Company's proprietary technologies. In addition to the research funding, the agreement provides for a license fee, milestone payments and royalty payments to the Company on sales of any products. In return, Synaptic granted Kissei worldwide exclusive rights to use selected receptors resulting from the collaboration to discover, develop, manufacture and market drugs that act through these receptors.

During 2000, the Company recognized $1,271,000 in revenue under this agreement. Revenues that have been recognized are not subject to repayment.

At December 31, 2000, the Company had recorded $354,000 in deferred revenue representing advance funding for research and license revenue, both of which will be recognized in 2001.

Grunenthal GmbH. Synaptic and Grunenthal are parties to a collaborative and licensing agreement pursuant to which they are collaborating to discover and develop drugs for the treatment of pain. Synaptic is using its receptor-targeted drug design technology to identify compounds of interest and Grunenthal is using its expertise to evaluate the compounds in pain model systems and conduct preclinical studies. Grunenthal will conduct clinical studies with promising compounds. The companies will each be responsible for their own research costs and equally share the development costs through Phase IIa clinical trials. Synaptic will retain manufacturing and marketing rights in the U.S., Canada and Mexico and share these rights in countries outside of Europe, South and Central America where Grunenthal retains these rights. To date, the Company has not recognized any revenue under this collaboration.

The R.W. Johnson Research Pharmaceutical Research Institute. Synaptic and The R.W. Johnson Pharmaceutical Research Institute ("PRI") are parties to a licensing agreement under which PRI was granted nonexclusive licenses under the Company's alpha 1 adrenergic receptor patents and benign prostatic hyperplasia functional use patent to develop and sell alpha-1a selective compounds for all therapeutic applications. PRI is required to make payments upon the achievement of certain milestones and pay royalties to Synaptic on sales of products, if any.

During 2000, the Company recognized $2,500,000 in revenue under this licensing arrangement. Revenue that has been recognized is not subject to repayment.

Eli Lilly and Company. Synaptic and Eli Lilly and Company ("Lilly") are parties to a collaborative and licensing agreement under which the Company granted Lilly an exclusive license to use all but two of the Company's serotonin drug discovery systems to promote the discovery and development of receptor subtype-selective drugs for the treatment of serotonin-related disorders. Through July 1999, Lilly provided funding to Synaptic to support a specified number of Company scientists who conducted research as part of the collaboration. Under the terms of the agreement, the collaboration and associated research funding ended on July 30, 1999. Lilly is required to pay royalties on sales of any products developed through the use of the Company's technology and is required to make payments upon the achievement of certain milestones.

During 1999 and 1998, the Company recognized $1,676,000 and $4,659,000, respectively, in revenue under this agreement. Revenues that have been

recognized are not subject to repayment.

Novartis Pharma AG. Synaptic and Novartis Pharma AG ("Novartis") are parties to two collaborative and licensing agreements under which the Company granted Novartis an exclusive worldwide license to use the Company's neuropeptide Y technology to develop, manufacture and sell compounds that work through neuropeptide Y receptor subtypes for the treatment of obesity and eating disorders. Through August 4, 1998, Novartis provided funding to Synaptic to support a specified number of the Company's scientists who conducted research as part of the collaboration. Under the terms of the agreements, the collaboration and associated research funding ended on August 4, 1998. After August 4, 2001, all of these licenses and rights become nonexclusive. Novartis is required to pay royalties on certain product sales and is required to make payments upon the achievement of certain milestones.

During 1998 the Company recognized $2,041,000 in revenue under this agreement. Revenues that have been recognized are not subject to repayment.

At December 31, 2000, Novartis held 695,715 shares of the Company's common stock, which represents 6.36% of the outstanding shares of the Company.

Glaxo Group Limited. Synaptic and Glaxo Group Limited of the United Kingdom ("Glaxo") are parties to a licensing agreement under which Glaxo currently holds a nonexclusive license under the Company's alpha 1 adrenergic receptor patents to develop and sell alpha-1a selective compounds for therapeutic applications other than the treatment of BPH. Synaptic is entitled to receive royalties on sales of all alpha-1a selective drugs sold by Glaxo so long as Synaptic has an issued patent relating to an alpha 1 adrenergic receptor subtype in at least one major market country.

During 1998, the Company recognized $2,000,000 in revenue under this licensing arrangement. Revenue that has been recognized is not subject to repayment.

Merck & Co., Inc. Synaptic and Merck & Co., Inc. ("Merck") were parties to a collaborative and licensing agreement. Synaptic had granted Merck licenses that were subsequently relinquished.

During 1999 and 1998, the Company recognized $83,000 and $482,000, respectively, in revenue under this agreement. Revenues that have been recognized are not subject to repayment.

