

SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

AMENDMENT NO. 2  
TO  
FORM S-3

REGISTRATION STATEMENT  
UNDER THE SECURITIES ACT OF 1933

BIOCRIST PHARMACEUTICALS, INC.  
(Exact name of Registrant as specified in its charter)

DELAWARE  
(State or other jurisdiction  
of incorporation or organization)

62-1413174  
(I.R.S. Employer  
Identification Number)

2190 PARKWAY LAKE DRIVE, BIRMINGHAM, ALABAMA 35244  
(205) 444-4600  
(Address, including zip code, and telephone number, including area code,  
of Registrant's principal executive offices)

CHARLES E. BUGG, PH.D.  
CHAIRMAN, CHIEF EXECUTIVE OFFICER AND PRESIDENT  
BIOCRIST PHARMACEUTICALS, INC.  
2190 PARKWAY LAKE DRIVE  
BIRMINGHAM, ALABAMA 35244  
(205) 444-4600  
(Name, address, including zip code, and telephone number, including  
area code, of agent for service of process)

COPIES TO:

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APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO THE PUBLIC:  
As soon as practicable after the effective date of this Registration Statement.

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

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

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and

list the Securities Act registration statement number of earlier effective registration statement for the same offering. / /

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

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

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THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL FILE A FURTHER AMENDMENT WHICH SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(A) OF THE SECURITIES ACT OF 1933 OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE COMMISSION, ACTING PURSUANT TO SAID SECTION 8(A), MAY DETERMINE.  
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SUBJECT TO COMPLETION, DATED SEPTEMBER 24, 1996

PROSPECTUS

2,000,000 SHARES

[BIOCRYST PHARMACEUTICALS, INC. LOGO]

COMMON STOCK  
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All of the shares of Common Stock offered hereby are being sold by BioCryst Pharmaceuticals, Inc. ("BioCryst" or the "Company"). The Common Stock of the Company is listed on the Nasdaq National Market tier of The Nasdaq Stock MarketSM under the symbol "BCRX." On September 23, 1996, the last sale price of the Common Stock as reported by Nasdaq was \$12.375 per share.

THE COMMON STOCK OFFERED HEREBY INVOLVES A HIGH DEGREE OF RISK. SEE "RISK FACTORS" BEGINNING ON PAGE 5.  
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THESE SECURITIES HAVE NOT BEEN APPROVED OR DISAPPROVED BY THE SECURITIES AND EXCHANGE COMMISSION OR ANY STATE SECURITIES COMMISSION NOR HAS THE SECURITIES AND EXCHANGE COMMISSION OR ANY STATE SECURITIES COMMISSION PASSED UPON THE ACCURACY OR ADEQUACY OF THIS PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

[CAPTION]

	PRICE TO PUBLIC	UNDERWRITING DISCOUNTS AND COMMISSIONS (1)	PROCEEDS TO COMPANY (2)
Per Share	\$	\$	\$
Total(3)	\$	\$	\$

- (1) The Company has agreed to indemnify the Underwriters against certain liabilities, including liabilities under the Securities Act of 1933, as amended. See "Underwriting."
- (2) Before deducting expenses of the offering estimated at \$ payable by the Company.
- (3) The Company has granted the Underwriters a 30-day option to purchase up to 300,000 additional shares of Common Stock on the same terms as set forth above to cover over-allotments, if any. If the Underwriters exercise such option in full, the total Price to Public, Underwriting Discounts and Commissions and Proceeds to Company will be \$ , \$ and \$ , respectively. See "Underwriting."

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The shares of Common Stock are being offered by the several Underwriters named herein, subject to prior sale, when, as and if accepted by them and subject to certain conditions. It is expected that certificates for the shares of Common Stock offered hereby will be available for delivery on or about , 1996 at the offices of Smith Barney Inc., 333 West 34th Street, New York, New York 10001.

SMITH BARNEY INC.

NEEDHAM & COMPANY, INC.

, 1996

INFORMATION CONTAINED HEREIN IS SUBJECT TO COMPLETION OR AMENDMENT. A REGISTRATION STATEMENT RELATING TO THESE SECURITIES HAS BEEN FILED WITH THE SECURITIES AND EXCHANGE COMMISSION. THESE SECURITIES MAY NOT BE SOLD NOR MAY OFFERS TO BUY BE ACCEPTED PRIOR TO THE TIME THE REGISTRATION STATEMENT BECOMES EFFECTIVE. THIS PROSPECTUS SHALL NOT CONSTITUTE AN OFFER TO SELL OR THE SOLICITATION OF AN OFFER TO BUY NOR SHALL THERE BE ANY SALE OF THESE SECURITIES IN ANY STATE IN WHICH SUCH OFFER, SOLICITATION OR SALE WOULD BE UNLAWFUL PRIOR TO THE REGISTRATION OR QUALIFICATION UNDER THE SECURITIES LAWS OF ANY SUCH STATE.

CURRENT PRODUCT DEVELOPMENT STATUS

Drug Discovery    Preclinical    Phase I    Phase I/II    Phase II    Phase III

PNP Inhibitors (BCX-34)

CTCL            topical

                  oral

Psoriasis        topical

Atopic dermatitis

HIV

[CHART REFLECTING STATUS OF COMPANY'S  
PHARMACEUTICAL DEVELOPMENT PROJECTS]

Rheumatoid arthritis

Transplant rejection

Ophthalmic disorders

Influenza Neuraminidase  
Inhibitors

Complement Inhibitors

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IN CONNECTION WITH THIS OFFERING, THE UNDERWRITERS MAY OVER-ALLOT OR EFFECT TRANSACTIONS WHICH STABILIZE OR MAINTAIN THE MARKET PRICE OF THE COMMON STOCK OF THE COMPANY AT A LEVEL ABOVE THAT WHICH MIGHT OTHERWISE PREVAIL IN THE OPEN MARKET. SUCH TRANSACTIONS MAY BE EFFECTED ON THE NASDAQ NATIONAL MARKET, OR OTHERWISE. SUCH STABILIZING, IF COMMENCED, MAY BE DISCONTINUED AT ANY TIME.

