

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

FORM 10-K/A

Annual Report Pursuant to Section 13 or 15(d) of the  
Securities Exchange Act of 1934.

For the fiscal year ended December 31, 1995

OR

Transition Report Pursuant to Section 13 or 15(d) of the  
Securities Exchange Act of 1934.

For the transition period from \_\_\_\_\_ to \_\_\_\_\_.

Commission File Number 000-23186

BIOCRYST PHARMACEUTICALS, INC.  
(Exact name of registrant as specified in its charter)

DELAWARE 62-1413174  
(State of other jurisdiction of (I.R.S. employer identification no.)  
incorporation or organization)

2190 Parkway Lake Drive; Birmingham, Alabama 35244  
(Address and zip code of principal executive offices)

(205) 444-4600  
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Name of each exchange on which registered
None	None

Securities registered pursuant to Section 12(g) of the Act:

Title of each class
Common Stock, \$.01 Par Value

Indicate by a 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 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 [ X ].

While it is difficult to determine the number of shares owned by non-affiliates, the Registrant estimates that the aggregate market value of the Common Stock on January 31, 1996 (based upon the closing price shown on the Nasdaq National Market on January 31, 1996) held by non-affiliates was approximately \$65,349,342. For this computation, the Registrant has excluded the market value of all shares of its Common Stock reported as beneficially owned by officers, directors and certain significant stockholders of the Registrant. Such exclusion shall not be deemed to constitute an admission that any such stockholder is an affiliate of the Registrant.

The number of shares of Common Stock, par value \$.01, of the Registrant outstanding as of January 31, 1996 was 9,512,409 shares.

DOCUMENTS INCORPORATED BY REFERENCE

None.

## PART I

### ITEM 1. BUSINESS

#### General

BioCryst Pharmaceuticals, Inc. ("BioCryst" or the "Company") is a pioneer in using structure-based drug design to discover and design novel, small-molecule pharmaceutical products for the treatment of immunological and infectious diseases and disorders. The Company is conducting three clinical trials with its lead drug, BCX-34, including a Phase III trial with a topical formulation for cutaneous T-cell lymphoma ("CTCL"), a Phase II trial with a topical formulation for psoriasis and a Phase I/II trial with an oral formulation for CTCL. BioCryst has additional drug discovery projects underway using its structure-based drug design technologies to develop inhibitors of influenza neuraminidase and enzymes and proteins involved in the complement cascade.

BioCryst's lead immunological drug program is targeting T-cell proliferative disorders, which arise when T-cells, which normally fight infection, attack normal body cells or multiply uncontrollably. These disorders are varied and include CTCL, a severe form of cancer, psoriasis, transplant rejection and certain autoimmune diseases. BioCryst has designed and synthesized several chemically distinct classes of compounds which inhibit purine nucleoside phosphorylase ("PNP"), an enzyme believed to be involved in T-cell proliferation. The Company has performed preclinical studies with BCX-34 and has completed a series of six Phase I clinical trials, three Phase I/II clinical trials and two Phase II clinical trials with topical BCX-34 and has completed one Phase I trial with oral and intravenous formulations of the drug. BCX-34 has been tested in over 230 subjects, and no significant drug-related side effects have been observed.

The completed Phase II trials of topical BCX-34 involved the treatment of CTCL and the treatment of psoriasis. These two dose-ranging clinical trials did not achieve a statistically significant outcome. A majority of the patients from the Phase II CTCL trial volunteered to roll over into an extended, open-label trial which demonstrated clinical improvement in 75% of the patients. The Company expects to initiate a pilot Phase I/II clinical trial for atopic dermatitis in the first half of 1996. In addition, the Company has initiated preclinical studies using an ophthalmic formulation of BCX-34.

BioCryst's scientists include recognized world leaders in the fields of X-ray crystallography and medicinal chemistry, two core disciplines associated with structure-based drug design. The Company has certain collaborative arrangements with The University of Alabama at Birmingham ("UAB"), which has one of the leading X-ray crystallography centers in the world and has been successful in characterizing a significant number of medically relevant protein targets. The Company believes that based upon its scientific staff and management, the number of compounds it has designed and its clinical development program, it is a leader in the practical application of structure-based drug design.

#### Background

The human immune system employs specialized cells and proteins, including cells known as T-cells and B-cells, to control infection and recognize and attack foreign disease-causing viruses, bacteria and parasites. The immune system can also cause diseases or disorders when it inappropriately identifies the body's own tissue as foreign and, among other things, produces T-cells that attack normal body cells. Such diseases are referred to as autoimmune diseases and include psoriasis, in which the immune system attacks skin tissue; multiple sclerosis, in which the immune system attacks the protective sheaths of certain nerve cells; and rheumatoid arthritis, in which the immune system attacks joint tissue. This immune system response also causes transplant rejection in which the T-cells of the immune system attack the transplanted organ or tissue. The immune system may also cause T-cells to multiply uncontrollably. T-cell proliferation in such cases is associated with cancers such as cutaneous T-cell lymphoma ("CTCL"). Within the past decade, drugs have been developed that treat autoimmune and related diseases by selectively suppressing the immune system. However, most current immunosuppressive drugs have dose-limiting side effects, including severe toxicity.

PNP Enzyme. The link between T-cell proliferative disorders and the PNP enzyme was first discovered approximately 20 years ago when a patient, who was genetically deficient in PNP, exhibited limited T-cell activity, but reasonably

normal activity of other immune functions. Since then, additional patients with inherited PNP deficiency have been reported. In most patients, the T-cell

population was less than 20% of normal levels, often as low as 1-3% of normal levels. However, B-cell function was normal in approximately two-thirds of these patients. These findings suggested that inhibition of PNP might produce selective suppression of T-cell function without significantly impairing B-cell function.

Studies of the immune system have revealed the mechanism by which PNP inhibition suppresses the proliferation of T-cells. In the absence of PNP, all four nucleoside substrates (inosine, deoxyinosine, guanosine and deoxyguanosine) accumulate in plasma and/or urine. It is the intracellular accumulation of deoxyguanosine that leads to the suppression of T-cell proliferation. This occurs by the following steps:

- (1) T-cells have a high capacity, because of their high concentration of an enzyme called deoxycytidine kinase, to add a phosphate group to deoxyguanosine (GdR), forming deoxyguanosine phosphate (dGMP), which is then converted by other enzymes to deoxyguanosine triphosphate (dGTP).
- (2) As the production of dGTP occurs, dGTP accumulates in the T-cell because of the inability of the T-cell to remove or break down this nucleotide.
- (3) High concentrations of dGTP inhibit the enzyme ribonucleoside diphosphate reductase.
- (4) Since ribonucleoside diphosphate reductase is necessary for DNA synthesis or cell proliferation, when ribonucleoside diphosphate reductase is inhibited, DNA synthesis is suppressed and T-cells cannot proliferate.

The dGTP-mediated suppression of cell proliferation via PNP inhibition is relatively selective for T-cells because these cells appear to have relatively high capacity to add phosphate groups to deoxyguanosine and limited ability to degrade or remove the dGTP so produced.

Products in Development

The following table summarizes BioCryst's development projects:

PROGRAM/ COMPOUND	INDICATION/ APPLICATION	DELIVERY FORM	STAGE OF DEVELOPMENT (1)
PNP Inhibitors (BCX-34)	CTCL	Topical	Phase III
	Psoriasis	Oral	Phase I/II (2) (3)
		Topical	Phase II
	Atopic Dermatitis	Oral	Pre-IND Safety Assessment
		Topical	Phase I/II (2) (4)
	Rheumatoid Arthritis	Oral	Pre-IND Safety Assessment
	Transplant Rejection	Oral	Pre-IND Safety Assessment
	Multiple Sclerosis	Oral	Pre-IND Safety Assessment
Ophthalmic Diseases and Disorders	Ophthalmic	Preclinical	
Influenza Neuraminidase Inhibitors	Influenza	Oral	Preclinical
Complement Inhibitors	Immunological Diseases and Disorders	Intravenous/ Oral	Drug Discovery

(1) The development process for the Company's products typically can be expected to consist of the following stages: (i) drug discovery; (ii) performance of three phases of preclinical studies to evaluate the safety and potential activity of the drug as follows: (A) laboratory tests, (B) pharmacology tests with animal models and (C) safety assessment; (iii)

preparation and submission of an investigational new drug ("IND") application to the United

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States Food and Drug Administration ("FDA"); (iv) performance of clinical and other studies to assess safety and parameters of use, if authorized by the FDA; (v) performance of clinical trials to establish safety and effectiveness, typically referred to as Phase I, II and III clinical trials, including one or more adequate and well-controlled Phase III clinical trials, if authorized by the FDA; (vi) preparation and submission to the FDA of a new drug application ("NDA"); and (vii) if the new product is approved by the FDA, commercialization of the product.

- (2) These clinical trials combine certain elements of both Phase I and Phase II clinical trials. See "Business - Government Regulation."
- (3) This trial may also include subjects with T-cell leukemia and other T-cell cancers.
- (4) This trial is scheduled to commence in the first half of 1996.

#### PNP Inhibitors (BCX-34)

BioCryst has designed and synthesized several chemically distinct classes of small molecule compounds (five of which include compounds patented in the United States) which inhibit the PNP enzyme. In in vitro preclinical studies, the Company's PNP inhibitor compounds selectively and potently suppressed human T-cells associated with certain T-cell proliferative disorders. One member of a patented class of PNP inhibitor compounds, BCX-34, which was designed and developed by BioCryst, to date has been the most promising of the Company's compounds as a potential treatment for a number of T-cell proliferative diseases and related disorders. The Company is in the clinical stage of development of topical and oral formulations of BCX-34 and has an intravenous formulation for future development. A topical formulation may be most suitable for treating certain dermal indications as a result of being able to directly administer drug to diseased skin thereby minimizing systemic absorption. An orally deliverable product may allow systemic application of the drug in diseases that either cannot be treated topically or can be treated more successfully with an oral formulation. An intravenous formulation may allow more precise dosage control and direct systemic application into the bloodstream and may permit usage of BCX-34 where other methods of delivery may not be suitable.

The Company has completed a series of six Phase I clinical trials, three Phase I/II clinical trials and two Phase II clinical trials with topical BCX-34 and has completed one Phase I trial with oral and intravenous formulations of the drug. BCX-34 has been tested in over 230 subjects, and no significant drug-related side effects have been observed. The Company is conducting a Phase III trial with topical BCX-34 for the treatment of CTCL, a Phase II trial with topical BCX-34 for the treatment of psoriasis and a Phase I/II trial with oral BCX-34 for the treatment of CTCL. The Company expects to initiate a pilot Phase I/II clinical trial for the topical treatment of atopic dermatitis in the first half of 1996. The Company is in the preclinical stage of development of an ophthalmic formulation of BCX-34 for direct delivery of the drug to the eye for treating certain T-cell proliferative disorders of the eye. While the Company has selected BCX-34 as its lead compound, the Company has a number of patented PNP inhibitor compounds which it believes may be suitable as alternative lead compounds for the treatment of T-cell proliferative disorders. No assurance can be given that the topical, oral, intravenous or ophthalmic formulations of BCX-34 will be successfully developed, will receive FDA approval or will prove to be commercially successful.

Cutaneous T-Cell Lymphoma. CTCL is a severe form of cancer which is characterized by the development of scaly patches on the skin, progressing to ulcers and tumors of the skin, lymph nodes and internal organs. CTCL is a chronic disease involving the proliferation of certain types of T-cells. CTCL affects approximately 5,000 to 10,000 people in the United States. There is no known cure and the median survival time is approximately four years after systemic progression of the disease. Existing therapies for CTCL are generally considered inadequate.

The Company is conducting a Phase III trial with topical BCX-34. This trial, being conducted at eight major medical centers, is a randomized, double-blind, placebo-controlled trial including 90 patients with early stage CTCL. Patients in this study apply either BCX-34 (1% concentration) or placebo cream over their entire body twice daily for six months. Supporting this trial is a two-stage

dose-ranging Phase II trial completed in 1995. The first stage of the Phase II trial was randomized, double-blinded and placebo-controlled and enrolled 30 patients at UAB and Washington University with CTCL. In this trial, patients applied one of three concentrations of BCX-34 (0.3%, 1% or 5%) and placebo cream to different targeted disease lesions twice a day for six weeks. This trial did not achieve a statistically significant outcome. Twenty-four of the study patients continued in an open-label trial applying BCX-34 (1%) to all disease lesions twice daily for six months. The results from the extended trial showed that seven patients had complete remissions (lesions cleared both clinically and histologically), two patients were clinically clear and nine patients had partial clearance. Six patients had stable or progressive disease or dropped out of the trial. There were no significant drug related adverse events. The foregoing results are not definitive, as positive Phase III clinical trial results are required to determine safety and efficacy of BCX-34. The Company believes the results of the open-label trial suggest that more than six weeks are required to obtain efficacy in the topical treatment of CTCL.

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The Company completed a Phase I oral and intravenous trial of BCX-34 in May 1995. In this trial, three CTCL patients received a single intravenous dose, followed a week later by a single oral dose, followed three weeks later by five day consecutive oral dosing. This pharmacology study suggested that BCX-34 is well tolerated systemically and that the drug is highly bioavailable in humans. In late 1995, the Company initiated a Phase I/II dose escalation oral trial in CTCL and other T-cell cancer patients. This is an open label trial designed to provide safety and pharmacokinetic data on BCX-34 as well as provide potential efficacy data.

Psoriasis. Psoriasis is a common chronic and recurrent disease involving T-cells characterized by red, thick scaling of the skin, which can develop at any time in life. In the United States, it is estimated that more than four million people suffer from some form of psoriasis and 150,000 to 260,000 new cases are diagnosed annually. About 10% of these cases are classified as "severe" and are most likely to require physician's care and drug intervention. In some cases, the condition may be accompanied by a form of arthritis which can be debilitating. Current therapies for psoriasis either are of limited benefit or have severe side effects.