Note 4 -- Property and Equipment

Property and equipment consists of the following as of December 31, 2000 and 1999:

	2000	1999
Scientific equipment	$ 7,943,000	$ 7,169,000
Furniture and fixtures	192,000	192,000
Office equipment	533,000	521,000
Leasehold improvements	2,352,000	2,452,000
Software	1,035,000	967,000
	12,055,000	11,301,000
Accumulated depreciation and amortization	(7,274,000)	(6,115,000)

	$ 4,781,000	$ 5,186,000

Note 5 -- Stockholders' Equity

Common Stock. In January 1998, warrants to purchase 137,648 shares of the Company's Common Stock were exercised at $9.50 per share. There are currently no common stock warrants outstanding.

Stockholders' Rights Plan. In November 1995, Synaptic's Board of Directors approved the adoption of a stockholders' rights plan (the "Rights Plan"). The Rights Plan provides for the distribution of one right (a "Right") with respect to each share of outstanding common stock and any new issuances of common stock. Upon completion of the initial public offering in December 1995, the Board of Directors designated Series A Junior Participating Preferred Stock and declared a dividend of one Right with respect to each share of common stock outstanding. Each Right will become exercisable to purchase from the Company, at an exercise price of $160.00, 1/1000th of a share of Series A Junior Participating Preferred Stock or that number of shares of common stock having a market value equal to two times the exercise price of the Right. The Rights generally become exercisable for the Series A Junior Participating Preferred Stock ten days following the announcement by any person or group of an intention to make a tender offer or exchange offer, the consummation of which would cause any person or group to become the owner of 15% or more of the outstanding common stock, and generally become exercisable for common stock ten days

following the
acquisition by any person or group of more than 15% of the outstanding common stock. The Rights will expire in the year 2005. The Rights Plan may discourage certain types of transactions involving an actual or potential change in control of the Company.

Each 1/1000th of a share of Series A Junior Participating Preferred Stock will have one vote. Each share of Series A Junior Participating Preferred Stock will be entitled to a preferential quarterly dividend per share equal to the larger of (i) an amount equal to any dividend declared on the common stock and (ii) $.00025. Additionally, in the event of a liquidation, each 1/1000th of a share of the Series A Junior Participating Preferred Stock would be entitled to a preferential liquidation payment equal to $0.01 plus an amount equal to the amount that would be distributed with respect to each share of common stock.

Preferred Stock. Synaptic is authorized to issue up to 1,000,000 shares of preferred stock, 200,000 of which is designated as Series A Junior Participating and 800,000 of which is undesignated. The Board of Directors is authorized to provide for the issuance of preferred stock in one or more classes or series and to fix the number of shares constituting any such class or series, and the voting powers, designations, preferences and relative, participating, optional or other special rights and qualifications, limitations or restrictions thereof, including the dividend rights, dividend rate, terms of redemption, redemption price or prices, conversion rights and liquidation preferences of the shares constituting any class or series, without any further vote or action by the shareholders of the Company.

Note 6 -- Incentive/Stock Plans

Synaptic currently has three stock incentive plans: the 1996 Incentive Plan (the "1996 Plan"), the 1988 Amended and Restated Incentive Plan (the "1988 Plan" and, together with the 1996 Plan, the "Incentive Plans") and the 1996

Nonemployee Director Stock Option Plan (the "Director Plan").

The Company has elected to follow APB No. 25 in accounting for its employee stock options because, as discussed below, the alternative fair value accounting provided for under Financial Accounting Standards Board Statement No. 123 "Accounting for Stock-Based Compensation" ("SFAS No. 123") requires use of option valuation models that were not developed for use in valuing employee stock options. Under APB No. 25, compensation expense is required to be recognized when the exercise price of the Company's employee stock options is at a price below the market price of the underlying stock on the date of grant.

Incentive Plans. The 1996 Plan and the 1988 Plan were adopted in October 1995 and June 1988, respectively. In May 1998, the Company's stockholders approved an amendment to the 1996 Plan that increased the maximum number of shares available for awards under the 1996 Plan from 1,100,000 to 2,100,000. Effective as of January 1, 1996, the 1996 Plan replaced the 1988 Plan with respect to all future stock and option awards by the Company to its employees and consultants. A committee of the Company's Board of Directors (the "Committee") approves the sale of shares and the granting of nonstatutory or incentive stock options. In addition, under the 1996 Plan, the Committee may grant stock appreciation rights to employees and consultants of the Company. The purchase price for shares and the exercise price of options are determined by the Committee (although, the exercise price of incentive stock options may be no less than the fair market value of the common stock on the date of grant).