IN CONNECTION WITH THIS OFFERING, THE UNDERWRITERS AND OTHER SELLING GROUP MEMBERS MAY ENGAGE IN PASSIVE MARKET MAKING TRANSACTIONS IN THE COMMON STOCK OF THE COMPANY ON NASDAQ IN

PROSPECTUS SUMMARY

The following summary is qualified in its entirety by the more detailed information and the financial statements and notes thereto appearing elsewhere in this Prospectus or incorporated herein by reference. Prospective investors should carefully consider the information set forth under the heading "Risk Factors."

THE COMPANY

BioCryst Pharmaceuticals, Inc. ("BioCryst" or the "Company") is an emerging 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 believes that structure-based drug design, by precisely designing compounds to fit the active site of target proteins, offers the potential for developing drugs for many indications that have improved efficacy and fewer side effects than currently marketed drugs for the same indications. The Company's development plan focuses on life threatening or significant clinical indications, including T-cell cancers, psoriasis, human immunodeficiency virus ("HIV") infection and influenza. The Company is conducting three clinical trials with its most advanced drug, BCX-34: a Phase III trial with a topical formulation for cutaneous T-cell lymphoma ("CTCL"), a Phase I/II trial with an oral formulation for CTCL and a Phase I/II trial with a topical formulation for atopic dermatitis. In addition, the Company expects to initiate by the end of 1996 (assuming satisfactory FDA reviews) a Phase III trial for the topical treatment of psoriasis, a Phase I/II trial for the oral treatment of psoriasis and a Phase I/II trial for the oral treatment of HIV infection. BioCryst has additional research projects underway to develop inhibitors of influenza neuraminidase, an enzyme believed to perform an essential role in the infectious cycle of flu, and enzymes involved in the complement cascade, which is implicated in several major inflammatory conditions. One of the elements of the Company's strategic plan is to leverage its clinical progress by entering into pharmaceutical collaborations with drug companies in major world markets. Recently, BioCryst entered into an exclusive license agreement with Torii Pharmaceutical Co., Ltd. ("Torii"), a Japanese pharmaceutical company, for the development and commercialization in Japan of BCX-34 and certain other purine nucleoside phosphorylase ("PNP") inhibitor compounds. PNP is an enzyme believed to be involved in T-cell proliferation.

BioCryst's lead drug program targets T-cell proliferative disorders, which arise when T-cells, immune system cells that 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. Additionally, the Company believes that by suppressing proliferation of the T-cell, the host to the HIV virus, it might be possible to treat HIV-infected patients. BioCryst has designed and synthesized several chemically distinct classes of compounds which inhibit PNP.

The Company has completed six Phase I clinical trials, three Phase I/II clinical trials and three 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 280 subjects, and no significant drug-related adverse side effects have been observed. The completed Phase II trials of topical BCX-34 were double-blinded, placebo-controlled and enrolled 30 CTCL patients and 130 psoriasis patients. A majority of the patients from the Phase II CTCL trial volunteered to roll over into an extended, open-label trial. In addition, the Company has initiated preclinical studies using an ophthalmic formulation of BCX-34 for potential use in treating uveitis and corneal transplant rejection.

BioCryst's objective is to be a leader in the use of structure-based drug design to develop clinically and commercially significant pharmaceutical products. The key elements of the Company's strategy include: (i) targeting immunological mechanisms to pursue multiple indications; (ii) utilizing advanced technologies to design traditional pharmaceuticals; (iii) pursuing a tiered clinical plan for BCX-34 and (iv) establishing additional research collaborations and strategic partnerships.

In May 1996, BioCryst entered into an exclusive license agreement with Torii of Tokyo, Japan to develop, manufacture and commercialize BCX-34 and certain

other PNP inhibitor compounds in Japan. Pursuant to the agreement, Torii has made an upfront license fee payment of \$1.5 million and purchased shares of Common Stock for \$1.5 million at a price of \$19.58 per share. The agreement further provides for potential milestone payments of up to \$19.0 million and royalties on future sales of licensed products in Japan. Torii has the right to develop BCX-34 and certain other PNP inhibitor compounds for three indications and may negotiate a license with BioCryst to develop the drug for additional indications.

THE OFFERING

Common Stock being offered..... 2,000,000 shares(1)  
Common Stock to be outstanding  
after the offering..... 12,837,237 shares(1) (2)  
Use of Proceeds..... Funding for research and product development  
programs and for general corporate purposes  
Nasdaq National Market symbol..... BCRX