The Company is conducting a Phase II trial with topical BCX-34 for the treatment of psoriasis. This trial, being conducted at four clinical research centers, is a randomized, double-blind, placebo-controlled trial which has enrolled 90 patients with plaque stage psoriasis. Patients in this study apply either BCX-34 (1% concentration) or placebo cream over their disease lesions twice daily for 12 weeks. The Company believes preliminary results will be available in the second quarter of 1996. Supporting this trial is a Phase II trial completed in December 1994. This Phase II trial was randomized, double-blinded and placebo-controlled and enrolled 40 patients at UAB with plaque stage psoriasis. In this trial, patients applied one of four concentrations of BCX-34 (0.1%, 0.3%, 1% or 5%) and placebo cream to different targeted disease lesions twice a day for six weeks. While there were no significant drug related adverse events, the trial did not achieve a statistically significant outcome.

Atopic Dermatitis. Atopic dermatitis, sometimes referred to as eczema, is a chronic skin condition occurring primarily in infants and children and, to a lesser extent, in adults. The disorder is characterized by severe itching, a rash with small bumps, redness, thickened skin from repeated scratching, and sometimes secondary infection of the skin. Between one and two million people in the United States are affected with atopic dermatitis.

Several biochemical mechanisms of the disease have been studied, including abnormal T-cell function. It is uncertain whether inhibiting T-cell proliferation with BCX-34 will be helpful in treating the disease, but other agents which inhibit T-cells have been successfully used in atopic dermatitis. These other agents generally cause side effects which can be severe. The Company plans to initiate a pilot Phase I/II clinical trial with topical BCX-34 for atopic dermatitis in 1996.

Rheumatoid Arthritis. Rheumatoid arthritis is an autoimmune disease that involves inflammation of the membranes lining joints, causing joint pain, swelling, and deformities. It is estimated that approximately four million people in the United States are afflicted with rheumatoid arthritis. There are many drugs used to treat the disease, but such drug treatments only alleviate the symptoms of rheumatoid arthritis. The Company believes T-cell controlling

agents such as PNP inhibitors and specifically an oral formulation of BCX-34 offer promise as a potential drug treatment for rheumatoid arthritis. Among other potential competitors, Ciba-Geigy ("Ciba") has rights to develop a class of PNP inhibitors, licensed from BioCryst, with potential application in the treatment of rheumatoid arthritis.

Transplant Rejection. Risk of rejection is one of the most frequent complications following transplant surgery. Rejection is caused by the body's immune response in which T-cells are generated to attack the transplanted organ or tissue. It is estimated that there are approximately 25,000 organ transplants, 30,000 corneal transplants and 6,000 bone marrow transplants each year in the United States. In general for organ and bone marrow transplants, rejection is an acute risk during the initial hospital stay for the transplant surgery and thereafter a chronic risk of varying degrees of severity. The Company believes selective suppression of the immune response may reduce the risk of rejection. The immunosuppressant drugs which are currently used to control or prevent rejection often cause significant detrimental side effects. A number of new drugs are in various stages of development by other researchers and companies for the control and prevention of transplant rejection. The Company is at the pre-IND safety assessment stage of development of an oral formulation of BCX-34 for treatment of transplant rejection.

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Multiple Sclerosis. Multiple sclerosis ("MS") is an autoimmune disease in which T-cells attack and progressively destroy the myelin sheath that envelops certain nerve cells in the brain and spinal cord. The disease is characterized by unpredictable attacks of neurological dysfunction that may include partial paralysis or tremors, lack of motor coordination, vision problems, and memory loss. MS afflicts approximately 300,000 people in the United States, approximately two-thirds of whom are women. The Company believes that T-cell controlling agents such as PNP inhibitors offer promise as a potential drug treatment for MS. BioCryst believes that an oral formulation of BCX-34, which is currently in the clinical stage of development for CTCL, may be useful for the treatment of MS. The first FDA approved treatment for any form of MS, a beta interferon, became available in 1993. Beta interferon is a large molecule protein which requires delivery by injection.

Ophthalmic Diseases and Disorders. There are a number of inflammatory diseases of the eye that involve T-cells. A leading ophthalmic inflammatory disease is uveitis which is characterized by eye swelling, ocular accumulation of fatty deposits and impaired vision. The most severe cases of uveitis, such as Behcet's syndrome and Vogt-Koyanagi-Harada syndrome, result in blindness. Clinical studies with currently approved immunosuppressants support the idea that T-cells participate in the pathogenesis of these diseases and that oral and ophthalmic formulations of BCX-34 may potentially be efficacious in treating these diseases. The Company is in the preclinical stage of development of an ophthalmic formulation of BCX-34 for direct delivery of the drug to the eye.

#### Influenza Neuraminidase Inhibitors

Influenza is a viral disease which afflicts up to 40 million people in the United States each year. It is particularly dangerous to the very young, the elderly and/or debilitated patients and those who have suppressed immune systems. The current standard for preventing flu is by vaccination, which is of limited benefit as vaccines are designed to resist a specific flu strain. No satisfactory treatment currently exists. Since the early 1980's, UAB scientists have been investigating the active site and function of the enzyme influenza neuraminidase. Influenza neuraminidase is an enzyme on the surface of the influenza virus which is associated with the spread of influenza and is believed to permit the influenza virus to invade human cells. Scientists at UAB and the Company have characterized the molecular structure of influenza neuraminidase and have initiated the design and synthesis of specific inhibitors of influenza neuraminidase. Research at UAB and the Company to date indicates that the active site for influenza neuraminidase remains substantially unchanged for the major strains of influenza. Funded in part by a National Institutes of Health ("NIH") Phase I Small Business Innovation Research ("SBIR") grant and a State of Alabama grant, the Company has developed lead compounds which in in vitro studies have indicated inhibition of influenza neuraminidase. The Company is in the preclinical stage of development of inhibitors of influenza neuraminidase. The Company believes that a neuraminidase inhibitor may be useful as a treatment for influenza. At least one major pharmaceutical company is engaged in clinical studies of an influenza neuraminidase inhibitor compound intended to treat

influenza, and it is believed that several other pharmaceutical companies are engaged in research to design or discover inhibitors of influenza neuraminidase.

#### Complement Inhibitors

The human body is equipped with immunological defense mechanisms to respond aggressively to infection or injury. One of these mechanisms, called complement, is a system of functionally linked proteins that interact with one another in a highly regulated manner. The complement system functions as a "cascade." Namely, once an activator of the system converts an inactive enzyme to an active enzyme, the activated enzyme then activates more proteins at the next stage which in turn activate other proteins. This mechanism, if inappropriately activated, can cause acute medical conditions, including, among other conditions, the inflammatory reactions that accompany hemodialysis, myocardial infarction, bypass surgery and post heart attack reperfusion injury. There are two pathways of complement activations, the classical pathway and the alternative pathway. The classical pathway is usually initiated by antigen-antibody complexes, while the alternative pathway is activated by bacterial, viral and parasite cell surfaces.

BioCryst is focusing its research efforts on designing protein and enzyme inhibitors to limit the rapid and aggressive damage caused by the complement cascade. The Company is initially focusing on designing inhibitors for factor D and factor B, enzymes playing a role in the alternative pathway, and the enzyme C1s, which plays a role in the classical pathway. Working with UAB scientists and funded in part by SBIR grants from the NIH, BioCryst has characterized the three-dimensional structure of factor D and has developed various assay systems for screening complement inhibitors. Due to the biochemical mechanism of the complement cascade, BioCryst believes complement inhibitors may have therapeutic applications in numerous acute and chronic immunological disorders.

#### Drug Discovery Methods

Drugs are chemical compounds that interact with target molecules, typically proteins, within the human body to affect a molecule's normal function. Ideally, drugs accomplish their intended therapeutic functions while creating as few side effects as possible. The interaction can be illustrated as follows: the drug molecule inserts itself in the target protein like a key inserted in a lock, and either stimulates, or more commonly suppresses, a protein's normal function. The results vary depending upon the role of the target protein. A drug that is selective or specific, i.e., that binds to or blocks the target protein without affecting other proteins or receptors, is generally more effective, less likely to cause side effects and can be administered in smaller doses.

#### Traditional Drug Discovery

Historically, most pharmaceutical companies have relied on costly and time-consuming screening to discover new chemical entities for development. While screening has been the basis for the discovery of virtually all drugs currently in use, the cost has been great. On average, it has generally been necessary to assess hundreds or thousands of chemical compounds to find a lead compound which successfully completes the development process. If screening produces a lead compound, the compound's mode of action is likely to be unknown and the risk of side effects caused by a lack of target specificity is high. Screening-based research has failed to yield acceptably safe and effective drugs for many important therapeutic needs.

Most pharmaceutical companies presently use some form of pharmacology-based rational drug design which primarily utilizes certain receptors or purified enzyme preparations in assays to identify lead compounds for discovery and to design molecules to perform specific therapeutic tasks. Development of lead compounds is conducted by a systematic empirical approach and computer modeling. While this approach is more refined than random screening, it still represents a costly and time-consuming effort which is limited by the amount and quality of information available about the target protein.

#### Structure-Based Drug Design

BioCryst believes that structure-based drug design further improves the advancements made by the rational drug design approach over traditional drug screening techniques. By identifying the target protein in advance and by

discovering the chemical and molecular structure of the protein, scientists believe it is possible to design a more optimal drug to interact with the protein.

Structure-based drug design is a drug discovery approach by which synthetic compounds are designed from detailed structural knowledge of the active sites of protein targets associated with particular diseases. The Company's structure-based drug design involves the integrated application of traditional biology and medicinal chemistry along with an array of advanced technologies, including X-ray crystallography, computational chemistry, computer modeling of molecular structures, molecular biology and protein biophysical chemistry, to focus on the three-dimensional molecular structure and active site characterization of the proteins that control cellular biology.

The initial targets for structure-based drug design are selected based on their involvement in the amplification or suppression of cellular biology activities integral to the course of a disease. Once a target is selected, it is obtained in purified form, either by isolation and purification from natural sources or through recombinant molecular biology technology. The purified protein target is crystallized and the crystals are subjected to X-ray diffraction analysis. The diffraction data, both of the protein alone and of the protein complexed with one or more "heavy atom derivatives" are used to determine the three-dimensional molecular structure of the target. This structure is then used as a blueprint for the drug design of a lead compound. The design occurs through an interactive study of the three-dimensional display of the protein target by a team of X-ray crystallographers, molecular modelers, synthetic chemists and pharmacologists. The compounds are modeled for their fit in the active site of the target, considering both steric aspects (i.e., geometric shape) and functional group interactions, such as hydrogen bonding and hydrophobic interactions.

The initial design phase is followed by the synthesis of the lead compound, quantitative measurements of its ability to interact with the target protein, and X-ray crystallographic analysis of the compound-target complex. This analysis reveals important, empirical information on how the compound actually binds to the target and the nature and extent of conformational changes induced in the target by the binding. These data, in turn, suggest ways to refine the lead

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compounds to improve its interaction with the target protein. The refined lead compound is then synthesized and complexed with the target and refined again in an iterative process. At each stage, the structure of the complex of the lead compound bound to the target protein is determined by X-ray crystallography, for further analysis and optimization.

Once a sufficiently potent compound has been designed and optimized, its activity is evaluated in a biological system to establish the compound's ability to function in a physiological environment. If the compound fails in the biological system, the design team is able to go back to the structural model and use the crystallographic data to adjust structural features of the compound to overcome the difficulty. This process continues until a designed compound exhibits the desired properties.

The compound is then evaluated in an experimental disease model. If the compound fails, the reasons for failure (e.g., adverse metabolism, plasma binding, distribution, etc.) are determined and, again, new or modified compounds are designed to overcome the deficiencies without interfering with their ability to interact with the active site of the target protein. The experimental drug is then ready for conventional drug development (e.g., studies in safety assessment, formulation, clinical trials, etc.). If problems occur during drug development, the drug design team may overcome them by further manipulation of the compound without altering the portion of the compound binding to the active site of the target protein.

This iterative analysis and compound modification is possible because of the structural data obtained from X-ray crystallographic analysis at each stage. It is this capability that holds forth the promise of structure-based drug design for potential increases in the efficiency of the drug discovery and development process with reductions in the total cost involved.

BioCryst scientists include recognized world leaders in the fields of X-ray crystallography and medicinal chemistry who collaborate with the Company's



distinguished Scientific Advisory Board members and consultants from UAB. UAB has one of the leading X-ray crystallography centers in the world and has been successful in characterizing a significant number of medically relevant protein targets. Several UAB scientists are consultants to BioCryst. In 1986, the Company entered into an agreement with UAB which granted BioCryst exclusive rights to any discoveries resulting from research relating to PNP and a right of first negotiation for other UAB discoveries in other areas in which BioCryst has UAB consultants. The Company believes that based upon its scientific staff and management, the number of promising compounds it has developed and their stage of clinical development, it is a leader in the practical application of structure-based drug design.

## Research and Development

### General

BioCryst initiated its research and development program in 1986, with drug synthesis beginning in 1987. The Company has assembled a scientific research staff with expertise in a broad base of advanced research technologies including protein biochemistry, X-ray crystallography, chemistry and pharmacology. Of the Company's 42 employees at January 31, 1996, 34 were employed in its research and development, preclinical studies and clinical trials programs. The Company's staff includes 17 persons with Ph.D.s.

The Company's research facilities include protein biochemistry and organic synthesis laboratories, in vitro and in vivo testing facilities, X-ray crystallography, computer and graphics equipment and formulation facilities.

In addition to its research programs pursued in-house, BioCryst collaborates with academic institutions to support research in areas of the Company's product development interests and to conduct its clinical trials. Usually, research assistance provided by outside academic institutions is performed in conjunction with additional in-house research. The faculty member supervising the outside research effort may also participate as a consultant to the Company's in-house effort. The Company's primary academic collaboration is with UAB and is described under "Business - Research and Development - UAB Collaborative Arrangements."

During the years ended December 31, 1993, 1994 and 1995, the Company spent an aggregate of \$16,854,709 on research and development. Of that amount, \$4,195,800 was spent in 1993, \$5,551,660 was spent in 1994 and

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\$7,107,249 was spent in 1995. Approximately \$10,359,000 of that amount was spent on in-house research and development and \$6,496,000 was spent on contract research and development.

### Grants and Technology Agreements

In 1991 and 1992, BioCryst was awarded three \$50,000 Phase I SBIR grants by the NIH. They were used to support the design and synthesis of inhibitors to influenza neuraminidase, factor D and aldose reductase. In 1992, the Company was also awarded \$47,500 by the Alabama Department of Economic and Community Affairs which was used in the design and synthesis of inhibitors of influenza neuraminidase. In February 1994, BioCryst was awarded a two-year \$500,000 Phase II SBIR grant by the NIH. The grant was used to support the design of inhibitors of factor D. There is no assurance that BioCryst will be awarded any future grants.