In general, options granted under the Incentive Plans vest over a four-year period. Unvested options are forfeited upon termination of the employee or consulting relationship. Vested options, if not exercised within a specified period of time following the termination of the employment or consulting relationship, are also forfeited. Options generally expire 10 years from the date of grant. Shares of common stock sold under the Incentive Plans are also generally subject to vesting. Options granted and shares sold to employees under the Incentive Plans generally become fully vested upon the occurrence of a change in control of the

Company (as defined) if the holders
thereof are terminated in connection with such change in control other than for cause (as defined). At December 31, 2000, 713,945 shares remain available for future awards under the 1996 Plan. As of December 31, 2000, no stock appreciation rights had been awarded under the 1996 Plan.

Director Plan. The Director Plan was adopted by the Board of Directors in March 1996 and approved by the stockholders in June 1996. In general, under the Director Plan, each nonemployee director of the Company is automatically granted an option on the date that he or she first becomes a member of the Board of Directors. In addition, on June 1 of each year, commencing in 1997, each nonemployee director is granted an additional option to purchase 2,500 shares of common stock at an exercise price equal to the fair market value on the date of grant. The maximum number of shares subject to the Director Plan is 250,000. In general, options granted under the Director Plan become exercisable as to 1/24th of the total number of shares subject to the option for each calendar month elapsed after the date of the option grant. In the event of a change in control of the Company (as defined) or the death or disability of the optionee, any unvested portion of the options will become exercisable in full. Options granted under the Director Plan will expire upon the earliest to occur of the following: (a) the expiration of ten years from the date of grant of the option, (b) one year after the optionee ceases to be a director of the Company by reason of death or disability of the optionee, or (c) three months after the date the optionee ceases to be a director of the Company for any reason other than death

or disability.

Option activities under the Incentive Plans and the Director Plan are detailed in the following table:

	1996 Plan	1988 Plan	Director Plan	Weighted Average Option Price Per Share
Outstanding at January 1, 1998	851,063	265,302	30,000	$10.47
Granted	339,543	-	15,000	$13.36
Exercised	(4,453)	(43,063)	-	$ 2.70
Canceled/Forfeited	(60,918)	(4,375)	-	$12.36
Outstanding at December 31, 1998	1,125,235	217,864	45,000	$11.39
Granted	432,100	-	20,000	$ 4.92
Exercised	(22,542)	(30,745)	-	$ 4.03
Canceled/Forfeited	(158,516)	(625)	-	$12.86
Outstanding at December 31, 1999	1,376,277	186,494	65,000	$ 9.69
Granted	145,750	-	15,000	$ 5.79
Exercised	(36,363)	(134,748)	-	$ 3.94
Canceled/Forfeited	(166,092)	-	(22,500)	$10.74
Outstanding at December 31, 2000	1,319,572	51,746	57,500	$ 9.80
Exercisable at December 31, 2000	487,699	51,746	44,687	$12.32
Exercisable at December 31, 1999	345,592	186,494	46,562	$ 9.90
Exercisable at December 31, 1998	202,195	211,276	30,000	$ 8.10

The following table discloses at December 31, 2000, for each of the following classes of options as determined by range of exercise price, the information regarding weighted-average exercise price and weighted-average remaining contractual life of each said class:

Option Class	Number Of Options Outstanding	Weighted Average Exercise Price of Outstanding Options	Weighted Average Remaining Contractual Life Of Outstanding Options	Number Of Options Currently Exercisable	Weighted Average Exercise Price of Options Currently Exercisable
Prices ranging from $1.76-$2.00	51,746	$ 1.80	2.8 years	51,746	$ 1.80
Prices ranging from $4.25-$8.4375	543,500	$ 5.03	9.2 years	20,937	$ 5.74

Prices ranging from $10.125-$15.25	730,072	$12.95	7.0 years	410,574	$12.93
Prices ranging from $16.50-$17.75	103,500	$16.61	5.4 years	100,875	$16.58

Other Disclosures. During 2000, 1999 and 1998, all options were granted with an exercise price equal to the market price of the common stock on the date of grant. Pro forma information regarding net income and earnings per share is required by SFAS No. 123, and has been determined as if the Company had been accounting for its employee stock options under the fair value method of SFAS No. 123. The weighted-average fair value of options granted during 2000, 1999 and 1998 approximated $4.07, $3.19 and $7.66, respectively. The fair value for these options was estimated at the date of grant using a Black-Scholes option pricing model with the following assumptions for 2000, 1999 and 1998, respectively: weighted average risk-free interest rates of 5.43%, 6.13% and 4.70%; no dividends; and a weighted-average expected life of the

options of 5 years. Weighted average volatility factors of the expected market price of the Company's common stock of .852, .741 and .628, were used for 2000, 1999 and 1998, respectively.