SUMMARY FINANCIAL INFORMATION

	YEARS ENDED DECEMBER 31,					SIX MONTHS ENDED JUNE 30,	
	1991	1992	1993	1994	1995	1995	1996
STATEMENT OF OPERATIONS							
DATA:							
Total operating revenues.....	\$ 83,333	\$ 137,614	\$ 302,375	\$ 269,126	\$ 222,329	\$ 94,691	\$ 1,521,279
Operating expenses:							
Research and development.....	706,807	3,018,774	4,195,800	5,551,660	7,107,249	3,752,843	3,414,457
General and administrative.....	641,448	1,085,355	1,098,206	1,904,046	2,209,488	1,041,999	1,562,688
Total operating expenses.....	1,348,255	4,104,129	5,294,006	7,455,706	9,316,737	4,794,842	4,977,145
Interest income.....	28,622	47,468	60,629	464,690	662,259	285,544	387,977
Interest expense.....	(45,792)	(131,927)	(264,994)	(215,985)	(144,115)	(77,501)	(55,629)
Other income (expense), net.....	(17,170)	(84,459)	(204,365)	248,705	518,144	208,043	332,348
Net loss.....	\$ (1,282,092)	\$ (4,050,974)	\$ (5,195,996)	\$ (6,937,875)	\$ (8,576,264)	\$ (4,492,108)	\$ (3,123,518)
Net loss per share(3).....	\$ (1.50)	\$ (1.31)	\$ (1.55)	\$ (1.02)	\$ (.96)	\$ (.54)	\$ (.31)
Weighted average shares outstanding(3).....	855,573	3,100,888	3,352,364	6,787,203	8,905,099	8,305,857	10,095,953

AS OF JUNE 30, 1996

	ACTUAL	AS ADJUSTED (4)
BALANCE SHEET DATA:		
Cash, cash equivalents and securities held-to-maturity.....	\$ 17,813,084	\$ 43,363,084
Working capital.....	17,022,751	42,572,751
Total assets.....	19,667,319	45,217,319
Long-term debt and capital lease obligations, excluding current portion.....	148,112	148,112
Accumulated deficit.....	(33,190,911)	(33,190,911)
Total stockholders' equity.....	17,803,185	43,353,185

(1) Excludes up to 300,000 shares of Common Stock that may be sold by the Company pursuant to the Underwriters' over-allotment option. See "Underwriting."

(2) Based on shares outstanding on August 31, 1996. Does not include (i) 1,590,000 shares of Common Stock issuable upon the exercise of

the outstanding options granted pursuant to the Company's amended and restated 1991 Stock Option Plan at a weighted average exercise price of \$5.70 per share and (ii) 1,012,841 shares of Common Stock issuable upon the exercise of outstanding warrants issued in connection with certain financing transactions at a weighted average exercise price of \$5.10 per share. See "Capitalization."

- (3) See Note 1 of Notes to Financial Statements for information concerning the computation of net loss per share and weighted average shares outstanding.
- (4) Adjusted to reflect the sale of the shares of Common Stock offered hereby (at an assumed public offering price of \$13.75 per share) and the receipt of the estimated net proceeds therefrom. See "Use of Proceeds."

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Unless otherwise indicated, information in this Prospectus assumes no exercise of the Underwriters' option to purchase from the Company up to 300,000 additional shares of Common Stock to cover over-allotments, if any. This Prospectus contains, in addition to historical information, forward-looking statements that involve risks and uncertainties. The Company's actual results could differ materially from the results discussed in the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in "Risk Factors," as well as those discussed elsewhere in this Prospectus.

4

#### RISK FACTORS

In addition to other information contained in this Prospectus, the following factors should be considered carefully in evaluating the Company and its business before purchasing any of the shares of Common Stock offered hereby.

#### EARLY STAGE OF DEVELOPMENT; UNCERTAINTY OF PRODUCT DEVELOPMENT; TECHNOLOGICAL UNCERTAINTY

BioCryst is at an early stage of development. All of the Company's compounds are in research and development, and no revenues have been generated from sales of its compounds. It will be a number of years, if ever, before the Company will recognize significant revenues from product sales or royalties. To date, most of the Company's resources have been dedicated to the research and development of pharmaceutical compounds based upon its purine nucleoside phosphorylase ("PNP") program for the treatment of T-cell proliferative diseases and disorders and for the development of inhibitors of influenza neuraminidase and enzymes and proteins involved in the complement cascade. The Company is conducting preclinical and clinical studies with its lead drug, BCX-34, and results from these studies may not support future human clinical testing or further development of the compound. T-cell proliferative diseases, as well as the other disease indications the Company is studying, are highly complex and their causes are not fully known. The Company's compounds under development will require significant additional, time-consuming and costly research and development, preclinical testing and extensive clinical testing prior to submission of any regulatory application for commercial use. Product development of new pharmaceuticals is highly uncertain, and unanticipated developments, clinical or regulatory delays, unexpected adverse side effects or inadequate therapeutic efficacy could slow or prevent product development efforts and have a material adverse effect on the Company. BioCryst's lead drug, BCX-34, reversibly inhibits T-cell activity, an essential component of the human immune system. In addition to any direct toxicities or side effects the drug may cause, BCX-34, while inhibiting T-cells, may compromise the immune system's ability to fight infection. Although the Company will monitor immunosuppression during drug dosing, there can be no assurance that the drug will not cause irreversible immunosuppression. There can be no assurance that the Company's research or product development efforts as to any particular compound will be successfully completed, that the compounds currently under development will be safe or efficacious, that required regulatory approvals can be obtained, that products can be manufactured at acceptable cost and with appropriate quality or that any approved products can be successfully marketed or will be accepted by patients, health care providers and third-party payors. Few drugs discovered by use of structure-based drug design have been successfully developed, approved by the United States Food and Drug Administration (the "FDA") or marketed. Within the pharmaceutical industry, treatment of the disease indications being pursued by the Company, especially T-cell proliferative diseases such as cutaneous T-cell lymphoma and psoriasis, have proven difficult. There can be no assurance that drugs resulting from the approach of structure-based drug design employed by the

Company will overcome the difficulties of drug discovery and development or result in commercially successful products. See "Business -- Product Research and Development."