In 1987, the Company entered into a research agreement under which BioCryst received approximately \$960,000 over four years from Ciba to fund its research of PNP inhibitors and Ciba was granted certain rights to enter into various option and license agreements for PNP inhibitors. In 1990, Ciba exercised its right pursuant to which the Company granted Ciba an exclusive option to enter into a worldwide exclusive license for several compounds in the Company's sixth class of PNP inhibitors. The license does not include BCX-34. Ciba signed that license agreement and paid the Company a \$500,000 fee (up to \$300,000 of which is refundable in certain circumstances) following patent issuance in 1993. The terms of the license also call for Ciba to make milestone payments based upon the estimated annual United States sales of the licensed products plus royalties. No assurance can be given that any additional revenues will be realized by the Company pursuant to the license. Ciba's other rights to enter

into various option and license agreements for PNP inhibitors have expired.

#### UAB Collaborative Arrangements

UAB has one of the leading X-ray crystallography centers in the world with approximately 99 full-time staff members and approximately \$9 million in research grants and contract funding in 1995. In 1986, the Company entered into an agreement with UAB which granted the Company exclusive rights to any discoveries resulting from research relating to PNP, and the right of first negotiation for UAB discoveries in other areas in which BioCryst has UAB consultants. In exchange for these rights, BioCryst issued securities to a foundation associated with UAB and paid research fees of approximately \$387,000. Since 1990, the Company has entered into several other research agreements with UAB to perform research for the Company. The agreements provide that UAB perform specific research for the Company in return for research payments and license fees. In November 1994, the Company entered into an agreement with UAB for the joint research and development relating to development of an influenza neuraminidase inhibitor. UAB has granted the Company certain rights to any discoveries resulting from research previously developed by UAB or jointly developed with BioCryst. The Company has agreed to fund three UAB research laboratories, to expend at least \$6 million for the project over a three-year period, to pay certain royalties on sales of any resulting product and to share in future payments received from other third-party collaborators. In July 1995, the Company entered into an agreement with UAB for the joint research and development relating to development of factor D inhibitors. UAB has also granted the Company certain rights to any discoveries resulting from research previously developed by UAB or jointly developed with BioCryst. The Company has agreed to fund two UAB research laboratories, to expend at least \$1 million for the project over a three-year period, to pay certain royalties on sales of any resulting product and to share in future payments received from other third-party collaborators. These two agreements have 25-year terms and are terminable by the Company upon three months' notice. BioCryst believes that due to the expertise of the faculty at UAB in the various disciplines employed by BioCryst in its structure-based drug design programs, including X-ray crystallography, and UAB's past performance in identifying and characterizing medically relevant protein targets, BioCryst's relationship with UAB is important to the success of BioCryst. No assurance can be given, however, that UAB's research will be beneficial to BioCryst or that BioCryst will be able to maintain its relationship with UAB.

#### Patents and Proprietary Information

The Company owns or has rights to certain proprietary information, issued patents and patent applications which relate to compounds it is developing. The Company actively seeks, when appropriate, protection for its products and proprietary information by means of United States and foreign patents, trademarks and contractual arrangements. In addition, the Company plans to rely upon trade secrets and contractual arrangements to protect certain of its proprietary information and products.

The Company has been issued five United States patents which expire between 2009 or 2010 and relate to compounds in classes two through six of its PNP inhibitor compounds. The Company's current lead compound, BCX-34, is covered by one of the composition of matter patents. A patent application involving compounds in class seven of the Company's PNP inhibitors is under examination at the PTO. The Company's patent application involving compounds in class one of its PNP inhibitors is in the process of being further examined by the PTO after an unsuccessful administrative appeal. The compound under a disputed option to Warner-Lambert is included in this class. See "Business - Legal Proceedings." A patent application on a new process to prepare BCX-34 and other PNP inhibitors has also been submitted to the PTO. In addition, a patent application covering novel inhibitors of influenza neuraminidase is under review by the PTO. There can be no assurance that any patents will provide the Company with sufficient protection against competitive products or otherwise be commercially valuable.

The Company depends upon the knowledge, experience and skills (which are not patentable) of its key scientific and technical personnel. To protect its rights to its proprietary information, the Company requires all employees, consultants, advisors and collaborators to enter into confidentiality agreements which prohibit the disclosure of confidential information to anyone outside the Company and require disclosure and assignment to the Company of their ideas,

developments, discoveries and inventions. There can be no assurance that these agreements will effectively prevent the unauthorized use or disclosure of the Company's confidential information. In the absence of patent protection, the Company's business may be adversely affected by competitors who develop substantially equivalent technology.

#### Marketing, Distribution and Sales

The Company has no experience in marketing, distributing or selling pharmaceutical products and will have to develop a pharmaceutical sales force and/or rely on collaborators, licensees or on arrangements with others to provide for the marketing, distribution and sales of any products it may develop. There can be no assurance that the Company will be able to establish marketing, distribution and sales capabilities or make arrangements with collaborators, licensees or others to perform such activities.

#### Competition

The pharmaceutical industry is intensely competitive. Many companies, including biotechnology, chemical and pharmaceutical companies, are actively engaged in activities similar to those of the Company, including research and development of drugs for the treatment of immunological and infectious diseases and disorders. Many of these companies have substantially greater financial and other resources, larger research and development staffs, and more extensive marketing and manufacturing organizations than the Company. In addition, some of them have considerable experience in preclinical testing, clinical trials and other regulatory approval procedures. There are also academic institutions, governmental agencies and other research organizations which are conducting research in areas in which the Company is working; they may also market commercial products, either on their own or through collaborative efforts.

BioCryst expects to encounter significant competition for the pharmaceutical products it plans to develop. Companies that complete clinical trials, obtain required regulatory approvals and commence commercial sales of their products before their competitors may achieve a significant competitive advantage. In addition, certain pharmaceutical and biotechnology firms, including major pharmaceutical companies and specialized structure-based drug design companies have announced efforts in the field of structure-based drug design and in the field of PNP inhibitors. The Company expects that the technology for structure-based drug design will attract significant additional competitors over time. In order to compete successfully, the Company's goal is to develop proprietary positions in patented drugs for therapeutic markets which have not been satisfactorily addressed by conventional research strategies and, in the process, extend its expertise in structure-based drug design.

#### Government Regulation

BioCryst's research and development activities are, and its future business will be, subject to significant regulation by numerous governmental authorities in the United States, primarily, but not exclusively, by the FDA, and other countries. Pharmaceutical products intended for therapeutic or diagnostic use in humans are governed principally by the Federal Food, Drug and Cosmetic Act and by FDA regulations in the United States and by comparable laws and regulations in foreign countries. The process of completing clinical testing and obtaining FDA approval for a new drug product requires a number of years and the expenditure of substantial resources.

Following drug discovery, the steps required before a new pharmaceutical product may be marketed in the United States include (1) preclinical laboratory and animal tests, (2) the submission to the FDA of an application for an IND, (3) clinical and other studies to assess safety and parameters of use, (4) adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug, (5) the submission of an NDA to the FDA, and (6) FDA approval of the NDA prior to any commercial sale or shipment of the drug.

Typically, preclinical studies are conducted in the laboratory and in animal model systems to gain preliminary information on the drug's pharmacology and toxicology and to identify any potential safety problems that would preclude testing in humans. The results of these studies are submitted to the FDA as part of the IND application. Testing in humans may commence 30 days after submission of the IND by the FDA unless the FDA objects, although companies typically

wait for approval from the FDA before commencing clinical trials. A three phase clinical trial program is usually required for FDA approval of a pharmaceutical product. Phase I clinical trials are designed to determine the metabolism and pharmacologic effects of the drug in humans, the side effects associated with increasing doses, and, possibly, to obtain early indications of efficacy. These studies generally involve a small number of healthy volunteer subjects, but may be conducted in people with the disease the drug is intended to treat. Phase II studies are conducted in an expanded population to evaluate the effectiveness of the drug for a particular indication and thus involve patients with the disease under study. These studies also provide evidence of the short term side effects and risks associated with the drug. Phase III studies are generally designed to provide the substantial evidence of safety and effectiveness of a drug required to obtain FDA approval. They often involve a substantial number of patients in multiple study centers and may include chronic administration of the drug in order to assess the overall benefit-risk relationship of the drug. A clinical trial may combine the elements of more than one phase and typically two or more Phase III studies are required. Upon completion of clinical testing which demonstrates that the product is safe and effective for a specific indication, an NDA may be submitted to the FDA. This application includes details of the manufacturing and testing processes, preclinical studies and clinical trials. The designation of a clinical trial as being of a particular Phase is not necessarily indicative that such a trial will be sufficient to satisfy the requirements of a particular Phase. For example, no assurance can be given that a Phase III clinical trial will be sufficient to support an NDA without further clinical trials. The FDA monitors the progress of each of the three phases of clinical testing and may alter, suspend or terminate the trials based on the data that have been accumulated to that point and its assessment of the risk/benefit ratio to the patient. Typical estimates of the total time required for completing such clinical testing vary between four and ten years. FDA approval of the NDA is required before the applicant may market the new product in the United States. The clinical testing and FDA review process for new drugs, which includes confirmation by the FDA that good laboratory, clinical, and manufacturing practices were maintained during testing and manufacturing, are likely to require substantial time, effort and expense. There can be no assurance that any approval will be granted to the Company on a timely basis, if at all. The FDA may refuse to approve an NDA if applicable statutory and/or regulatory criteria are not satisfied, or may require additional testing or information. There can be no assurance that such additional testing or the provision of such information, if required, will not have a material adverse effect on the Company. The regulatory process can be modified by Congress or the FDA in specific situations.

In 1988, the FDA issued regulations intended to expedite the development, evaluation, and marketing of new therapeutic products to treat life-threatening and severely debilitating illnesses for which no satisfactory alternative therapies exist. These regulations provide for early consultation between the sponsor and the FDA in the design of both preclinical studies and clinical trials. Phase I clinical trials may sometimes be carried out in people with the disease that the drug is intended to treat rather than in healthy volunteers, as is customary, followed by studies to establish effectiveness in Phase II. If the results of Phase I and Phase II trials support the safety and effectiveness of the therapeutic agent, and their design and execution are deemed satisfactory upon review by the FDA, marketing approval can be sought at the end of Phase II trials. NDA approval granted under these regulations may be restricted by the FDA as necessary to ensure safe use of the drug. In addition, post-marketing clinical studies may be required. If after approval a post-marketing clinical study establishes that the drug does not perform as expected, or if post-marketing restrictions are not adhered to or are not adequate to ensure safe use of the drug, FDA approval may be withdrawn. The

expedited approval may shorten the traditional drug development process by an estimated two to three years. There can be no assurance, however, that any compound the Company may develop will be eligible for evaluation by the FDA under the 1988 regulations or, if eligible, will be approved for marketing at all or, if approved for marketing, will be approved for marketing sooner than would be traditionally expected.

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a "rare disease or condition," which generally is a disease or condition that affects populations of fewer than 200,000 individuals in the

United States. Orphan drug designation must be requested before submitting an NDA, and after the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are publicized by the FDA. Under current law, orphan drug designation grants certain U.S. marketing exclusivity to the first company to receive FDA approval to market such designated drug, subject to certain limitations. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory approval process. In October 1993, the Company obtained from the FDA an orphan drug designation for BCX-34 to treat CTCL, and may request orphan drug designation for more of its products and/or additional indications as part of its overall regulatory strategy in the future. There is no assurance, however, that any of its products will receive an orphan drug designation or be the first to be approved by the FDA for the designated indication and, hence, obtain orphan drug marketing exclusivity. Although obtaining FDA approval to market a product with an orphan drug designation can be advantageous, there can be no assurance that the scope of protection or the level of marketing exclusivity that is currently afforded by orphan drug designation and marketing approval will remain in effect in the future. There can be no assurance that the Company will receive FDA approval to market BCX-34 to treat CTCL and thus receive orphan drug designation for BCX-34 to treat CTCL. In addition, it is possible that other competitors of the Company could obtain orphan drug designation for product candidates that are not the same as BCX-34 though they are intended for use to treat CTCL.

In June 1995, the Company notified the FDA that it had submitted incorrect efficacy data to the FDA pertaining to its Phase II dose-ranging studies of BCX-34 for CTCL and psoriasis. Upon learning of the error, the Company initiated internal and external audits and submitted corrected analyses to the FDA. In addition, the Company hired a new Vice President of Clinical Development and outside expert personnel to manage clinical development and monitor studies, developed additional standard operating procedures, and contracted with a contract research organization to assist the Company in monitoring its trial for BCX-34 for CTCL.

In November 1995, the FDA inspected the Company in relation to a February 1995 48-hour skin stripping study involving application of BCX-34. At the conclusion of the inspection, the FDA issued to the Company a Form FDA 483 including the observation that there was no documentation of any monitoring of the study or of several other studies. The Company responded to this and the other observation in the Form FDA 483. Although the FDA has not raised any additional questions in the matter, the Company does not know whether its responses were satisfactory to the FDA, and there can be no assurance that even if the FDA finds the responses to be satisfactory, it will not seek to impose administrative, civil, or other sanctions in connection with the studies.

Even after initial FDA approval has been obtained, further studies may be required to provide additional data on safety or to gain approval for the use of a product as a treatment in clinical indications other than those for which the product was initially tested. The FDA may also require post-marketing testing and surveillance programs to monitor the drug's effects. Side effects resulting from the use of pharmaceutical products may prevent or limit the further marketing of products.

Once the sale of a product is approved, the FDA regulates production, distribution, marketing, advertising and other activities under the Federal Food, Drug, and Cosmetic Act and the FDA's implementing regulations. A post-marketing testing, surveillance and reporting program may be required to continuously monitor the product's usage and effects. Product approvals may be withdrawn, or other actions may be ordered, or sanctions imposed if compliance with regulatory requirements is not maintained. Other countries in which any products developed by the Company or its licensees may be marketed impose a similar regulatory process.

In addition to regulations enforced by the FDA, the Company also is subject to regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act and other similar Federal, state and local regulations governing permissible laboratory activities, waste disposal handling of toxic, dangerous or radioactive materials and other matters. The Company believes that it is in compliance with such regulations.