The Black-Scholes option valuation model was developed for use in estimating the fair value of traded options, which have no vesting restrictions and are fully transferable. In addition, option valuation models require the input of highly subjective assumptions including the expected stock price volatility. Because the Company's employee stock options have characteristics significantly different from those of traded options, and because changes in the subjective input assumptions can materially affect the fair value estimate, in management's opinion, the existing models do not necessarily provide a reliable single measure of the fair value of its employee stock options.

For purposes of pro forma net loss disclosures, the estimated fair value of options granted subsequent to 1994 is amortized to expense over the options' vesting period. The Company's pro forma net loss information is as follows:

	2000	1999	1998
Pro forma net loss	$ (15,814,000)	$ (16,801,000)	$ (7,863,000)
Pro forma net loss per share	$ (1.46)	$ (1.56)	$ (0.74)

For certain options granted prior to 1997, the Company recorded pursuant to APB No. 25 deferred compensation expense representing the difference between the exercise price thereof and the market value of the common stock as of the date of grant. This compensation expense was being amortized over the vesting period of each option granted. Amortization of deferred compensation under the Incentive Plans amounted to approximately $50,000 and $79,000 during 1999 and 1998, respectively. In addition, approximately $11,000 and $20,000 of deferred compensation, as it relates to the Incentive Plans was reversed during 1999 and 1998, respectively, due to the forfeiture of the unvested options. At December 31, 1999, this deferred compensation had been amortized.

Note 7 -- Income Taxes

The liability method is used in accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse.

At December 31, 2000 and 1999, the Company had net operating loss ("NOL") carryforwards of $57,000,000 and $45,000,000, respectively, for Federal income tax purposes that will expire principally in the years 2002 through 2020. In addition, Synaptic had research and development credit carryforwards of approximately $1,610,000, which will expire principally in 2002 through 2018. For financial reporting purposes, a valuation allowance has been recognized to offset the deferred tax assets related to these carryforwards. Due to the limitations imposed by the Tax Reform Act of 1986, and as a result of significant changes in the Company's ownership in 1993 and 1997, the utilization of $25,000,000 of net operating loss carryforwards is subject to annual limitation. The utilization of the research and development credits is similarly limited.

At December 31, 2000, the Company had NOL carryforwards of $41,637,000 and research and development credits of $475,000 for State income tax purposes. In November 2000, $5,650,000 in gross State NOL carryforwards was sold under the State of New Jersey's Technology Business Tax Certificate Transfer Program (the "Program"). The Program allows qualified technology and biotechnology businesses

in New Jersey to sell unused amounts of NOL carryforwards and defined research and development credits for cash. The tax value sold was $509,000 and the proceeds received by the Company were $407,000, which was recorded as an income tax benefit in the statement of operations.

A reconciliation of the Company's income tax expense (benefit) at U.S. federal statutory tax rates to recorded income tax provision is as follows:

	2000	1999	1998
Tax at U.S. statutory rates	$(4,713,000)	$(5,141,000)	$(2,208,000)
State income taxes	(823,000)	(898,000)	(386,000)
Research and development credit	-	-	(110,000)
Expiration/sale of state NOLs	(71,000)	248,000	2,000
Other	(30,000)	(16,000)	50,000
Valuation allowance recorded	5,230,000	5,807,000	2,652,000
Recorded tax provision (benefit)	(407,000)	-	-

Significant components of the Company's federal deferred tax assets as of December 31, 2000 and 1999 are as follows:

	2000	1999
Deferred tax assets:		
Net operating loss carryforwards	$ 21,930,000	$ 17,233,000
Research and development credit carryforwards	1,610,000	1,610,000
Book over tax amortization	2,171,000	1,638,000

Total deferred tax assets	25,711,000	20,481,000
Valuation allowance	(25,711,000)	(20,481,000)
Net deferred tax assets	-	-

Note 8 -- Commitments

Synaptic leases facilities under an agreement expiring on December 31, 2015 (the "lease").

Rent expense for the years ended December 31, 2000, 1999 and 1998 approximated $1,895,000, $1,749,000, and $693,000, respectively, and included executory costs of $524,000, $579,000 and $120,000, respectively.

As of December 31, 2000, future minimum annual payments under the lease, inclusive of executory costs, are as follows:

2001	2,074,000
2002	1,634,000
2003	1,634,000
2004	1,634,000
2005	1,886,000
Thereafter	20,872,000
Total	$ 29,734,000

The Company is subleasing 5,000 square feet and 23,008 square feet of its premises to two non-affiliated third parties under agreements expiring in 2001 and 2010, respectively. During 2000, the Company

recognized $104,000 in
rental income under these agreements, which is included in other income. Additionally, under the non-cancelable portions of these sublease agreements, the Company expects to recognize an aggregate of $2,146,000 in rental income, inclusive of executory costs.