#### UNCERTAINTY ASSOCIATED WITH PRECLINICAL AND CLINICAL TESTING

Before obtaining regulatory approvals for the commercial sale of any of its products, BioCryst must undertake extensive preclinical and clinical testing to demonstrate their safety and efficacy in humans. The Company has limited experience in conducting clinical trials. To date, the Company has conducted initial preclinical testing of certain of its compounds and is testing topical and oral formulations of BCX-34 in various clinical trials. The results of initial preclinical and clinical testing of compounds under development by the Company are neither necessarily predictive of results that will be obtained from subsequent or more extensive preclinical and clinical testing nor necessarily acceptable to the FDA to support applications for marketing permits. Even if the results of subsequent clinical tests are positive, products, if any, resulting from the Company's research and development programs are not likely to be commercially available for several years. Additionally, the Company has made and may in the future make changes to the formulation of its drugs and/or to the processes for manufacturing its drugs. Any such future changes in formulation or manufacturing processes could result in delays in conducting further preclinical and clinical testing, in unexpected adverse events in further preclinical and clinical testing, and/or in additional development expenses. Furthermore, there can be no assurance

5

that clinical studies of products under development will be acceptable to the FDA or demonstrate the safety and efficacy of such products at all or to the extent necessary to obtain regulatory approvals of such products. The Company's Phase II trial with topical BCX-34 for the treatment of psoriasis completed in April 1996 did not achieve a statistically significant outcome. See "Business -- PNP Inhibitors (BCX-34)." Companies in the industry have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. The failure to comply with data integrity (Good Clinical Practice ("GCP")) requirements or to adequately demonstrate the safety and efficacy of a therapeutic product under development could delay or prevent regulatory approval of the product, and would have a material adverse effect on the Company.

The rate of completion of clinical trials is dependent upon, among other factors, the rate of enrollment of patients. Patient accrual is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the study and the existence of competitive clinical trials. Delays in planned patient enrollment in the Company's current trials or future clinical trials may result in increased costs and/or program delays which could have a material adverse effect on the Company.

#### GOVERNMENT REGULATION; NO ASSURANCE OF PRODUCT APPROVAL

The research, testing, manufacture, labeling, distribution, advertising, marketing and sale of drug products are subject to extensive regulation by governmental authorities in the United States and other countries. Prior to marketing, compounds developed by the Company must undergo an extensive regulatory approval process required by the FDA and by comparable agencies in other countries. This process, which includes preclinical studies and clinical trials of each compound to establish its safety and effectiveness and confirmation by the FDA that good laboratory, clinical and manufacturing practices were maintained during testing and manufacturing, can take many years, requires the expenditure of substantial resources and gives larger companies with greater financial resources a competitive advantage over the Company. To date, no compound or drug candidate being evaluated by the Company has been submitted for approval to the FDA or any other regulatory authority for marketing, and there can be no assurance that any such product or compound will ever be approved for marketing or that the Company will be able to obtain the labeling claims desired for its products or compounds. The Company is and will continue to be dependent upon the laboratories and medical institutions conducting its preclinical studies and clinical trials to maintain both good laboratory and good clinical practices and, except for the formulating and packaging of small quantities of its drug formulations which the Company is currently undertaking, upon the manufacturers of its compounds to maintain compliance with current good manufacturing practice ("GMP") requirements. Data obtained from preclinical studies and clinical trials are subject to varying interpretations which could delay, limit or prevent FDA regulatory approval.

Delays or rejections may be encountered based upon changes in FDA policy for drug approval during the period of development and FDA regulatory review. Similar delays also may be encountered in foreign countries. Moreover, even if approval is granted, such approval may entail commercially unacceptable limitations on the labeling claims for which a compound may be marketed. Even if such regulatory approval is obtained, a marketed drug or compound and its manufacturer are subject to continual review and inspection, and later discovery of previously unknown problems with the product or manufacturer may result in restrictions or sanctions on such product or manufacturer, including withdrawal of the product from the market, and other enforcement actions.

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. The FDA inspected the Company in November 1995 in relation to a study involving the topical application of BCX-34 concluded in early 1995, and in June 1996 the FDA inspected the Company and one of its clinical sites in relation to a Phase II dose-ranging study of BCX-34 for CTCL and a Phase II dose-ranging study for psoriasis, both of which were concluded in early 1995. After each inspection, the FDA issued to the Company a List of Inspectional Observations ("Form FDA 483") setting forth certain deficient GCP procedures followed by the Company, some of which resulted in submission to the FDA of efficacy data which reported false statistical significance. The FDA also issued a Form FDA 483 to the principal investigator at one of the Company's clinical sites citing numerous significant deficiencies

6

in the conduct of the Phase II dose-ranging studies of BCX-34 for CTCL and psoriasis. These deficiencies included improper delegations of authority by the principal investigator, failures to follow the protocols, institutional review board deviations, and discrepancies or deficiencies in documentation and reporting. The CTCL and the psoriasis dose-ranging Phase II clinical trials did not result in an overall statistically significant drug effect and as a result of the FDA inspections the FDA may not accept data from these studies. As a consequence of the FDA inspections and such resulting Form 483s, the Company's ongoing clinical studies, and in particular, the Phase III trial with topical BCX-34 for CTCL, are likely to receive increased scrutiny since the same clinical site which received the 483 is involved in that trial; this may delay the regulatory review process or require the Company to increase the number of patients at other sites to obtain approval (which can not be assured on a timely basis or at all). The Company has adjusted certain of its procedures, but there can be no assurance that the FDA will find such adjustments to be in compliance with FDA requirements or that, even if it does find such adjustments to be in compliance, it will not seek to impose administrative, civil or other sanctions in connection with the earlier studies. Administrative sanctions could include refusing to accept earlier studies and requiring the Company to repeat one or more clinical studies, which would be the only studies the FDA would accept for purposes of substantive scientific review of any NDA by the agency. See "Business -- Government Regulation."