For marketing outside the United States, the Company will be subject to foreign regulatory requirements governing human clinical trials and marketing approval for drugs and devices. The requirements relating to the conduct of clinical trials, product licensing, pricing and reimbursement vary widely from country to

country.

#### Human Resources

As of January 31, 1996, the Company had 42 employees, of whom 34 were engaged in research and development and eight were in general and administrative functions. The Company's scientific staff (17 of whom hold Ph.D. degrees) has diversified experience in biochemistry, pharmacology, X-ray crystallography, synthetic organic chemistry, computational chemistry, medicinal chemistry and pharmacology. The Company considers its relations with its employees to be satisfactory.

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#### Scientific Advisory Board and Consultants

BioCryst has assembled a Scientific Advisory Board comprised of seven members (the "Scientific Advisors") who are leaders in certain of the Company's core disciplines or who otherwise have specific expertise in its therapeutic focus areas. The Scientific Advisory Board meets as a group at scheduled semi-annual meetings and the Scientific Advisors meet more frequently, on an individual basis, with the Company's scientific personnel and management to discuss the Company's ongoing research and drug discovery and development projects.

The Company also has consulting agreements with a number of other scientists (the "Consultants") with expertise in the Company's core disciplines or in its therapeutic focus areas who are consulted from time to time by the Company.

The Scientific Advisors and the Consultants are reimbursed for their expenses and receive nominal cash compensation in connection with their service and have been issued options and/or shares of Common Stock. The Scientific Advisors have been issued a total of 4,975 shares of Common Stock for nominal consideration and granted stock options to purchase a total of 63,000 shares of Common Stock at a weighted average exercise price of \$5.55 per share. Consultants have also been granted stock options to purchase a total of 47,000 shares at a weighted average exercise price of \$4.41 per share. The Scientific Advisors and the Consultants are all employed by or have consulting agreements with entities other than the Company, some of which may compete with the Company in the future. The Scientific Advisors and the Consultants are expected to devote only a small portion of their time to the business of the Company, although no specific time commitment has been established. They are not expected to participate actively in the Company's affairs or in the development of the Company's technology. Certain of the institutions with which the Scientific Advisors and the Consultants are affiliated may adopt new regulations or policies that limit the ability of the Scientific Advisors and the Consultants to consult with the Company. The loss of the services of certain of the Scientific Advisors and the Consultants could adversely affect the Company to the extent that the Company is pursuing research or development in areas of such Scientific Advisors' and Consultants' expertise. To the extent members of the Company's Scientific Advisory Board or the Consultants have consulting arrangements with or become employed by any competitor of the Company, the Company could be materially adversely affected. One member of the Scientific Advisory Board, Dr. Gordon N. Gill, is a member of the Board of Directors of the Agouron Institute. The Agouron Institute is a shareholder in, and has had contractual relationships with, Agouron Pharmaceuticals, Inc., a company utilizing core technology which is similar to the core technology employed by BioCryst.

Any inventions or processes independently discovered by the Scientific Advisors or the Consultants may not become the property of the Company and will probably remain the property of such persons or of such persons' employers. In addition, the institutions with which the Scientific Advisors and the Consultants are affiliated may make available the research services of their personnel, including the Scientific Advisors and the Consultants, to competitors of the Company pursuant to sponsored research agreements. The Company requires the Scientific Advisors and the Consultants to enter into confidentiality agreements which prohibit the disclosure of confidential information to anyone outside the Company and require disclosure and assignment to the Company of their ideas, developments, discoveries or inventions. However, no assurance can be given that competitors of the Company will not gain access to trade secrets and other proprietary information developed by the Company and disclosed to the Scientific Advisors and the Consultants.

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## ITEM 2. PROPERTIES

The Company's administrative offices and principal research facility are located in 22,800 square feet of leased office space in Riverchase Industrial/Research Park in Birmingham, Alabama. The lease runs through March 31, 2000. The Company believes that its facilities are adequate for its current operations. Additional facilities will be necessary to manufacture sufficient quantities under good manufacturing practices to conduct extensive clinical trials or if the Company undertakes commercial manufacturing. See Note 6 to the Financial Statements.

## ITEM 3. LEGAL PROCEEDINGS

In October 1991, the Company granted an option to Warner-Lambert to license BioCryst's class one PNP inhibitors on terms and conditions to be negotiated by the parties. In June 1993, that option was extended at Warner-Lambert's request until September 1994, or completion of Warner-Lambert's clinical trials (whichever first occurred), while being restricted to only BCX-5, one PNP inhibitor compound in BioCryst's class one inhibitors. The Company's patent application for compounds in this class of PNP inhibitor compounds is in the process of being further examined by the PTO after an unsuccessful administrative appeal. Upon exercise of the option, any license negotiated by the parties would have required an upfront payment, milestone payments and royalties on agreed-upon terms. In September 1994, Warner-Lambert requested a further extension of its option, and a dispute has arisen between the parties as to, among other things, whether or not the option has expired and whether or not BioCryst is obligated to negotiate further with Warner-Lambert the terms of a licensing agreement.

On February 6, 1995, the Company filed a complaint for a declaratory judgment against Warner-Lambert in the Circuit Court of Shelby County, Alabama to resolve the dispute. Warner-Lambert counter-claimed against the Company, alleging that the Company breached the option, seeking unspecified compensatory, consequential and incidental damages and lost profits.

The Company believes that the conditions precedent to the exercise of Warner-Lambert's option have not been satisfied, that the option has expired, and that Warner-Lambert's breach of contract allegations lack merit. The Company believes that it has complied with its obligations under the option agreement, and intends to continue to vigorously pursue this action. There can be no assurance, however, that the Company will prevail or that Warner-Lambert will not prevail in its counter claims.

The Company is not a party to any other litigation.

## ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

None.

## PART II

### ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS

The Company's common stock trades on the Nasdaq National Market tier of The Nasdaq Stock Market<sup>SM</sup> under the symbol BCRX. Public trading commenced on March 4, 1994. Prior to that date, there was no public market for the Company's stock. The following table sets forth the low and high prices as reported by Nasdaq for each quarter in 1995 and 1994:

	1995		1994	
	Low	High	Low	High
	---	---	---	---
First quarter	\$4.63	\$7.00	\$5.50	\$6.75
Second quarter	5.50	13.75	3.38	5.88
Third quarter	7.75	12.25	3.75	5.88
Fourth quarter	8.50	11.25	4.38	6.13

The last sale price of the common stock on January 31, 1996 as reported by

Nasdaq was \$9.63 per share.

As of January 31, 1996, there were approximately 520 holders of record of the common stock.

The Company has never paid cash dividends and does not anticipate paying cash dividends.

#### ITEM 6. SELECTED FINANCIAL DATA

	Years Ended December 31, (In thousands, except per share)				
Statement of Operations Data:	1995	1994	1993	1992	1991
Total revenues	\$ 885	\$ 734	\$ 363	\$ 185	\$ 112
Research and development expenses	\$ 7,107	\$ 5,552	\$ 4,196	\$ 3,019	\$ 707
Net loss	\$ (8,576)	\$ (6,938)	\$ (5,196)	\$ (4,051)	\$ (1,282)
Net loss per share	\$ (.96)	\$ (1.02)	\$ (1.55)	\$ (1.31)	\$ (1.50)
Weighted average shares outstanding	8,905	6,787	3,352	3,101	856

  

	December 31, (In thousands)				
Balance Sheet Data:	1995	1994	1993	1992	1991
Cash, cash equivalents and securities	\$ 11,414	\$ 10,873	\$ 2,873	\$ 1,284	\$ 3,164
Total assets	13,056	12,803	5,203	3,555	3,578
Long-term debt and obligations under capital leases, excluding current portion	300	573	855	931	150
Accumulated deficit	(30,067)	(21,491)	(14,553)	(9,357)	(5,306)
Total stockholders' equity	11,326	11,176	2,877	1,534	2,951

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#### ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

This Annual Report on Form 10-K contains certain statements of a forward-looking nature relating to future events or the future financial performance of the Company. Such statements are only predictions and the actual events or results may differ materially from the results discussed in the forward-looking statements. Factors that could cause or contribute to such differences include those discussed below as well as those discussed in other filings made by the Company with the Securities and Exchange Commission.

##### Overview

Since its inception in 1986, the Company has been engaged in research and development activities (including conducting preclinical studies and clinical trials) and organizational efforts, including recruiting its scientific and management personnel, establishing laboratory facilities, engaging its Scientific Advisory Board and raising capital. The Company has not received any revenue from the sale of pharmaceutical products and does not expect to receive such revenues to a significant extent for at least several years, if at all. The Company has incurred operating losses since its inception.

The Company's future business, financial condition and results of operations are dependent on the Company's ability to successfully develop, market and manufacture its pharmaceutical products for the treatment of major immunological and infectious diseases and disorders. Inherent in this process are a number of factors that the Company must carefully manage in order to be successful. Some of these factors are: conducting preclinical studies and clinical trials of its compounds that demonstrate such compounds' safety and effectiveness; obtaining additional financing to support the Company's operations; developing collaborative arrangements with corporate partners, academic institutions and consultants to support research and development efforts and to conduct such



clinical trials; obtaining regulatory approval for such compounds; entering into agreements for product development, manufacturing and commercialization; developing the capacity to manufacture, market and sell its products either directly or with collaborative partners; competing effectively with other pharmaceutical and biotechnological products for human therapeutic applications; obtaining adequate reimbursement from third-party payors for its products; retaining and attracting key personnel; protecting its proprietary rights; and avoiding infringement claims by third parties. No assurance can be given that the Company will be able to manage such factors successfully. The failure to manage such factors successfully could have a material adverse effect on the Company's business, financial condition and results of operations.

Year Ended December 31, 1995 Compared with the Year Ended December 31, 1994

Collaborative and other research and development revenue decreased 17.4% to \$222,329 in 1995 from \$269,126 in 1994, primarily as a result of 1994 including \$50,000 from non-recurring contract research. Interest and other income increased 42.5% to \$662,259 in 1995 from \$464,690 in 1994, primarily due to higher rates and the investment of funds received from the Company's initial public offering of common stock in March 1994 and private placements of common stock in September 1994 and May 1995.

Research and development expenses increased 28.0% to \$7,107,249 in 1995 from \$5,551,660 in 1994. The increase was primarily attributable to expenses associated with conducting clinical trials, preclinical studies and large scale synthesis of BCX-34 (generic name peldesine) and increased personnel costs and expenses associated with joint research and development contracts with UAB for the influenza neuraminidase and complement projects and outside research on PNP inhibitors.

General and administrative expenses increased 16.0% to \$2,209,488 in 1995 from \$1,904,046 in 1994. The increase was primarily the result of increased franchise taxes, increased stockholder and investor communication expenses associated with being a public company and higher business insurance costs. These increases were partially offset by two non-recurring charges in 1994 - payments made pursuant to a consulting agreement entered into upon the former president's termination in the second quarter of 1994 and contractual deferred compensation paid to the former president of the Company upon the initial public offering in the first quarter of 1994.

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Interest expense decreased 33.3% to \$144,115 in 1995 from \$215,985 in 1994. The decrease was primarily due to a decline in capitalized lease obligations, along with long-term debt, resulting in lesser interest expense. The Company obtained most of its leases in connection with the move to its new facilities in April 1992.

Year Ended December 31, 1994 Compared with the Year Ended December 31, 1993

Collaborative and other research and development revenue decreased 11.0% to \$269,126 in 1994 from \$302,375 in 1993, primarily as a result of the exercise of an option for a license by Ciba in 1993 compared to \$219,126 from a Phase II SBIR grant and \$50,000 from contract research in 1994. Interest and other income increased 666.4% to \$464,690 in 1994 from \$60,629 in 1993, primarily due to higher rates and the investment of funds received from the Company's initial public offering.

Research and development expenses increased 32.3% to \$5,551,660 in 1994 from \$4,195,800 in 1993. The increase was primarily attributable to expenses associated with conducting clinical trials, preclinical studies and large scale synthesis of BCX-34 and the effect of additional research and clinical personnel hired since the first quarter of 1993.

General and administrative expenses increased 73.4% to \$1,904,046 in 1994 from \$1,098,206 in 1993. The increase was primarily due to the additional costs associated with added personnel, additional business insurance, payments made pursuant to a consulting agreement entered into upon the former president's termination, costs associated with being a public company, increased legal expenses and contractual deferred compensation paid to the former president of the Company upon the initial public offering in the first quarter of 1994 which were offset in part by the non-recurring effect of writing off costs of a public offering withdrawn in the second quarter of 1993.

Interest expense decreased 18.5% to \$215,985 in 1994 from \$264,994 in 1993. The decrease was primarily due to a decline in capitalized lease obligations, along with long-term debt, resulting in lesser interest expense. The Company obtained most of its leases in connection with the move to its new facilities in April 1992.

#### Liquidity and Capital Resources

Cash expenditures have exceeded revenues since the Company's inception. Operations have principally been funded through an initial public offering of common stock, private placements of equity and debt securities, equipment lease financing, facility leases, collaborative and other research and development agreements (including a license and options for licenses), research grants and interest income. In addition, the Company has attempted to contain costs and reduce cash flow requirements by renting scientific equipment or facilities, contracting with third parties to conduct certain research and development and using consultants. The Company expects to incur additional expenses, resulting in significant losses, as it continues and expands its research and development activities and undertakes additional preclinical studies and clinical trials of compounds which have been or may be discovered. The Company also expects to incur substantial administrative, manufacturing and commercialization expenditures in the future as it seeks FDA approval for its compounds and establishes its manufacturing capability under Good Manufacturing Practices, and substantial expenses related to the filing, prosecution, maintenance, defense and enforcement of patent and other intellectual property claims.

At December 31, 1995, the Company's cash, cash equivalents and securities held-to-maturity were \$11,414,044.

The Company received \$500,000 in June 1993 as a license fee from Ciba. The Company is required to refund up to \$300,000 of the fee if sales of any resultant products are below specified levels (see Note 10).

The Company has financed its equipment purchases primarily with lease lines of credit. The Company currently has a \$500,000 line of credit with its bank to finance capital equipment. In January 1992, the Company entered into an operating lease for its current facilities which, based on an extension signed in December 1994, expires on March 31, 2000, with an option to lease for an additional three years at current market rates. The operating lease requires the Company to pay monthly rent (ranging from \$10,241 and escalating annually to a minimum of \$12,457 per month in the final year), and a pro rata share of operating expenses and real estate taxes in excess of base year amounts.