The Company is party to a license agreement with a major research university. Under the terms of this agreement, the Company received a worldwide nonexclusive license under a patent issued in January 1991, which patent expires in 2008. The Company is committed under this agreement to pay royalties on future net sales of products employing the technology or falling under claims of the patents covered by this agreement.

Synaptic has an employment agreement with its Chairman, President and Chief Executive Officer which provides for severance payments of up to one year of base salary upon the occurrence of certain events, including early termination and termination upon a change in control, as defined. In addition to severance payments, under certain circumstances, the agreement calls for immediate vesting of any unvested shares of common stock and stock options.

At December 31, 2000, the Company had entered into agreements with its Senior Vice President and Chief Financial Officer, its Vice President for Research and its Vice President of Business Development which provide for severance payments in amounts equal to 50% of annual base salary, on substantially the same terms as stated above. In addition to severance, under certain circumstances, the agreements call for immediate vesting of any unvested

shares of common stock and stock options.

Note 9 -- Employee Benefit Plans

The Company established a defined contribution employee retirement plan (the "Plan") effective January 1, 1990, conforming to Section 401(k) of the Internal Revenue Code ("IRC"). All eligible employees with six months service may elect to have a portion of their salary deducted and contributed to the Plan up to the maximum allowable limitations of the IRC. Synaptic matches 50% of each participant's contribution up to the first 5% of annual compensation (as defined) with a maximum employer contribution of 2.5% of a participant's compensation. The Company's matching portion, which amounted to approximately $117,000, $133,000 and $117,000 for the years ended December 31, 2000, 1999 and 1998, respectively, vests over a six-year period.

The Company currently provides medical, dental, long-term disability and life insurance benefits for its full-time employees. The Company does not presently provide any post-retirement health benefits.

Note 10 -- Quarterly Data (Unaudited)

The following tables present selected unaudited information relating to the results of operations of the Company for the past eight quarters.

(in thousands, except per share information)

	2000				
	1st	2nd	3rd	4th	Year
Total revenues	$ 214	$ 354	$ 2,903	$ 365	$ 3,836
Total expenses	4,503	5,014	5,306	5,389	20,212
Net loss	(3,704)	(4,094)	(1,998)	(4,063)	(13,859)
Basic and diluted Net loss per share	(.34)	(.38)	(.18)	(.37)	(1.28)

	1999				
	1st	2nd	3rd	4th	Year
Total revenues	$ 644	$ 843	$ 314	$ 54	$ 1,855
Total expenses	5,192	5,106	4,823	4,531	19,652
Net loss	(3,811)	(3,568)	(3,887)	(3,855)	(15,121)
Basic and diluted Net loss per share	(.36)	(.33)	(.36)	(.36)	(1.41)

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Part III

Item 10. Directors and Executive Officers of the Registrant

The information required by this item is incorporated herein by reference from the information under the captions "ELECTION OF DIRECTORS" and "COMPENSATION AND OTHER INFORMATION CONCERNING OFFICERS, DIRECTORS AND CERTAIN STOCKHOLDERS" contained in the Proxy Statement.

Item 11. Executive Compensation

The information required by this item is incorporated herein by reference from the information under the caption "COMPENSATION AND OTHER INFORMATION CONCERNING OFFICERS, DIRECTORS AND CERTAIN STOCKHOLDERS" contained in the Proxy Statement.

Item 12. Security Ownership of Certain Beneficial Owners and Management

The information required by this item is incorporated herein by reference from the information under the caption "SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT" contained in the Proxy Statement.

Item 13. Certain Relationships and Related Transactions

The information required by this item is incorporated herein by reference from the information under the caption "COMPENSATION AND OTHER INFORMATION CONCERNING OFFICERS, DIRECTORS AND CERTAIN STOCKHOLDERS" contained in the Proxy Statement.

Part IV

Item 14. Exhibits, Financial Statement Schedules and Reports on Form 8-K

(a) (1) Financial Statements

Reference is made to the Index to Financial Statements under Item 8, Part II hereof.

(2) Financial Statement Schedules

The Financial Statement Schedules have been intentionally omitted either because they are not required or because the information has been included in the notes to the Financial Statements included in this Report on Form 10-K.