Such sanctions or other government regulation may delay or prevent the marketing of products being developed by the Company, impose costly procedures upon the Company's activities and confer a competitive advantage to larger companies or companies that are more experienced in regulatory affairs and that compete with the Company. There can be no assurance that FDA or other regulatory approval for any products developed by the Company will be granted on a timely basis, or at all. Delay in obtaining or failure to obtain such regulatory approvals will materially adversely affect the marketing of any products which may be developed by the Company, as well as the Company's results of operations. See "Business -- Government Regulation."

#### HISTORY OF OPERATING LOSSES; ACCUMULATED DEFICIT; UNCERTAINTY OF FUTURE PROFITABILITY

BioCryst, to date, has generated no revenue from product sales and has incurred losses since its inception. As of June 30, 1996, the Company's accumulated deficit was approximately \$33.2 million. Losses have resulted principally from costs incurred in research activities aimed at discovering, designing and developing the Company's pharmaceutical product candidates and from general and administrative costs. These costs have exceeded the Company's revenues, which to date have been generated primarily from collaborative arrangements, licenses, research grants and from interest income. The Company expects to incur significant additional operating losses over the next several



years and expects such losses to increase as the Company's research and development and clinical trial efforts expand. The Company's ability to achieve profitability depends upon its ability to develop drugs and to obtain regulatory approval for its products, to enter into agreements for product development, manufacturing and commercialization, and to develop the capacity to manufacture, market and sell its products. There can be no assurance that the Company will ever achieve significant revenues or profitable operations. See "Management's Discussion and Analysis of Financial Condition and Results of Operations."

#### ADDITIONAL FINANCING REQUIREMENTS; UNCERTAINTY OF ADDITIONAL FUNDING

The Company has incurred negative cash flows from operations in each year since its inception. The Company expects that the funding requirements for its operating activities will increase substantially in the future due to expanded research and development activities (including preclinical studies and clinical trials), the development of manufacturing capabilities and the development of marketing and distribution capabilities. The Company anticipates that its capital resources after the consummation of this offering will be adequate to satisfy its capital requirements through 1998. However, this is a forward-looking statement, and no assurance can be given that there will be no change that would consume available resources significantly before such time. The Company's future capital requirements will depend on many factors, including continued scientific progress in its research, drug discovery and development programs, the magnitude of these programs, progress with preclinical studies and clinical trials, prosecuting and enforcing patent claims, competing technological and market developments, changes in existing collaborative research or development relationships, the ability of the Company to

7

establish additional collaborative relationships, and the cost of manufacturing scale-up and effective marketing activities and arrangements. The Company anticipates, based on its current business plan, that it will be necessary to raise additional funds in 1999 or earlier. Additional funds, if any, may possibly be raised through financing arrangements or collaborative relationships and/or the issuance of preferred or common stock or convertible securities, on terms and prices significantly more favorable than those of the Common Stock in this offering, which could have the effect of diluting or adversely affecting the holdings or rights of existing stockholders of the Company. In addition, collaborative arrangements may require the Company to transfer certain material rights to such corporate partners. If adequate funds are not available, the Company will be required to delay, scale back or eliminate one or more of its research, drug discovery or development programs or attempt to obtain funds through arrangements with collaborative partners or others that may require the Company to relinquish some or all of its rights to certain of its intellectual property, product candidates or products. No assurance can be given that additional financing will be available to the Company on acceptable terms, if at all. See "Management's Discussion and Analysis of Financial Condition and Results of Operations -- Liquidity and Capital Resources."

#### COMPETITION

The Company is engaged in the pharmaceutical industry, which is characterized by extensive research efforts, rapid technological progress and intense competition. There are many public and private companies, including well-known pharmaceutical companies, chemical companies, specialized biotechnology companies and academic institutions, engaged in developing synthetic pharmaceuticals and biotechnological products for human therapeutic applications that represent significant competition to the Company. Existing products and therapies and improvements thereto will compete directly with products the Company is seeking to develop and market, and the Company is aware that other companies or institutions are pursuing development of new drugs and technologies directly targeted at applications for which the Company is developing its drug compounds. Many of the Company's competitors have substantially greater financial and technical resources and production and marketing capabilities and experience than does the Company. The Company has granted Ciba-Geigy Corporation ("Ciba") a worldwide exclusive license to several compounds in the Company's sixth group of PNP inhibitors. Additionally, the Company granted an option to license a separate PNP inhibitor compound to Warner-Lambert Company ("Warner-Lambert"). A dispute has arisen between the Company and Warner-Lambert regarding this option. See "Business -- Legal Proceedings." Such arrangements with Ciba and Warner-Lambert do not include BCX-34 or most of the Company's other compounds. No assurance can be given that Ciba or Warner-Lambert will or will not develop compounds under such arrangements, will be able to obtain FDA approval for any licensed compounds,

that any such licensed compounds if so approved will be able to be commercialized successfully, or that the Company will realize any revenues pursuant to such arrangements. If commercialized, these compounds could compete directly against other compounds, including BCX-34, being developed by the Company.