At December 31, 1995, the Company had long-term capital lease and operating lease obligations which provide for aggregate minimum payments of \$531,747 in 1996, \$502,077 in 1997 and \$306,714 in 1998. The Company is required

to expend \$6 million over the three-year period ending December 31, 1997 on its influenza neuraminidase project and \$1 million over the three-year period ending July 18, 1998 on its Complement project in order to maintain a worldwide license from UAB. In addition, the Company has committed to conducting certain clinical trials and animal studies in 1996 for an aggregate amount of approximately \$1.2 million at December 31, 1995.

The Company plans to finance its needs principally from its existing capital resources and interest thereon, from payments under collaborative and licensing agreements with corporate partners, through research grants, and to the extent available, through lease or loan financing and future public or private financings. The Company believes that its available funds will be sufficient to fund the Company's operations through the end of 1996. The Company's long-term capital requirements and the adequacy of its available funds will depend upon many factors, including results of research and development, results of product testing, relationships with strategic partners, changes in the focus and direction of the Company's research and development programs, competitive and technological advances and the FDA regulatory process. Additional funding, whether through additional sales of securities or collaborative or other arrangements with corporate partners or from other sources, may not be available when needed or on terms acceptable to the Company. Insufficient funds may require the Company to delay, scale-back or eliminate certain of its research and development programs or to license third parties to commercialize products

or technologies that the Company would otherwise undertake itself.

The Company believes that inflation has not had a material impact on its operations.

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ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

BALANCE SHEETS

	December 31,	
	1995	1994
Assets		
Cash and cash equivalents (Note 4)	\$ 6,134,968	\$ 2,678,059
Securities held-to-maturity	5,279,076	8,194,802
Prepaid expenses and other current assets	279,386	244,847
Total current assets	11,693,430	11,117,708
Furniture and equipment, net (Note 2)	1,362,783	1,685,123
Total assets	\$ 13,056,213	\$12,802,831
Liabilities and Stockholders' Equity		
Accounts payable	\$ 210,177	\$ 148,114
Accrued expenses	187,673	171,012
Accrued taxes, other than income	350,223	23,726
Accrued vacation	110,704	134,727
Current maturities of long-term debt (Note 5)	28,782	25,416
Current maturities of capital lease obligations (Note 6)	241,745	250,383
Total current liabilities	1,129,304	753,378
Long-term debt (Note 5)	18,560	47,342
Capital lease obligations (Note 6)	281,851	526,151
Deferred license fee (Note 10)	300,000	300,000
Stockholders' equity (Notes 8 and 9):		
Preferred stock, \$.01 par value, shares authorized - 5,000,000; none issued and outstanding		
Common stock, \$.01 par value; shares authorized - 45,000,000; shares issued and outstanding - 9,504,331 - 1995; 7,907,166 - 1994	95,043	79,072
Additional paid-in capital	41,298,848	32,588,017
Accumulated deficit	(30,067,393)	(21,491,129)
Total stockholders' equity	11,326,498	11,175,960
Commitments and contingency (Notes 6 and 10)		
Total liabilities and stockholders' equity	\$ 13,056,213	\$12,802,831

See accompanying notes to financial statements.

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STATEMENTS OF OPERATIONS

	Years Ended December 31,		
	1995	1994	1993

Revenues:

Collaborative and other research and development (Notes 1 and 10)	\$ 222,329	\$ 269,126	\$ 302,375
Interest and other	662,259	464,690	60,629
	-----	-----	-----
Total revenues	884,588	733,816	363,004
	-----	-----	-----
Expenses:			
Research and development	7,107,249	5,551,660	4,195,800
General and administrative	2,209,488	1,904,046	1,098,206
Interest	144,115	215,985	264,994
	-----	-----	-----
Total expenses	9,460,852	7,671,691	5,559,000
	-----	-----	-----
Net loss	\$(8,576,264)	\$(6,937,875)	\$(5,195,996)
	=====	=====	=====
Net loss per share (Note 1)	\$ (.96)	\$ (1.02)	\$ (1.55)
Weighted average shares outstanding (Note 1)	8,905,099	6,787,203	3,352,364

See accompanying notes to financial statements.

STATEMENTS OF STOCKHOLDERS' EQUITY

	Preferred and Other Capital*	Common Stock	Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Equity
	-----	-----	-----	-----	-----
Balance at December 31, 1992	\$ 2,620,629	\$ 33,065	\$ 8,237,624	\$ (9,357,258)	\$ 1,534,060
Exercise of 8,750 shares of common stock under the stock option plan		87	17,413		17,500
Sale of 436,667 shares of Series A Preferred Stock at \$3.00 per share, less issuance cost	1,165,856				1,165,856
Sale of 994,165 shares of Series B Preferred Stock at \$6.00 per share, less issuance cost	5,355,159				5,355,159
Net loss				(5,195,996)	(5,195,996)
	-----	-----	-----	-----	-----
Balance at December 31, 1993	9,141,644	33,152	8,255,037	(14,553,254)	2,876,579
Sale of 2,310,900 shares of common stock at \$6.50 per share, less issuance cost		23,109	13,229,538		13,252,647
Conversion of Series A Preferred Stock into 709,160 shares of common stock upon the Company's IPO	(3,786,485)	7,092	3,779,393		
Conversion of Series B Preferred Stock into 994,165 shares of common stock upon the Company's IPO	(5,355,159)	9,942	5,345,217		
Sale of 515,000 shares of common stock at \$3.88 per share, less issuance cost		5,150	1,972,712		1,977,862
Exercise of 99,540 shares of common stock under the stock option plan, less 36,796 shares exchanged		627	6,120		6,747
Net loss				(6,937,875)	(6,937,875)
	-----	-----	-----	-----	-----
Balance at December 31, 1994		79,072	32,588,017	(21,491,129)	11,175,960
Sale of 1,570,000 shares of common stock at \$5.50 per share, less issuance cost		15,700	8,594,550		8,610,250
Exercise of 13,834 shares of common stock under the stock option plan		138	50,556		50,694
Sale of 13,331 shares of common stock under the employee stock purchase plan at \$4.94 per share		133	65,725		65,858
Net loss				(8,576,264)	(8,576,264)
	-----	-----	-----	-----	-----
Balance at December 31, 1995		\$ 95,043	\$41,298,848	\$ (30,067,393)	\$ 11,326,498
	=====	=====	=====	=====	=====

\* Represents Series A Preferred Stock at December 31, 1992 and Series A and B Preferred Stock at December 31, 1993.

See accompanying notes to financial statements.

STATEMENTS OF CASH FLOWS

	Years Ended December 31,		
	1995	1994	1993
Operating activities			
Net loss	\$ (8,576,264)	\$ (6,937,875)	\$ (5,195,996)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	554,025	607,399	603,532
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	(34,539)	149,638	(230,813)
Accounts payable	62,063	80,541	(232,266)
Accrued expenses	16,661	(452,038)	204,263
Accrued taxes, other than income	326,497	(1,461)	(24,813)
Accrued vacation	(24,023)	38,439	78,774
Net cash used in operating activities	(7,675,580)	(6,515,357)	(4,797,319)
Investing activities			
Purchases of furniture and equipment	(231,685)	(357,760)	(327,216)
Purchase of marketable securities	(11,397,640)	(13,433,567)	
Maturities of marketable securities	14,313,366	5,238,765	
Net cash provided by/(used in) investing activities	2,684,041	(8,552,562)	(327,216)
Financing activities			
Issuance of short-term notes payable			1,741,000
Sale and leaseback of furniture and equipment			242,828
Principal payments of debt and capital lease obligations	(278,354)	(364,542)	(2,108,225)
Deferred license			300,000
Sale of preferred stock, net of issuance costs			6,521,015
Exercise of stock options	50,694	6,747	17,500
Sale of common stock under the Employee Stock Purchase Plan	65,858		
Sale of common stock, net of issuance costs	8,610,250	15,230,509	
Net cash provided by financing activities	8,448,448	14,872,714	6,714,118
Increase (decrease) in cash and cash equivalents	3,456,909	(195,205)	1,589,583
Cash and equivalents at beginning of period	2,678,059	2,873,264	1,283,681
Cash and cash equivalents at end of period	\$ 6,134,968	\$ 2,678,059	\$ 2,873,264

See accompanying notes to financial statements.

## NOTES TO FINANCIAL STATEMENTS

### Note 1 - Accounting Policies

#### Basis of Presentation

BioCryst Pharmaceuticals, Inc. (the "Company") is a pharmaceutical company using structure-based drug design to discover and design novel, small-molecule pharmaceutical products for the treatment of immunological and infectious diseases and disorders. The Company has three research projects, of which only one is in clinical trials. While the prospects for a project may increase as the project advances to the next stage of development, a project can be terminated at any stage of development. Until the Company generates revenues from either a research project or an approved product, its ability to continue research and development is dependent upon its ability to raise funds. The Company relies on sole suppliers to manufacture its BCX-34 compound for clinical trials and is evaluating supply sources for commercial production.

#### Net Loss Per Share

Net loss per share is computed using the weighted average number of shares of common stock outstanding. Common equivalent shares from convertible subordinated debt, convertible preferred stock, unused stock awards and unexercised stock options and warrants are excluded from the computation as their effect is anti-dilutive, except that, pursuant to requirements of the Securities and Exchange Commission, common and common equivalent shares issued at a price substantially below the anticipated public stock offering price during the

12-month period prior to the Company's initial public offering in March 1994 have been included in the calculation as if they were outstanding for all periods presented (using the treasury method and the public offering price).

#### Securities Held-to-Maturity

The Company is required to classify debt and equity securities as held-to-maturity, available-for-sale or trading. The appropriateness of each classification is reassessed at each reporting date. The only dispositions were maturities of securities held to maturity. At December 31, 1995, securities held-to-maturity, all current, consisted of \$2,714,385 of U.S. Treasury and Agency securities and \$2,564,691 of high-grade domestic corporate debt carried at amortized cost. The amortized cost of these securities at December 31, 1995 approximated market value.

#### Furniture and Equipment

Furniture and equipment are recorded at cost. Depreciation is computed using the straight-line method with estimated useful lives of five and seven years. Leased laboratory equipment is amortized over the lease lives of three and five years. Leasehold improvements are amortized over the remaining lease period.

#### Income Taxes

The liability method is used in accounting for income taxes in accordance with Statement of Financial Accounting Standards No. 109 ("Statement No. 109"). 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.

#### Revenue Recognition

Research and development revenue on cost-reimbursement agreements is recognized as expenses are incurred, up to contractual limits. Research and development and option payments are recognized as revenue when irrevocably received, and payments received which are related to future performance are deferred and taken into income as earned over a specified future performance period.

#### Statements of Cash Flows

For purposes of the statements of cash flows, the Company considers cash equivalents to be all cash held in money market accounts or investments in debt instruments with maturities of three months or less at the time of purchase.

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#### Stock-Based Compensation

The Company accounts for stock-based compensation under Accounting Principles Board Opinion No. 25, Accounting for Stock Issued to Employees (APB Opinion No. 25). Under APB No. 25, the Company's stock option and employee stock purchase plans qualify as noncompensatory plans. Consequently, no compensation expense is recognized.

#### Use of Estimates

Management is required to make estimates and assumptions that affect the amounts reported in the financial statements. Actual results could differ from those estimates.

#### Reclassifications

The 1994 financial statements have been reclassified to conform to the 1995 financial statements. The changes had no effect on the results of operations previously reported.

#### Note 2 - Furniture and Equipment

Furniture and equipment consisted of the following at December 31:

1995

1994

Furniture and fixtures	----- \$	----- \$
Office equipment	78,560	61,845
Laboratory equipment	197,389	128,936
Leased laboratory equipment	765,873	639,225
Leasehold improvements	1,220,778	1,670,651
	802,987	783,122
	-----	-----
	3,065,587	3,283,779
Less accumulated depreciation and amortization	1,702,804	1,598,656
	-----	-----
Furniture and equipment, net	\$1,362,783	\$1,685,123
	=====	=====

Statement of Financial Accounting Standards No. 121 ("Statement No. 121"), Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to be Disposed Of, was issued in March 1995 effective for fiscal years beginning after December 15, 1995. The Company does not anticipate having to recognize any significant impairment losses when Statement No. 121 is adopted in 1996.

#### Note 3 - Line of Credit

The Company had an unused line of credit of \$500,000 at December 31, 1995.

#### Note 4 - Concentration of Credit and Market Risk

The Company invests its excess cash principally in marketable securities from a diversified portfolio of institutions with strong credit ratings and in U.S. government and agency bills and notes, and by policy, limits the amount of credit exposure at any one institution. These investments are generally not collateralized and primarily mature within one year. The Company has not realized any losses from such investments. The Company has one primary bank in which it keeps funds in excess of the amounts insured by the Federal Deposit Insurance Corporation. Approximately \$4,868,045 of the cash is invested in the Fidelity Institution Cash Portfolio, which invests in treasury notes and repurchase agreements. The Fidelity Institution Cash Portfolio is not insured.

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#### Note 5 - Long-term Debt

Long-term debt consisted of the following at December 31:

	1995	1994
	-----	-----
Installment note, payable \$2,757 monthly, including interest at 12.9% through May 1997	\$47,342	\$72,758
Less current maturities	28,782	25,416
	-----	-----
Long-term debt, non-current portion	\$18,560	\$47,342
	=====	=====

The installment note is secured by equipment with an original value of \$171,200 and a carrying value of \$14,300 at December 31, 1995. Annual maturities of long-term debt are \$28,782 in 1996 and \$18,560 in 1997. The Company paid \$144,115, \$215,985 and \$132,484 in interest on debt and lease obligations for the years ended December 31, 1995, 1994 and 1993, respectively.

#### Note 6 - Leases

The Company entered into several capital lease obligations totaling \$1,324,653 in 1992 and \$345,998 in 1993 under agreements to obtain laboratory and office equipment. The leases have terms ranging from 36 to 60 months and contain renewal options. Assets under capital leases are capitalized using interest rates appropriate at the inception of each lease.