(3) Exhibits

Exhibit No.	Description
3.1(a)	Amended and Restated Certificate of Incorporation of the Company, filed December 19, 1995 (incorporated by reference to Exhibit 3.1(a) to the Company's Quarterly Report on Form 10-Q filed for the quarter ended June 30, 1996, Commission File Number 0-27324)
3.1(b)	Certificate of Designations of Series A Junior Participating Preferred Stock filed December 19, 1995 (incorporated by reference to Exhibit 3.1(b) to the Company's Quarterly Report on Form 10-Q filed for the quarter ended December 31, 1995, Commission File Number 0-27324)
3.1(c)	Certificate of Amendment of the Amended and Restated Certificate of Incorporation of the Company, filed June 5, 1996 (incorporated by reference to Exhibit 3.1(c) to the Company's Quarterly Report on Form 10-Q filed for the quarter ended June 30, 1996, Commission File Number 0-27324)
3.2	Amended and Restated By-Laws of the Company, as amended on March 24, 1999 (incorporated by reference to Exhibit 3.2 to the Company's Quarterly Report on Form 10-Q filed for the quarter ended March 31, 1999, Commission File Number 0-27324)
4.1	Specimen of Certificate of Common Stock of the Company (incorporated by reference to Exhibit 4 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)

4.2	Rights Agreement dated as of December 11, 1995, between the Company and Chase Mellon Shareholder Services, as Rights Agent (incorporated by reference to Exhibit 4.2 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1995, Commission File Number 0-27324)
*10.1	Research, Option and License Agreement dated as of January 25, 1991, between the Company and Eli Lilly and Company, as amended by Addendum dated as of January 1, 1995 (incorporated by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)
*10.2	Research Collaboration and License Agreement dated as of November 30, 1993, between the Company and Merck & Co., Inc., as amended by Amendment No. 1 dated as of February 15, 1995, and as modified by the Letter Agreement dated August 25, 1995 (incorporated by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)
*10.3	Research and License Agreement dated as of August 4, 1994, between the Company and Ciba-Geigy Limited (predecessor-in-interest of Novartis AG, the parent of Novartis Pharma AG) (incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)
+10.4	1988 Amended and Restated Incentive Plan of the Company (incorporated by reference to Exhibit 10.9 to the Company's Registration Statement on Form S-1, as amended (File Number

	33-98366), which became effective on December 13, 1995)
+10.5	Form of Restricted Stock Purchase Agreement under the 1988 Amended and Restated Incentive Plan of the Company (incorporated by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)
+10.6	Form of Incentive Stock Option Agreement under the 1988 Amended and Restated Incentive Plan of the Company (incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)
+10.7	Form of Nonqualified Stock Option Agreement under the 1988 Amended and Restated Incentive Plan of the Company (incorporated by reference to Exhibit 10.12 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)

10.8	Third Amended and Restated Registration Rights Agreement dated as of January 19, 1993, as amended by Amendment No. 1 dated as of August 4, 1994 (incorporated by reference to Exhibit 10.13 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)
10.9	Form of Common Stock Purchase Warrant dated as of January 1993 (incorporated by reference to Exhibit 10.15 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)
10.10	License Agreement dated June 3, 1991, between the Company and the Trustees of Columbia University in the City of New York (incorporated by reference to Exhibit 10.16 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)
+10.11	Employment Agreement dated as of February 14, 1994, between the Company and Robert I. Taber (incorporated by reference to Exhibit 10.21 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)
+10.12	Employment Agreement dated as of April 6, 1995, between the Company and Richard L. Weinshank (incorporated by reference to Exhibit 10.24 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)
10.13	Form of Indemnification Agreement between the Company and each of its executive officers and directors (incorporated by reference to Exhibit 10.25 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)
+10.14	1996 Incentive Plan of the Company, as amended on May 12, 1998 (incorporated by reference to Exhibit 10.14 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1998, Commission File Number 0-27324)
+10.15	Incentive Stock Option Agreement dated October 1, 1993, between the Company and Kathleen P. Mullinix (incorporated by reference to Exhibit 10.28 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)
+10.16	Incentive Stock Option Agreement dated February 14, 1994, between the Company and Robert I. Taber (incorporated by

reference to Exhibit 10.29 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)