Many of the Company's competitors have significantly greater experience in conducting preclinical studies and clinical trials of new pharmaceutical products and in obtaining FDA and other regulatory approvals for health care products. Accordingly, BioCryst's competitors may succeed in obtaining approvals for their products more rapidly than the Company and in developing products that are safer or more effective or less costly than any that may be developed by the Company and may also be more successful than the Company in the production and marketing of such products. Many of the Company's competitors also have current GMP facilities and significantly greater experience in implementing GMP or in obtaining and maintaining the requisite regulatory standards for manufacturing. Moreover, other technologies are, or may in the future become, the basis for competitive products. Competition may increase further as a result of the potential advances from structure-based drug design and greater availability of capital for investment in this field. There can be no assurance that the Company's competitors will not succeed in developing technologies and products that are more effective than any being developed by the Company or that would render the Company's technology and product candidates obsolete or noncompetitive. See "Business -- Competition."

8

#### DEPENDENCE ON COLLABORATIVE PARTNERS; RELATIONSHIP WITH THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

The Company's strategy for research, development and commercialization of certain of its products is to rely in part upon various arrangements with corporate partners, licensees and others. As a result, the Company's products are dependent in large part upon the subsequent success of such third parties in performing preclinical studies and clinical trials, obtaining regulatory approvals, manufacturing and marketing. The Company has recently entered into an exclusive license agreement with Torii to develop, manufacture and commercialize in Japan BCX-34 and certain other PNP inhibitor compounds for three indications. The Company has also entered into collaborative arrangements with Ciba and intends to pursue additional collaborations in the future. See "Business -- Collaborative Arrangements." There can be no assurance that the Company will be able to negotiate additional acceptable collaborative arrangements or that such arrangements will be successful. No assurance can be given that the Company's collaborative partners will be able to obtain FDA approval for any licensed compounds, that any such licensed compounds, if so approved, will be able to be commercialized successfully, or that the Company will realize any revenues pursuant to such arrangements. Although the Company believes that parties to collaborative arrangements generally have an economic motivation to succeed in performing their contractual responsibilities, the amount and timing of resources which they devote to these activities are not within the control of the Company. There can be no assurance that such parties will perform their obligations as expected or that current or potential collaborators will not pursue treatments for other diseases or seek alternative means of developing treatments for the diseases targeted by collaborative programs with the Company or that any additional revenues will be derived from such arrangements. If any of the Company's collaborators breaches or terminates its agreement with the Company or otherwise fails to conduct its collaborative activities in a timely manner, the development or commercialization of the product candidate or research program under such collaboration agreement may be delayed, the Company may be required to undertake unforeseen additional responsibilities or to devote unforeseen additional resources to such development or commercialization, or such development or commercialization could be terminated. The termination or cancellation of collaborative arrangements could also adversely affect the Company's financial condition, intellectual property position and operations. In addition, disagreements between collaborators and the Company have in the past and could in the future lead to delays in the collaborative research, development or commercialization of certain product candidates, or could require or result in legal process or arbitration for resolution. These consequences could be time-consuming, expensive and could have material adverse effects on the Company. See "Business -- Legal Proceedings."

The successful commercialization of the Company's compounds and product candidates is also dependent upon the Company's ability to develop collaborative arrangements with academic institutions and consultants to support research and development efforts and to conduct clinical trials. The Company's primary

academic collaboration is with The University of Alabama at Birmingham ("UAB"). The Company is highly dependent upon its collaborative arrangements with UAB to support its ongoing research and development programs and the termination or cessation of such relationship could have a material adverse effect upon the Company. There can be no assurance that the Company's current arrangements with UAB will continue or that the Company will be able to develop successful collaborative arrangements with academic institutions and consultants in the future. See "Business -- Collaborative Arrangements -- UAB Collaborative Arrangements."

#### UNCERTAINTY OF PROTECTION OF PATENTS AND PROPRIETARY RIGHTS

The Company's success will depend in part on its ability to obtain and enforce patent protection for its products, preserve its trade secrets, and operate without infringing on the proprietary rights of third parties, both in the United States and in other countries. In the absence of patent protection, the Company's business may be adversely affected by competitors who develop substantially equivalent technology. See "Business -- Patents and Proprietary Information." Because of the substantial length of time and expense associated with bringing new products through development and regulatory approval to the marketplace, the pharmaceutical and biotechnology industries place considerable importance on obtaining and maintaining patent and trade secret protection for new technologies, products and processes. To date, the Company has been issued five United States patents related to its PNP inhibitor compounds. Two patent applications relating to additional PNP inhibitor compounds are

9

pending at the U.S. Patent and Trademark Office ("PTO"). The Company's patent application involving two additional PNP inhibitor compounds has been allowed. The compound under the disputed option to Warner-Lambert is included in this group. See "Business--Legal Proceedings." The Company may require a license from Warner-Lambert to market a product containing one or both of these compounds. No assurance can be given that such a license would be available or obtainable on terms acceptable to BioCryst. A patent application on a new process to prepare BCX-34 and other PNP inhibitors has also been submitted to the PTO. In addition, two patent applications relating to inhibitors of influenza neuraminidase have been filed at the PTO, one of which has been allowed. The Company has filed certain corresponding foreign patent applications and intends to file additional foreign patent applications and additional United States patent applications, as appropriate. There can be no assurance that patents will be issued from such applications, that the Company will develop additional products that are patentable or that present or future patents will provide sufficient protection to the Company's present or future technologies, products and processes. In addition, there can be no assurance that others will not independently develop substantially equivalent proprietary information, design around the Company's patents or obtain access to the Company's know-how or that others will not successfully challenge the validity of the Company's patents or be issued patents which may prevent the sale of one or more of the Company's product candidates, or require licensing and the payment of significant fees or royalties by the Company to third parties in order to enable the Company to conduct its business. Legal standards relating to the scope of claims and the validity of patents in the fields in which the Company is pursuing research and development are still evolving, are highly uncertain and involve complex legal and factual issues. No assurance can be given as to the degree of protection or competitive advantage any patents issued to the Company will afford, the validity of any such patents or the Company's ability to avoid infringing any patents issued to others. Further, there can be no guarantee that any patents issued to or licensed by the Company will not be infringed by the products of others. Litigation and other proceedings involving the defense and prosecution of patent claims can be expensive and time consuming, even in those instances in which the outcome is favorable to the Company, and can result in the diversion of resources from the Company's other activities. An adverse outcome could subject the Company to significant liabilities to third parties, require the Company to obtain licenses from third parties or require the Company to cease any related research and development activities or sales.