Certain capital lease obligations noted above were sale leaseback transactions. Equipment having a book value of \$826,720 and \$267,497 in 1992 and 1993, respectively, were sold for \$776,720 and \$242,828 in 1992 and 1993, respectively. The losses, principally representing sales taxes, have been deferred and are being amortized over the 60-month lease term.

	Capital Leases	Operating Leases
1996	\$341,679	\$190,068
1997	337,419	164,658
1998	162,642	144,072
1999		148,395
2000		37,371
	-----	-----
Total minimum lease payments	841,740	\$684,564
		=====
Less amounts representing interest	318,144	
	-----	
Present value of future minimum lease payments (including current portion of \$241,745)	\$523,596	
	=====	

Rent expense for operating leases was \$183,522, \$151,914 and \$95,343 in 1995, 1994 and 1993, respectively.

#### Note 7 - Income Taxes

The Company has not had taxable income since incorporation and, therefore, has not paid any income tax. Deferred tax assets of approximately \$11,250,000 and \$7,100,000 at December 31, 1995 and 1994, respectively, have been recognized principally for the net operating loss and research and development credit carryforwards and have been reduced by a valuation allowance of \$11,250,000 and \$7,100,000 at December 31, 1995 and 1994, respectively, which will remain until it is more likely than not that the related tax benefits will be realized.

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At December 31, 1995, the Company had net operating loss and research and development credit carryforwards of approximately \$25,600,000 and \$1,400,000, respectively, which will expire in 2005 through 2010. Use of the net operating losses and research and development credits will be subject to a substantial annual limitation due to the ownership provisions of the Tax Reform Act of 1986. The annual limitation is expected to result in the expiration of a portion of net operating losses and credits before utilization, which has been considered by the Company in its computations under Statement No. 109. Additional sales of the Company's equity securities may result in further annual limitations on the use of operating loss carryforwards and research and development credit carryforwards against taxable income in future years.

#### Note 8 - Stockholders' Equity

The Company was incorporated on November 17, 1989 as a Nevada corporation. On December 29, 1989 it exchanged 384,901 shares of its common stock and 33,350 shares of its 8% Cumulative Convertible Preferred Stock, Series 1989 for the predecessor partnership interests of the general partner and limited partners. The partnership was dissolved as of January 15, 1990 and its assets and liabilities were transferred to the Company in an exchange accounted for in a manner similar to a pooling of interests. In 1991, the Company formed a wholly-owned subsidiary, BioCryst Pharmaceuticals, Inc., a Delaware corporation; thereafter the Company was merged into BioCryst Pharmaceuticals, Inc., the surviving corporation.

#### Warrants

As part of financing arrangements, the Company has, at certain times, issued warrants to purchase 1,314,341 shares of the Company's common stock at no less than its estimated fair value at the date of grant. In return for their guarantees of an expired line of credit, three directors each received warrants (included in the 1,314,341 warrants) to purchase 49,400 shares of common stock at \$6.00 per share. All warrants are exercisable at various five-year periods through 1998. In lieu of a cash exercise, the warrant holder may elect a net issue exercise. Under a net issue exercise, the shares to be issued are equal to the product of (a) the number of shares of common stock purchasable under the warrant being exercised, and (b) the fair market value of one share of common stock minus the exercise price divided by (c) the fair market value of one share of common stock. At December 31, 1995 and 1994, 1,314,341 shares of the Company's common stock were reserved for issuance under warrant agreements and the weighted average per share exercise price was \$4.95 on



those dates. Nowarrants have been exercised as of December 31, 1995.

#### Options

In November 1991, the Board of Directors adopted the 1991 Stock Option Plan (the "Plan") for key employees and consultants of the Company and reserved 500,000 shares of common stock for the Plan. The Plan was approved by the stockholders on December 19, 1991. The term of the Plan is for ten years and includes both incentive stock options and non-statutory options. The option price for the incentive stock options shall not be less than the fair market value of common stock on the grant date. The option price per share for non-statutory stock options may not be less than 85% of the fair market value of common stock on the date of grant. The options generally vest 25% after one year and monthly thereafter on a pro rata basis over the next three years until fully vested after four years.

There are 3,378,886 shares reserved for future issuance for the options and warrants discussed above and the Stock Purchase Plan discussed in Note 9.

The stockholders on April 16, 1993 and on March 1, 1994 (approving the Board of Directors' action of December 1993) authorized an amended and restated 1991 Stock Option Plan and approved an additional 1,000,000 shares of common stock for issuance (the "Amended Plan"). The Amended Plan includes an increase of common stock reserved for issuance to 1,500,000 shares and establishes an automatic option grant program. The automatic option grant program grants options to new non-employee Board members to purchase 25,000 shares of common stock at an exercise price of the fair market value at the grant date for a maximum of ten years and is subject to vesting restrictions and early termination upon the optionee's cessation of Board service. The vesting and exercise provisions of the options issued under the Amended Plan are subject to acceleration, under certain circumstances, upon the occurrence of a hostile tender offer for more than 50% of the outstanding stock of the Company or if the Company is acquired. On May 29,

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1995, the stockholders approved extending the automatic option grant to cover non-employee Board members not previously eligible for an automatic grant and approved an additional 500,000 shares of common stock for issuance, increasing the common stock reserved for issuance to 2,000,000 shares. The following is an analysis of stock options for the three years ending December 31, 1995:

	Options Available -----	Options Outstanding -----	Average Exercise Price -----
Balance December 31, 1992	148,862	351,138	\$2.19
Option plan amended	1,000,000		
Options granted	(610,915)	610,915	5.37
Options exercised		(8,750)	2.00
Options canceled	6,906	(6,906)	2.39
	-----	-----	
Balance December 31, 1993	544,853	946,397	4.24
Options granted	(515,850)	515,850	4.72
Options exercised		(99,540)	2.01
Options canceled	58,532	(58,532)	5.79
	-----	-----	
Balance December 31, 1994	87,535	1,304,175	4.53
Option plan amended	500,000		
Options granted	(384,800)	384,800	8.57
Options exercised		(13,834)	3.66
Options canceled	45,079	(45,079)	4.63
	-----	-----	
Balance December 31, 1995	247,814 =====	1,630,062 =====	5.49

#### Note 9 - Employee Benefit Plan

On January 1, 1991, the Company adopted an employee retirement plan (the "401(k) Plan") under Section 401(k) of the Internal Revenue Code covering all employees. Employee contributions may be made to the 401(k) Plan up to limits established by the Internal Revenue Service. Company matching contributions may be made at

the discretion of the Board of Directors. The Company did not make a contribution to the 401(k) Plan during the years ended December 31, 1995 and 1994. The Company made a contribution of \$10,000 in 1993.

On May 29, 1995, the stockholders approved an employee stock purchase plan (the "Stock Purchase Plan") effective February 1, 1995. The Company has reserved 200,000 shares of common stock under the Stock Purchase Plan. Eligible employees may authorize up to 15% of their salary to purchase common stock at the lower of 85% of the beginning or 85% of the ending price during the six-month purchase intervals. No more than 3,000 shares may be purchased by any one employee at the six-month purchase dates and no employee may purchase stock having a fair market value at the commencement date of \$25,000 or more in any one calendar year. On July 31, 1995, 13,331 shares of common stock were purchased under the Stock Purchase Plan at a price of \$4.94 per share.

Note 10 - Collaborative and Other Research and Development Contracts

The Company granted Ciba-Geigy ("Ciba") an option for \$100,000 in February 1990 to acquire exclusive licenses to a class of inhibitors arising from research performed by the Company by February 1991. The option was exercised on April 15, 1993 and a \$500,000 fee was paid to the Company in June 1993. Milestone payments are due upon approval of a new drug application. The Company will also receive a royalty based upon a percentage of sales of any resultant products. Up to \$300,000 of the initial fee received is refundable if sales of any resultant products are below specified levels.

Prior to 1994, the Company received funding for three Phase I Small Business Innovation Research Program (the "SBIR") grants with the National Institutes of Health (the "NIH") for \$50,000 each. The Company was awarded a Phase II SBIR grant for factor D from the NIH in February 1994. The Phase II SBIR grant is for \$500,000 over a two-year period.

In 1990, the Company entered into several contracts with The University of Alabama at Birmingham ("UAB") to perform research for the Company for an aggregate amount of approximately \$188,000, which has been paid as of December 31, 1993. On November 7, 1991, the Company entered into a joint research and license agreement with UAB. UAB will perform specific research on factor D for the Company for a period of approximately three years in return for research and license fees. The agreement was replaced by a new agreement on July 18, 1995 granting the Company a worldwide license in exchange for funding UAB research in the amount of \$188,000 annually and sharing any royalties or sublicense fees arising from the joint research. In 1995, 1994 and 1993, the Company expensed \$68,638, \$85,456 and \$85,456 respectively, under the original agreement and expensed \$47,000 in 1995 under the new agreement. The Company is required to expend \$1,000,000 on the project under the new agreement over a three-year period in order to maintain its exclusive worldwide license. On November 17, 1994, the Company entered into another agreement for a joint research and license agreement on influenza neuraminidase granting the Company a worldwide license. Under this agreement, the Company funds UAB research in the amount of \$300,000 annually and UAB shares any royalties or sublicense fees arising from the joint research. Under the agreement, \$300,000 was expensed in 1995 and no amounts were expensed in 1994. The Company is required to expend \$6,000,000 on the project over a three-year period in order to maintain its exclusive worldwide license.

Note 11 - Quarterly Financial Information (Unaudited)  
(In thousands, except per share)

	First	Second	Third	Fourth
	-----	-----	-----	-----
1995 Quarters:				
Revenues	\$ 157	\$ 223	\$ 265	\$ 240
Net loss	(2,908)	(1,584)	(1,915)	(2,169)
Net loss per share	(.37)	(.18)	(.20)	(.23)
1994 Quarters:				
Revenues	\$ 93	\$ 188	\$ 245	208
Net loss	(1,564)	(1,866)	(1,633)	(1,875)
Net loss per share	(.35)	(.25)	(.22)	(.24)

Note 12 - Litigation

The Company previously granted an option to license one PNP inhibitor to Warner-Lambert on terms and conditions to be negotiated. That option is in dispute and the Company filed a complaint for a declaratory judgment to resolve the dispute on February 6, 1995. Warner-Lambert has counter-claimed, alleging breach of the option and seeking unspecified compensatory, consequential and incidental damages and lost profits. The Company believes that the conditions precedent to the exercise of Warner-Lambert's option have not been satisfied, that the option has expired, and that Warner-Lambert's breach of contract allegations lack merit. The Company believes that it has complied with its obligations and intends to continue to vigorously pursue this action. While there can be no assurances as to the outcome, the Company believes that the ultimate outcome will not have an adverse impact on the Company's financial position.

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#### REPORT OF INDEPENDENT AUDITORS

The Board of Directors  
BioCryst Pharmaceuticals, Inc.

We have audited the accompanying balance sheets of BioCryst Pharmaceuticals, Inc. as of December 31, 1995 and 1994, and the related statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 1995. 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 generally accepted auditing standards. 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 BioCryst Pharmaceuticals, Inc. at December 31, 1995 and 1994 and the results of its operations and its cash flows for each of the three years in the period ended December 31, 1995, in conformity with generally accepted accounting principles.

/s/ Ernst & Young LLP

Birmingham, Alabama  
January 24, 1996

#### ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

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#### PART III

#### ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

The directors and executive officers of the Company are as follows:

Name	Age	Position(s) with the Company
Charles E. Bugg, Ph.D.	54	Chairman, President, Chief Executive Officer and Director
John A. Montgomery, Ph.D.	71	Executive Vice President, Secretary, Chief Scientific Officer and Director
Ronald E. Gray	55	Chief Financial Officer, Assistant

		Secretary and Treasurer
John L. Higgins	25	Vice President, Corporate Development
William W. Featheringill (1) (2)	53	Director
Edwin A. Gee, Ph.D. (1) (2)	76	Director
Zola P. Horovitz, Ph.D.	61	Director
John Pappajohn (1)	67	Director
Lindsay A. Rosenwald, M.D.	40	Director
Joseph H. Sherrill, Jr.	54	Director
William M. Spencer, III (1) (2)	75	Director
Randolph C. Steer, M.D., Ph.D. (2)	46	Director

(1) Member of the Compensation Committee ("Compensation Committee").

(2) Member of the Audit Committee ("Audit Committee").

Charles E. Bugg, Ph.D. was named Chairman of the Board, Chief Executive Officer and Director in November 1993, and named President in early 1995. Prior to joining the Company, Dr. Bugg had served as the Director of the Center for Macromolecular Crystallography, the Associate Director of the Comprehensive Cancer Center and a Professor of Biochemistry at UAB since 1975. He was a Founder of BioCryst and served as the Company's first Chief Executive Officer from 1987-1988 while on a sabbatical from UAB. Dr. Bugg also served as Chairman of the Company's Scientific Advisory Board from January 1986 to November 1993. He is Chairman of the U.S. National Committee for Crystallography under the National Research Council; past president of the American Crystallographic Association; and Editor-in-Chief of Acta Crystallographica, a set of journals published by the International Union of Crystallography. He also continues to hold the position of Professor Emeritus in Biochemistry and Molecular Genetics at UAB.

John A. Montgomery, Ph.D. has been a Director since November 1989 and has been Executive Vice President, Secretary and Chief Scientific Officer since joining the Company in February 1990. Dr. Montgomery was a Founder of BioCryst. Prior to joining the Company, Dr. Montgomery served as Senior Vice President of Southern Research Institute ("SRI") of Birmingham from January 1981 to February 1990. Dr. Montgomery has extensive experience in the area of discovery and development of novel pharmaceutical products and is widely published. He continues to hold the position of Distinguished Scientist at SRI, a position he has held since February 1990.

Ronald E. Gray joined BioCryst in January 1993 as Chief Financial Officer. In 1994, Mr. Gray received the additional title of Treasurer and Assistant Secretary. Prior to joining BioCryst, from June 1992 to September 1992, Mr. Gray was Chief Financial Officer of The ACB Companies, a collection agency. From July 1988 to March 1992, Mr. Gray was Chief Financial Officer and Secretary of Image Data Corporation, a medical imaging company. He was Vice President of Finance, Secretary and Treasurer of CyCare Systems, Inc., a health care information processing company, from September 1974 to April 1988.