+10.17	Incentive Stock Option Agreement dated February 7, 1994, between the Company and Lisa L. Reiter (incorporated by reference to Exhibit 10.30 to the Company's Registration Statement on Form S-1, as amended (File Number 33-98366), which became effective on December 13, 1995)
+10.18	Incentive Stock Option Agreement dated as of March 21, 1996, between the Company and Kathleen P. Mullinix (incorporated by reference to Exhibit 10.25 to the Company's Quarterly Report on Form 10-Q filed for the quarter ended March 31, 1996, Commission File Number 0-27324)
+10.19	Incentive Stock Option Agreement dated as of March 21, 1996, between the Company and Robert L. Spence (incorporated by reference to Exhibit 10.26 to the Company's Quarterly Report on Form 10-Q filed for the quarter ended March 31, 1996, Commission File Number 0-27324)
+10.20	Incentive Stock Option Agreement dated as of March 21, 1996, between the Company and Lisa L. Reiter (incorporated by reference to Exhibit 10.27 to the Company's Quarterly Report on Form 10-Q filed for the quarter ended March 31, 1996, Commission File Number 0-27324)
+10.21	Nonqualified Stock Option Agreement dated as of March 21, 1996, between the Company and Richard L. Weinshank (incorporated by reference to Exhibit 10.28 to the Company's Quarterly Report on Form 10-Q filed for the quarter ended March 31, 1996, Commission File Number 0-27324)
+10.22	Form of Incentive Stock Option Agreement under the 1996 Incentive Plan (incorporated by reference to Exhibit 10.29 to the Company's Quarterly Report on Form 10-Q filed for the quarter ended March 31, 1996, Commission File Number 0-27324)
+10.23	Form of Nonqualified Stock Option Agreement under the 1996 Incentive Plan (incorporated by reference to Exhibit 10.30 to the Company's Quarterly Report on Form 10-Q filed for the quarter ended March 31, 1996, Commission File Number 0-27324)
***10.24	Research and License Agreement dated as of May 31, 1996, between the Company and Ciba-Geigy Limited (predecessor-in-interest of Novartis AG, parent of Novartis Pharma AG) (incorporated by reference to Exhibit 10.31 to the Company's Quarterly Report on Form 10-Q/A filed for the quarter ended June 30, 1996, Commission File Number 0-27324)
***10.25	Supplement No. 1 to Research and License Agreement dated as of August 4, 1994, between the Company and Ciba-Geigy Limited (predecessor-in-interest of Novartis AG, parent of Novartis Pharma AG) (incorporated by reference to Exhibit 10.32 to the Company's Quarterly Report on Form 10-Q/A filed for the quarter ended June 30, 1996, Commission File Number 0-27324)

10.26	1996 Nonemployee Director Stock Option Plan of the Company

	(incorporated by reference to Exhibit 10.33 to the Company's Quarterly Report on Form 10-Q filed for the quarter ended June 30, 1996, Commission File Number 0- 27324)
10.27	Form of Stock Option Agreement under the 1996 Nonemployee Director Stock Option Plan of the Company (incorporated by reference to Exhibit A attached to Exhibit 10.33 to the Company's Quarterly Report on Form 10-Q filed for the quarter ended June 30, 1996, Commission File Number 0-27324)
**10.28	Addendum No. 2 to Research, Option and License Agreement dated as of October 31, 1996, between the Company and Eli Lilly and Company (incorporated by reference to Exhibit 10.35 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1996, Commission File No. 0-27324)
***10.29	Amendment No.2 to Research Collaboration and License Agreement dated as of October 9, 1996, between the Company and Merck & Co., Inc. (incorporated by reference to Exhibit 10.36 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1996, Commission File No. 0-27324)
+10.30	Incentive Stock Option Agreement dated as of December 13, 1996, between the Company and Kathleen P. Mullinix (incorporated by reference to Exhibit 10.37 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1996, Commission File No. 0-27324)
+10.31	Form of Incentive Stock Option Agreement dated as of December 13, 1996, entered into between the Company and each of Robert L. Spence, Robert I. Taber, Lisa L. Reiter and Richard L. Weinshank (incorporated by reference to Exhibit 10.38 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1996, Commission File No. 0-27324)
***10.32	Collaborative Research and License Agreement dated as of July 28, 1997, between the Company and the Warner-Lambert Company (incorporated by reference to Exhibit 10.39 to the Company's Quarterly Report on Form 10-Q filed for the quarter ended September 30, 1997, Commission File Number 0- 27324)
+10.33	Executive Employment Agreement effective as of October 1,1997, between the Company and Dr. Kathleen P. Mullinix (incorporated by reference to Exhibit 10.34 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1997, Commission File No. 0-27324)
10.34	Lease Agreement dated November 19, 1997, between the Company and Century Associates, which becomes effective January 1, 1998 (incorporated by reference to Exhibit 10.35 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1997, Commission File No. 0-27324)

10.35	Amendment No. 3 to Research Collaboration and License Agreement dated as of December 1, 1997, between the Company and Merck & Co., Inc. (incorporated by reference to Exhibit 10.36 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1997, Commission File No. 0-27324)
+10.36	Amended and Restated Employment Agreement dated as of January 1, 1998, between the Company and Robert L. Spence (incorporated by reference to Exhibit 10.37 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1997, Commission File No. 0-27324)