The Company's success is also dependent upon the skills, knowledge and experience (none of which is patentable) of its scientific and technical personnel. To help protect its rights, 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 requires disclosure and assignment to the Company of their ideas, developments, discoveries and inventions. There can be no assurance, however, that these agreements will provide adequate protection for the Company's trade

secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information.

The Company's management and scientific personnel have been recruited primarily from other pharmaceutical companies and academic institutions. In many cases, these individuals are continuing research in the same areas with which they were involved prior to joining BioCryst and may be restricted by agreement from disclosing to the Company trade secrets they learned elsewhere. As a result, the Company could be subject to allegations of violation of such agreements and similar claims and litigation regarding such claims could ensue.

#### DEPENDENCE ON KEY MANAGEMENT AND QUALIFIED PERSONNEL

The Company is highly dependent upon the efforts of its senior management and scientific team. The loss of the services of one or more members of the senior management and scientific team could significantly impede the achievement of development objectives. Although the Company maintains, and is the beneficiary of, a \$2.0 million key-man insurance policy on the life of Charles E. Bugg, Ph.D., Chairman of the Board of Directors, Chief Executive Officer and President, the Company does not believe the proceeds would be adequate to compensate for his loss. Due to the specialized scientific nature of the Company's business, the Company is also highly dependent upon its ability to attract and retain qualified scientific, technical and key management personnel. There is intense competition for

10

qualified personnel in the areas of the Company's activities, and there can be no assurance that the Company will be able to continue to attract and retain qualified personnel necessary for the development of its existing business and its expansion into areas and activities requiring additional expertise, such as production and marketing. The loss of, or failure to recruit, scientific, technical and managerial personnel could have a material adverse effect on the Company. In addition, the Company relies on members of its Scientific Advisory Board and consultants to assist the Company in formulating its research and development strategy. All of the members of the Scientific Advisory Board and all of the Company's consultants are employed by other employers, and each such member or consultant may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to the Company. See "Business -- Human Resources," "--Scientific Advisory Board and Consultants" and "Management."

#### LACK OF MANUFACTURING, MARKETING OR SALES CAPABILITY

The Company has not yet manufactured or marketed any products and currently does not have the facilities to manufacture its product candidates in commercial quantities under GMP as prescribed and required by the FDA. To be successful, the Company's products must be manufactured in commercial quantities under GMP and at acceptable costs. Although the Company is formulating and packaging under GMP conditions small amounts of certain drug formulations which are the subject of preclinical studies and clinical trials, the current facilities of the Company are not adequate for commercial scale production. Therefore, the Company will need to develop its own GMP manufacturing facility and/or depend on its collaborators, licensees or contract manufacturers for the commercial manufacture of its products. The Company has no experience in such commercial manufacturing and no assurance can be given that the Company will be able to make the transition to commercial production successfully or at an acceptable cost. In addition, no assurance can be given that the Company will be able to make arrangements with third parties to manufacture its products on acceptable terms, if at all. The inability of the Company to manufacture or provide for the manufacture of any products it may develop on a cost-effective basis would have a material adverse effect on the Company. See "Business -- Manufacturing."

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 its collaborators, licensees or 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.

#### UNCERTAINTY OF THIRD-PARTY REIMBURSEMENT AND PRODUCT PRICING

Successful commercialization of any pharmaceutical products the Company may

develop will depend in part upon the availability of reimbursement or funding from third-party health care payors such as government and private insurance plans. There can be no assurance that third-party reimbursement or funding will be available for newly approved pharmaceutical products or will permit price levels sufficient to realize an appropriate return on the Company's investment in its pharmaceutical product development. The U.S. Congress is considering a number of legislative and regulatory reforms that may affect companies engaged in the health care industry in the United States. Although the Company cannot predict whether these proposals will be adopted or the effects such proposals may have on its business, the existence and pendency of such proposals could have a material adverse effect on the Company in general. In addition, the Company's ability to commercialize potential pharmaceutical products may be adversely affected to the extent that such proposals have a material adverse effect on other companies that are prospective collaborators with respect to any of the Company's pharmaceutical product candidates.

Third-party payors are continuing their efforts to contain or reduce the cost of health care through various means. For example, third-party payors are increasingly challenging the prices charged for medical products and services. Also, the trend toward managed health care in the United States and the concurrent growth of organizations, such as health maintenance organizations, which can control or significantly influence the purchase of health care services and products, as well as legislative proposals to reform health care or reduce government insurance programs, may result in lower prices for

11

pharmaceutical products. The cost containment measures that health care providers are instituting and the effect of any health care reform could materially adversely affect the Company's ability to sell its products if successfully developed and approved.