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John L. Higgins joined BioCryst in August 1994 as Director, Corporate Development. In July 1995 he was promoted to Vice President, Corporate Development. From July 1992 to July 1994, Mr. Higgins was a member of the health care banking team of Dillon, Read & Co. Inc., an investment banking firm. While at Dillon Read, he focused on financing and advisory assignments for biotechnology and managed care companies. Mr. Higgins is a member of Colgate University's Board of Trustees. From August 1988 to May 1992 he attended Colgate University and graduated with an A.B. in economics in 1992.

William W. Featheringill was elected a Director in May 1995. Mr. Featheringill was Chairman and Chief Executive Officer of MACESS Corporation, which designs and installs paperless data management systems for the managed care industry, from 1988 to November 1995. MACESS Corporation merged with Sungard Data Systems in late 1995. From 1985 to June 1994, Mr. Featheringill was the developer, Chairman and Chief Executive Officer of Complete Health Services, Inc., a health maintenance organization which grew, under his direction, to become one of the largest HMOs in the southeastern United States. Complete Health Services, Inc. was acquired by United HealthCare Corporation in June 1994. Mr. Featheringill also serves as President and Director of Private Capital Corporation, a venture capital management company, since 1975 and serves as a member of the Board of Directors of Citation Corporation.

Edwin A. Gee, Ph.D. was elected a Director in August 1993. Dr. Gee has been active as an executive in biotechnology, pharmaceutical and specialty chemical companies since 1970. He serves as the Chairman of Oncogene Science, one of the leading biotechnology companies for the diagnosis and treatment of cancer. He served as President, Chairman of the Board and Chief Executive Officer of International Paper Company from 1978 until his retirement in 1985. Prior to 1978, Dr. Gee was a Senior Vice President, member of the Executive Committee and a Director of E.I. du Pont de Nemours and Company.

Zola P. Horovitz, Ph.D. was elected a Director in August 1994. Dr. Horovitz spent 36 years with the Squibb Institute for Medical Research and Bristol-Myers Squibb Pharmaceutical Research Institute in Princeton, serving as Vice President of Business Development and Planning at the time of his retirement in 1994. He also serves as a member of the Board of Directors of InfoMed Holdings, Inc., Procept Corporation, Diacrin, Inc., Magainin Pharmaceuticals, Inc. and Synaptic Pharmaceutical Corp.

John Pappajohn has been a Director of the Company since December 1991. Since 1969, Mr. Pappajohn has been the sole owner of Pappajohn Capital Resources, a venture capital fund, and President of Equity Dynamics, Inc., a financial consulting firm in Des Moines, Iowa. Mr. Pappajohn also serves as a Director of Core, Inc., Drug Screening Systems, Inc., Fuisz Technologies, Inc., OncorMed, Inc., PACE Health Systems, Inc., and United Systems Technologies, Inc.

Lindsay A. Rosenwald, M.D. has been a Director of the Company since December 1991. He is a founder of several biopharmaceutical companies, including Neose Technologies, Inc. and Interneuron Pharmaceuticals, Inc. In August 1991, Dr. Rosenwald founded the Castle Group, Ltd., a New York-based venture capital and merchant banking firm, and in March 1993 he founded Paramount Capital, Inc., an investment bank specializing in the health sciences industry. In June 1994, Dr. Rosenwald founded Aries Financial Services, Inc., a money management firm, specializing in the health sciences industry. Dr. Rosenwald served as Managing Director of Corporate Finance at the investment banking firm of D.H. Blair & Co., Inc. from June 1987 to February 1992, and as Senior Securities analyst at the investment banking firm of Ladenburg, Thalmann & Co., Inc. from September 1986 to June 1987. Dr. Rosenwald is also Chairman of the Board of Directors of Interneuron Pharmaceuticals, Inc., a director of Sparta Pharmaceuticals, Inc., Atlantic Pharmaceuticals, Inc., Ansan, Inc., Xenometrix, Inc., Neose Technologies, Inc., Titan Pharmaceuticals, Inc. and Boston Life Sciences, Inc.

Joseph H. Sherrill, Jr. was elected a Director in May 1995. Mr. Sherrill served as President of R.J. Reynolds ("RJR") Asia Pacific, based in Hong Kong, where he oversaw RJR operations across Asia, including licensing, joint ventures and a full line of operating companies from August 1989 to retirement in October 1994. Prior management positions with RJR include Senior Vice President of Marketing for R.J. Reynolds International, President and Chief Operating Officer of R.J. Reynolds Tabacos de Brasil, and President and General Manager of R.J. Reynolds Puerto Rico. Mr. Sherrill also serves as a member of the Board of Directors of Savers Life Insurance Company.

William M. Spencer, III has been a Director of the Company since its inception. Mr. Spencer is also a private investor in Birmingham, Alabama. He served as Chairman of the Board of BioCryst from its founding in 1986 until April 1992. He

co-founded and operated Motion Industries from 1946 through its merger into Genuine Parts Company in 1976. He has founded several businesses and serves on the Board of Directors of numerous private corporations.

Randolph C. Steer, M.D., Ph.D. was elected a Director in February 1993. Dr. Steer has been active as a consultant to biotechnology and pharmaceutical companies since 1989. From April 1985 to March 1989, he served as the Chairman, and from 1988 to 1989, he served as the President and Chief Executive Officer of, Advanced Therapeutics Communications International, Inc., a drug regulatory consulting group. Prior to 1985, he had executive-level industry experience at both Ciba and at Marion Laboratories, Inc. (now a division of Marion Merrell Dow Inc.) where he served as Medical Director and Associate Director, Medical Affairs, respectively. Dr. Steer serves on the Board of Directors of Techne Corporation.

In accordance with the terms of the Company's Composite Certificate of

Incorporation ("Certificate of Incorporation"), the Board of Directors has been divided into three classes with members of each class holding office for staggered three-year terms. Mr. Pappajohn's and Dr. Rosenwald's terms expire at the 1996 annual meeting of stockholders, Dr. Horovitz's, Mr. Spencer's and Dr. Steer's terms expire at the 1997 annual meeting, and Dr. Bugg's, Dr. Montgomery's and Dr. Gee's terms expire at the 1998 annual meeting (in all cases subject to the election and qualification of their successors or to their earlier death, resignation or removal). Mr. Featheringill and Mr. Sherrill were named Directors in May 1995 and have been nominated for election at the 1996 annual meeting of stockholders for terms expiring in 1999. At each annual stockholder meeting commencing with the 1996 annual meeting, the successors to the Directors whose terms expire are elected to serve from the time of their election and qualification until the third annual meeting of stockholders following their election and until a successor has been duly elected and qualified. The provisions of the Company's Certificate of Incorporation governing the staggered Director election procedure can be amended only by a shareholder's vote of at least 75% of the eligible voting securities. There are no family relationships among any of the directors and executive officers of the Company.

The Company has an Audit Committee, consisting of Messrs. Featheringill, Gee, Pappajohn and Spencer, which is responsible for the review of internal accounting controls, financial reporting and related matters. The Audit Committee also recommends to the Board the independent accountants selected to be the Company's auditors and reviews the audit plan, financial statements and audit results.

The Company also has a Compensation Committee consisting of Messrs. Featheringill, Gee, Spencer and Steer. The Compensation Committee is responsible for the annual review of officer compensation and other incentive programs and is authorized to award options under the Company's 1991 Stock Option Plan.

ITEM 11. EXECUTIVE COMPENSATION

The following table ("Summary Compensation Table") sets forth the annual and long-term compensation paid by the Company during the 1995, 1994 and 1993 fiscal years to the Company's Chief Executive Officer and each of the Company's four other most highly compensated executive officers whose annual salary and bonus for the 1995 fiscal year exceeded \$100,000 (collectively the "Named Executive Officers"):

Name and Principal Position	Year	Annual Compensation			Long-term Compensation
		Salary	Bonus	Other Annual Compensation	Awards-Securities Underlying Options
Charles E. Bugg, Ph.D. Chairman, President and Chief Executive Officer	1995	\$207,000	\$50,000(1)	0	100,000
	1994	200,000	50,000(1)	0	100,000
	1993	22,500(2)	0	0	200,000
John A. Montgomery, Ph.D. Executive Vice President, Secretary and Chief Scientific Officer	1995	130,008	0	0	11,000
	1994	109,833	0	0	11,000
	1993	86,268	0	0	40,000
William J. Cook, M.D., Ph.D. Senior Vice President, Research & Development and Medical Director	1995	179,032	0	0	0
	1994	58,333(3)	0	0	72,500
	1993	0	0	0	0
John L. Higgins Vice President, Corporate Development	1995	103,728	0	0	50,000
	1994	22,046(4)	0	1,050(5)	23,500
	1993	0	0	0	0

(1) Paid pursuant to an Employment Agreement dated November 19, 1993 between the Company and Dr. Bugg. See "Executive Compensation - Employment Agreement."

(2) Paid pursuant to a Consulting Agreement dated May 1, 1988, as amended, between the Company and Dr. Bugg.

(3) Dr. Cook joined BioCryst in September 1994 and resigned January 1, 1996.

(4) Mr. Higgins joined BioCryst in August 1994 and became an executive officer in July 1995.

(5) The other annual compensation represents reimbursed moving expenses.

#### Employment Agreement

Charles E. Bugg, Ph.D. entered into an employment agreement with the Company on November 19, 1993 (the "Agreement"). Under the terms of the Agreement, Dr. Bugg will serve as Chairman of the Board of Directors and Chief Executive Officer of the Company. Dr. Bugg will receive annual compensation of \$200,000 and a discretionary bonus of \$50,000. The Board may, in its discretion, grant other cash or stock bonuses to Dr. Bugg as an award or incentive. Dr. Bugg is also entitled to all employee benefits generally made available to executive officers. Dr. Bugg may, if he desires, also hold positions at The University of Alabama at Birmingham, provided that he does not devote more than ten percent of his time to such activities. The term of the Agreement is for three years unless terminated (i) by the Company for cause or (ii) upon the permanent disability of Dr. Bugg.

Pursuant to the Agreement, Dr. Bugg received in December 1993 an option to purchase 200,000 shares of Common Stock of the Company at \$6.00 per share under the Company's 1991 Stock Option Plan, which became exercisable

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upon the consummation of the Company's initial public offering in March 1994. Dr. Bugg will also receive, on the last day of each year during the term of the Agreement, an additional option to purchase between 25,000 and 100,000 shares of Common Stock of the Company under the Company's 1991 Stock Option Plan. The exact number of shares will be determined by the plan administrator based on Dr. Bugg's performance and the results of operations of the Company during such year. Dr. Bugg received an option to purchase 100,000 shares of common stock at the end of each of 1994 and 1995.

Dr. Bugg will receive an additional stock option to purchase 100,000 shares of Common Stock under the Company's 1991 Stock Option Plan upon BioCryst's submission to the FDA of any new drug application and another additional stock option to purchase 100,000 shares of Common Stock under the Company's 1991 Stock Option Plan upon the final approval by the FDA of each such new drug application. The exercise price shall be the fair market value of the Company's Common Stock on the date such additional stock option is granted. These additional stock options will vest 25% one year after the date of issuance and the remaining 75% will vest at the rate of 1/48 per month thereafter.

The options may be exercised immediately in the event of a merger or acquisition of the Company. The options may be exercised within 24 months of Dr. Bugg's death or permanent disability. In the event Dr. Bugg's employment is terminated for cause he may exercise the options within three months of the date of such termination to the extent such options were exercisable immediately prior to such termination. In the event Dr. Bugg's employment is terminated for a reason other than cause, death or permanent disability, the options then outstanding shall become immediately exercisable in full.

All options granted to Dr. Bugg pursuant to the Agreement are intended to qualify as incentive stock options as defined in Section 422 of the Internal Revenue Code of 1986, as amended, except to the extent the portion of such options which become exercisable in any year have an aggregate exercise price in excess of \$100,000. All options shall expire no later than ten years from the date of grant.

#### Option Grants in 1995

The following table shows, with respect to the Company's Named Executive Officers, certain information with respect to option grants in 1995. All of the grants were made under the Company's 1991 Stock Option Plan. No stock appreciation rights were granted during such year.

Potential Realizable  
Value at Assumed

Name	Number of Securities Underlying Options Granted	% of Total Options Granted	Exercise Price Per Share	Expiration Date	Annual Rates of Stock Price Appreciation for Option Term(1)	
					5%	10%
Charles E. Bugg, Ph.D.	100,000	26.0%	\$ 8.88	12/18/2005	\$558,144	\$1,414,446
John A. Montgomery, Ph.D.	11,000	2.9	8.88	12/18/2005	61,396	155,589
William J. Cook, M.D., Ph.D.	0	0				
John L. Higgins	5,000	1.3	6.38	04/04/2005	20,046	50,801
	26,000	6.8	8.00	06/20/2005	130,810	331,498
	14,000	3.6	10.13	07/04/2005	89,146	225,913
	5,000	1.3	8.88	12/18/2005	27,907	70,722

(1) Amounts represent hypothetical gains that could be achieved for the respective options at the end of the ten-year option term. The assumed 5% and 10% rates of stock appreciation are mandated by rules of the Securities and Exchange Commission and do not represent the Company's estimate of the future market price of the Common Stock.

#### Aggregate Option Exercises in 1995 and Year-end Option Values

The following table shows, with respect to the Company's Named Executive Officers, the number and value of unexercised options held by the Named Executive Officers as of December 31, 1995. No stock appreciation rights were exercised during the 1995 fiscal year and no such rights were outstanding at the end of that year.

Name	Number of Securities Underlying Unexercised Options (1)		Values of Unexercised In-the-Money Options (2)	
	Exercisable	Unexercisable	Exercisable	Unexercisable
Charles E. Bugg, Ph.D.	262,500	175,000	\$ 1,037,500	\$ 384,375
John A. Montgomery, Ph.D.	60,250	39,250	349,594	107,281
William J. Cook, M.D., Ph.D.	23,854	48,646	118,346	241,967
John L. Higgins	6,875	66,625	34,297	131,141

(1) The Named Executive Officers did not exercise any stock options during 1995.

(2) Amounts reflect the net values of outstanding stock options computed as the difference between \$9.25 per share (the fair market value at December 31, 1995) and the exercise price therefor.