***10.37	Cooperation Agreement dated as of January 12, 1998, between the Company and Grunenthal GmbH (incorporated by reference to Exhibit 10.38 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1997, Commission File No. 0-27324)
+10.38	Amended and Restated Employment Agreement dated as of February 7, 1998, between the Company and Lisa L. Reiter (incorporated by reference to Exhibit 10.39 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1997, Commission File No. 0-27324)
10.39	Amendment No.4 to Research Collaboration and License Agreement dated as of March 2,1998, between the Company and Merck & Co., Inc. (incorporated by reference to Exhibit 10.40 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1997, Commission File No. 0-27324)
***10.40	Option and License Agreement dated as of March 2, 1998, between the Company and Glaxo Group Limited (incorporated by reference to Exhibit 10.41 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1997, Commission File No. 0-27324)
+10.41	Employment Agreement dated as of April 1, 1998, between the Company and Theresa A. Branchek (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed for the quarter ended March 31, 1998, Commission File Number 0-27324)
+10.42	Incentive Stock Option Agreement dated as of May 12, 1998, between the Company and Theresa A. Branchek (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed for the quarter ended June 30, 1998, Commission File Number 0-27324)
+10.43	Nonqualified Stock Option Agreement dated as of May 12, 1998, between the Company and Theresa A. Branchek (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed for the quarter ended June 30, 1998, Commission File Number 0-27324)

10.44	Amendment No. 1 to Cooperation Agreement between the Company and Grunenthal GmbH (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed for the quarter ended September 30, 1998, Commission File Number 0-27324)
10.45	First Amendment to Lease dated as of November 25, 1998, between ARE-215 College Road, LLC, and the Company (incorporated by reference to Exhibit 10.45 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1998, Commission File No. 0-27324)
10.46	Amendment No. 5 to Research Collaboration and License Agreement dated as of December 1, 1998, between the Company and Merck & Co., Inc. (incorporated by reference to Exhibit 10.46 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1998, Commission File No. 0-27324)
10.47	Addendum No. 3 to Research, Option and License Agreement effective as of January 1, 1999, between the Company and Eli Lilly and Company (incorporated by reference to Exhibit 10.47 to the Company's Annual Report on Form 10-K filed for the fiscal year ended December 31, 1998, Commission File No.

	0-27324)
23.1	Consent of Independent Auditors, Ernst & Young LLP
24	Powers of Attorney

* Portions of this Exhibit were omitted and confidential treatment thereof has been granted by the Secretary of the Securities and Exchange Commission in response to the Registrant's Application Requesting Confidential Treatment under Rule 406 under the Securities Act of 1933, as amended.

** Portions of this Exhibit have been omitted and filed separately with the Secretary of the Securities and Exchange Commission pursuant to the Registrant's Application Requesting Confidential Treatment under Rule 24b-2 under the Securities Exchange Act of 1934, as amended.

*** Portions of this Exhibit were omitted and confidential treatment thereof has been granted by the Secretary of the Securities and Exchange Commission in response to the Registrant's Application Requesting Confidential Treatment under Rule 246-2 under the Securities Act of 1933, as amended.

\+ Management contracts and compensatory plans or arrangements

(b) Reports on Form 8-K

There were no reports on Form 8-K filed by the Registrant during the fourth quarter of the fiscal year ended December 31, 2000.

Supplemental Information

Copies of the Registrant's Proxy Statement and copies of the form of proxy to be used at the Annual Meeting of Stockholders to be held on May 10, 2001, will be furnished to the Securities and Exchange Commission at the time they are distributed to the Registrant's stockholders.

Imitrex(R) and Zantac(R) are registered trademarks of Glaxo Wellcome Inc. Hytrin(R) is the registered trademark of Abbott Laboratories. Claritin(R) is the registered trademark of Schering Corporation. Propulsid(R) is the

registered trademark of Johnson & Johnson. All other brand names or trademarks appearing in this Report are the property of their respective owners.

SIGNATURE PAGE

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

SYNAPTIC PHARMACEUTICAL CORPORATION

Date: March 23, 2001

By: /s/ Kathleen P. Mullinix

Name: Kathleen P. Mullinix
Title: Chairman, President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1934, this report has been signed by the following persons on behalf of the registrant in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Kathleen P. Mullinix Kathleen P. Mullinix, Ph.D.	Chairman, President and Chief Executive Officer	March 23, 2001
/s/ Robert L. Spence Robert L. Spence	Senior Vice President and Chief Financial Officer (Principal Accounting Officer)	March 23, 2001
* Zola P. Horovitz, Ph.D.	Director	March 23, 2001
* John E. Lyons	Director	March 23, 2001
* Patrick J. McDonald	Director	March 23, 2001
*	Director	March 23, 2001

Sandra Panem, Ph.D.

*	Director	March 23, 2001

Alison Taunton-Rigby, Ph.D.

* By: /s/ Kathleen P. Mullinix

Name: Kathleen P. Mullinix, Ph.D.
Title: Attorney-in-Fact