#### Director Compensation

Directors do not receive a fee for attending Board or committee meetings. Outside directors are reimbursed for expenses incurred in attending Board or committee meetings and while representing the Company in conducting certain business. Individuals who first become non-employee Board members on or after March 3, 1994, at the time of commencement of Board service, receive a grant of options to purchase up to 25,000 shares pursuant to the automatic option grant program under the Company's 1991 Stock Option Plan, and, under the Company's 1991 Stock Option Plan each non-employee director, including those persons presently serving as directors, will receive grants of options to purchase 25,000 additional shares of Common Stock every four years while they continue to serve as directors. All current outside directors of the Company have received options to purchase 25,000 shares of Common Stock. Dr. Horovitz and Dr. Steer also serve as consultants to the Company for a quarterly fee of \$4,000 each.

#### Compensation Committee Interlocks and Insider Participation

The Compensation Committee consists of Mr. Featheringill, Dr. Gee, Mr. Spencer



and Dr. Steer. Certain members of the Compensation Committee are parties to transactions with the Company. See "Item 13. Certain Relationships and Related Transactions."

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth information regarding beneficial ownership of the Company's Common Stock as of January 31, 1996 by (i) each director, (ii) each of the Named Executive Officers, (iii) all directors and executive officers of the Company as a group and (iv) each person known to the Company to be the beneficial owner of more than five percent of the Company's Common Stock:

Name and Address	Number of Common Shares Beneficially Owned(1)	Percentage of Outstanding Shares
William W. Featheringill 402 Office Park Drive Birmingham, Alabama 35223	1,000,000	10.5%
Lindsay A. Rosenwald, M.D. 375 Park Avenue, 15th Floor New York, New York 10152	740,934 (2)	7.4
John Pappajohn 2116 Financial Center Des Moines, Iowa 50309	735,295 (3)	7.3
Bernard B. Levine, M.D. 210 Riverside Drive New York, New York 10025	515,000	5.4
William M. Spencer, III	362,788 (4)	3.8
Charles E. Bugg, Ph.D.	334,241 (5)	3.4
Joseph H. Sherrill, Jr.	311,000 (6)	3.3
John A. Montgomery, Ph.D.	124,936 (7)	1.3
Randolph C. Steer, M.D., Ph.D.	38,542 (8)	*
William J. Cook, M.D., Ph.D.	26,267 (9)	*
Edwin A. Gee, Ph.D.	25,000 (8)	*
John L. Higgins	11,480 (10)	*
Zola P. Horovitz, Ph.D.	9,895 (8)	*
All executive officers and directors as a group (13 persons)	3,758,263 (11)	34.1

(\*) Less than one percent.

(1) Gives effect to the shares of Common Stock issuable within 60 days after January 31, 1996 upon the exercise of all options, warrants and other rights beneficially held by the indicated stockholder on that date.

(2) Includes 400,819 shares of Common Stock issuable upon exercise of certain common stock warrants, 9,895 shares issuable upon exercise of stock options and 3,125 shares which Dr. Rosenwald holds jointly with his spouse. Also includes 44,345 shares of Common Stock and warrants to purchase 49,000 shares held by Dr. Rosenwald's spouse individually and as custodian for their minor children, as to which Dr. Rosenwald disclaims beneficial ownership. Dr. Rosenwald has granted options to 10 individuals to purchase an aggregate of 60,293 shares of Common Stock held by him at purchase prices ranging from \$0.60 to \$7.20 per share.

(3) Includes 549,400 shares of Common Stock issuable upon exercise of common stock warrants and 9,895 shares issuable upon exercise of stock options. Also includes 100,000 shares of Common Stock held by Mr. Pappajohn's spouse. Mr. Pappajohn disclaims beneficial ownership of the 100,000 shares held by his

spouse.

(4) Includes 49,400 shares of Common Stock issuable upon exercise of certain common stock warrants, 9,895 shares issuable upon exercise of stock options and 10,000 shares held by Mr. Spencer's spouse. Mr. Spencer disclaims beneficial ownership of the 10,000 shares held by his spouse.

(5) Includes 268,749 shares issuable upon exercise of stock options.

(6) Includes 5,000 shares held by Mr. Sherrill's spouse. Mr. Sherrill disclaims beneficial ownership of the 5,000 shares held by his spouse.

(7) Includes 63,437 shares issuable upon exercise of stock options.

(8) Includes shares issuable upon exercise of stock options.

(9) Includes 24,270 shares issuable upon exercise of stock options and 100 shares held by Dr. Cook's daughter. Dr. Cook resigned January 1, 1996.

(10) Includes 8,344 shares issuable upon exercise of stock options and 1,000 shares held jointly with his spouse.

(11) See Notes (1) through (10).

#### ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

In May 1995, the Company sold an aggregate of 1,570,000 shares of Common Stock at a purchase price of \$5.50 per share to a group of investors including William W. Featheringill (1,000,000 shares) and Joseph H. Sherrill, Jr. (100,000 shares), Directors of the Company who were not Directors at the time of purchase, and Charles E. Bugg, Ph.D. (5,000 shares), William M. Spencer, III (100,000 shares) and John Pappajohn (20,000 shares), Directors of the Company.

Dr. Bugg, an executive officer and Director of the Company, is a Professor Emeritus of UAB and is paid an annual stipend of \$8,040 by UAB. The Company paid approximately \$808,000 to UAB in 1995 for conducting certain clinical trials, research and data analysis.

Dr. Montgomery, an executive officer and Director of the Company, is a former executive officer of the SRI. The Company paid approximately \$250,000 to SRI in 1995 for certain research, laboratory rental and supplies. Dr. Montgomery is currently a Distinguished Scientist at SRI and was paid approximately \$18,922 by SRI in 1995 for various consulting services unrelated to the services performed by SRI for the Company.

#### PART IV

#### ITEM 14. EXHIBITS, FINANCIAL STATEMENT SCHEDULES AND REPORTS ON FORM 8-K

##### (a) Financial Statements

	Page in Form 10-K
The following financial statements appear in Item 8 of this Form 10-K:	
Balance Sheets at December 31, 1995 and 1994	18
Statements of Operations for the years ended December 31, 1995, 1994 and 1993	19
Statements of Stockholders' Equity for the years ended December 31, 1995, 1994 and 1993	20
Statements of Cash Flows for the three ended December 31, 1995, 1994 and 1993	21
Notes to Financial Statements	22 to 27
Report of Independent Auditors	28

No financial statement schedules are included because the information is either provided in the financial statements or is not required under the related instructions or is inapplicable and such schedules therefore have been omitted.

(b) Reports on Form 8-K

None

(c) Exhibits

Number	Description
3.1	Composite Certificate of Incorporation of Registrant. Incorporated by reference to Exhibit 3.1 to the Company's Form 10-Q for the second quarter ending June 30, 1995 dated August 11, 1995.
3.2	Bylaws of Registrant. Incorporated by reference to Exhibit 3.1 to the Company's Form 10-Q for the second quarter ending June 30, 1995 dated August 11, 1995.
4.1	See Exhibits 3.1 and 3.2 for provisions of the Composite Certificate of Incorporation and Bylaws of the Registrant defining rights of holders of Common Stock of the Registrant.
10.1	Common Stock Purchase Warrant dated October 15, 1991 to purchase 500,000 shares of Common Stock issued to John Pappajohn. Incorporated by reference to Exhibit 10.6 to the Company's Form S-1 Registration Statement (Registration No. 33-73868).
10.2	Common Stock Purchase Warrant dated October 15, 1991 to purchase 500,000 shares of Common Stock issued to Lindsay Rosenwald. Incorporated by reference to Exhibit 10.7 to the Company's Form S-1 Registration Statement (Registration No. 33-73868).
10.3	1991 Stock Option Plan, as amended and restated. Incorporated by reference to Exhibit 99.1 to the Company's Form S-8 Registration Statement (Registration No. 33-95062).
10.4	Form of Notice of Stock Option Grant and Stock Option Agreement. Incorporated by reference to Exhibit 99.2 and 99.3 to the Company's Form S-8 Registration Statement (Registration No. 33-95062).

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Number	Description
10.5	Warehouse Lease dated January 17, 1992 between Principal Mutual Life Insurance Company and the Registrant. Incorporated by reference to Exhibit 10.21 to the Company's Form S-1 Registration Statement (Registration No. 33-73868).
10.6	Master Equipment Lease dated January 22, 1992 between Boston Financial & Equity Corporation and the Registrant. Incorporated by reference to Exhibit 10.22 to the Company's Form S-1 Registration Statement (Registration No. 33-73868).
10.7	Equipment Leases dated July 25, 1992, February 25, 1993, August 25, 1993, and November 25, 1993 between Ventana Leasing, Inc. and the Registrant. Incorporated by reference to Exhibit 10.23 to the Company's Form S-1 Registration Statement (Registration No. 33-73868).
10.8	Common Stock Purchase Warrants issued in connection with the issuance of Series A Convertible Preferred Stock. Incorporated by reference to Exhibit 10.32 to the Company's Form S-1 Registration Statement (Registration No. 33-73868).

- 10.9 Private Placement Agency Agreement dated July 1, 1993 between the Registrant and Paramount Capital, Inc., as amended. Incorporated by reference to Exhibit 10.33 to the Company's Form S-1 Registration Statement (Registration No. 33-73868).
- 10.10 Subscription and Preferred Stock Agreement and Confidential Investor Questionnaire among the Registrant and the purchasers of Series B Convertible Preferred Stock. Incorporated by reference to Exhibit 10.34 to the Company's Form S-1 Registration Statement (Registration No. 33-73868).
- 10.11 Fourth Amended and Restated Registration Rights Agreement among the Registrant and certain securityholders. Incorporated by reference to Exhibit 10.35 to the Company's Form S-1 Registration Statement (Registration No. 33-73868).
- 10.12 Common Stock Purchase Warrants issued in connection with the issuance of Series B Convertible Preferred Stock. Incorporated by reference to Exhibit 10.36 to the Company's Form S-1 Registration Statement (Registration No. 33-73868).
- 10.13 Common Stock Purchase Warrants dated December 7, 1993 to purchase 49,400 shares of Common Stock issued to each of John Pappajohn, Lindsay A. Rosenwald and William M. Spencer. Incorporated by reference to Exhibit 10.37 to the Company's Form S-1 Registration Statement (Registration No. 33-73868).
- 10.14 Employment Agreement dated November 19, 1993 between the Registrant and Charles E. Bugg, Ph.D. Incorporated by reference to Exhibit 10.38 to the Company's Form S-1 Registration Statement (Registration No. 33-73868).
- 10.15# License Agreement dated April 15, 1993 between Ciba-Geigy Corporation and the Registrant. Incorporated by reference to Exhibit 10.40 to the Company's Form S-1 Registration Statement (Registration No. 33-73868).
- 10.16 Stock Purchase Agreement dated September 21, 1994 between Registrant and Bernard B. Levine to purchase 515,000 shares of common stock. Incorporated by reference Exhibit 10.2 to the Company's Form 10-Q for the third quarter ending September 30, 1994 dated November 10, 1994.
- 10.17 Registration Rights Agreement dated September 21, 1994 between Registrant and Bernard B. Levine. Incorporated by reference Exhibit 10.3 to the Company's Form 10-Q for the third quarter ending September 30, 1994 dated November 10, 1994.
- 10.18 Employee Stock Purchase Plan. Incorporated by reference to Exhibit 99.4 to the Company's Form S-8 Registration Statement (Registration No. 33-95062).

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Number	Description
10.19	First Amendment to Lease Agreement between Registrant and Principal Mutual Life Insurance Company, Inc. for office/warehouse space. Incorporated by reference to Exhibit 10.21 to the Company's Form 10-K for the year ending December 31, 1994 dated March 28, 1995.
10.20	Form of Stock Purchase Agreement dated May 1995 between Registrant and various parties to purchase 1,570,000 shares of common stock. Incorporated by reference to Exhibit 10.22 to the Company's Form 10-Q for the second quarter ending June 30, 1995 dated August 11, 1995.
10.21	Form of Registration Rights Agreement dated May 1995 between Registrant and various parties. Incorporated by reference to Exhibit 10.23 to the Company's Form 10-Q for the second

quarter ending June 30, 1995 dated August 11, 1995.

23.1 Consent of Independent Auditors

27.1 Financial Data Schedule

- -----  
# Confidential treatment granted.

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SIGNATURES

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 in the City of Birmingham, State of Alabama, on this 24th day of September, 1996.

BIOCRYS T PHARMACEUTICALS, INC.

By: /s/Charles E. Bugg  
-----

Charles E. Bugg, Ph.D.  
Chairman and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934 this report has been signed by the following persons in the capacities indicated on September 24th, 1996:

Signature	Title(s)
/s/Charles E. Bugg ----- (Charles E. Bugg, Ph.D.)	Chairman, President, Chief Executive Officer and Director
/s/John A. Montgomery ----- (John A. Montgomery, Ph.D.)	Executive Vice President, Secretary, Chief Scientific Officer and Director
/s/Ronald E. Gray ----- (Ronald E. Gray)	Chief Financial Officer (Principal Financial and Accounting Officer)
/s/William W. Featheringill ----- (William W. Featheringill)	Director
/s/Edwin A. Gee ----- (Edwin A. Gee, Ph.D.)	Director
/s/Zola P. Horovitz ----- (Zola P. Horovitz, Ph.D.)	Director
_____ (Lindsay A. Rosenwald, M.D.)	Director
/s/William M. Spencer, III ----- (William M. Spencer, III)	Director
/s/Joseph H. Sherrill, Jr. ----- (Joseph H. Sherrill, Jr.)	Director
/s/Randolph C. Steer ----- (Randolph C. Steer, M.D., Ph.D.)	Director

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CONSENT OF INDEPENDENT AUDITORS

We consent to the incorporation by reference in the Registration Statements (Form S-8 No. 33-81110 and 33-95062) pertaining to the BioCryst Pharmaceuticals, Inc. 1991 Stock Option Plan of our report dated January 24, 1996, with respect to the financial statements of BioCryst Pharmaceuticals, Inc. included in the Annual Report (Form 10-K/A) for the year ended December 31, 1995.

/s/ Ernst & Young LLP

Birmingham, Alabama  
September 20, 1996

<ARTICLE> 5

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This schedule contains summary financial information extracted from the BioCryst Pharmaceuticals, Inc. Financial Statements, and is qualified in its entirety by reference to such financial statements.

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