#### RISK OF PRODUCT LIABILITY; AVAILABILITY OF INSURANCE

The Company's business may be affected by potential product liability risks which are inherent in the testing, manufacturing and marketing of pharmaceutical and other products under development by the Company. There can be no assurance that product liability claims will not be asserted against the Company, its collaborators or licensees. The use of products developed by the Company in clinical trials and the subsequent sale of such products is likely to cause BioCryst to bear all or a portion of those risks. The Company does not have product liability insurance but does maintain coverage for clinical trials in the amount of \$1.0 million per occurrence and in the aggregate. No assurance can be given that such insurance will be adequate to cover claims made with respect to the clinical trials. There can be no assurance that the Company will be able to obtain or maintain adequate product liability insurance on acceptable terms or that such insurance will provide adequate coverage against potential liabilities. Furthermore, there can be no assurance that any collaborators or licensees of BioCryst will agree to indemnify the Company, be sufficiently insured or have a net worth sufficient to satisfy any such product liability claims.

#### HAZARDOUS MATERIALS; COMPLIANCE WITH ENVIRONMENTAL REGULATIONS

The Company's research and development involves the controlled use of hazardous materials, chemicals and various radioactive compounds. Although the Company believes that its safety procedures for handling and disposing of such materials comply with the standards prescribed by state and federal regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident, the Company could be held liable for any damages that result and any such liability could exceed the resources of the Company. The Company may incur substantial costs to comply with environmental regulations if the Company develops manufacturing capacity.

#### CONTROL BY EXISTING MANAGEMENT AND STOCKHOLDERS; EFFECT OF CERTAIN ANTI-TAKEOVER CONSIDERATIONS

Upon completion of the offering, the Company's directors, executive officers and certain principal stockholders and their affiliates will own beneficially approximately 29.0% of the Common Stock. Accordingly, such holders, if acting together, may have the ability to exert significant influence over the election of the Company's Board of Directors and other matters submitted to the Company's stockholders for approval. The voting power of these holders may discourage or prevent any proposed takeover of the Company unless the terms thereof are approved by such holders. Pursuant to the Company's Composite Certificate of

Incorporation (the "Certificate of Incorporation"), shares of Preferred Stock may be issued by the Company in the future without stockholder approval and upon such terms as the Board of Directors may determine. The rights of the holders of Common Stock will be subject to, and may be adversely affected by, the rights of the holders of any Preferred Stock that may be issued in the future. The issuance of Preferred Stock could have the effect of discouraging a third party from acquiring a majority of the outstanding Common Stock of the Company and preventing stockholders from realizing a premium on their shares. The Company's Certificate of Incorporation also provides for staggered terms for the members of the Board of Directors. A staggered Board of Directors and certain provisions of the Company's by-laws and of Delaware law applicable to the Company could delay or make more difficult a merger, tender offer or proxy contest involving the Company.

#### SHARES ELIGIBLE FOR FUTURE SALE

Upon completion of this offering, the Company will have 12,837,237 shares of Common Stock outstanding. Of these shares, a total of approximately 8,018,809 shares (including the 2,000,000 shares offered hereby and shares tradeable under Rule 144(k) of the Securities Act of 1933, as amended (the "Securities Act")) will be freely tradeable in the public market without restriction and approximately 4,818,428 shares will be "restricted securities" within the meaning of Rule 144 under the Securities Act (excluding any shares tradeable under Rule 144(k) of the Securities Act). All such "restricted securities" may be sold only in compliance with Rule 144 or pursuant to registration under the Securities Act or an exemption therefrom. As of August 31, 1996, an additional 1,012,841 shares of

12

Common Stock may be issued from time to time upon the exercise of outstanding warrants. Warrants for the purchase of 701,000 of such shares are exercisable at \$4.40 per share and expire on October 15, 1996. The holders of such warrants can elect a net issue exercise, in lieu of a cash exercise, whereby the shares to be issued would be 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. Such shares, upon issuance pursuant to the net issue exercise option, could be freely tradeable under Rule 144(k), although some holders are "affiliates" within the meaning of Rule 144 and as such are subject to certain Rule 144 restrictions. Any shares of Common Stock issued upon the exercise of warrants other than by a net issue exercise (except for warrants to purchase 247,616 shares of Common Stock which have been held for less than three years) shall be restricted securities within the meaning of Rule 144. Certain persons and entities holding, or having the right to purchase upon exercise of outstanding warrants issued in connection with certain financing transactions, an aggregate of approximately 6,569,722 shares of Common Stock (not including the shares of Common Stock offered hereby), have the right to require the Company to register their shares under the Securities Act in certain circumstances. The holders of 848,333 of such 6,569,722 shares currently have their shares of Common Stock registered with the Securities and Exchange Commission (the "Commission") on a Form S-3. The Company intends to withdraw such registration statement for a period of 90 days following the date of this Prospectus. In addition, the Company intends to register, subject to certain restrictions, 1,000,000 shares of Common Stock with the Commission on a Form S-3 90 days after the date of this Prospectus. The Company has registered on Form S-8 under the Securities Act 2,191,250 shares of Common Stock, including the 1,991,250 shares reserved for issuance under the 1991 Stock Option Plan and the 200,000 shares of Common Stock reserved for issuance under the Company's Employee Stock Purchase Plan (the "Purchase Plan"). Of such 1,991,250 shares of Common Stock reserved for issuance under the 1991 Stock Option Plan, 1,590,000 shares were subject to options outstanding as of August 31, 1996. Upon the exercise of the current vested portion of such options, approximately 546,244 shares would be eligible for immediate sale in the public market, subject to Rule 144 volume restrictions applicable to affiliates and an additional 348,071 shares would be eligible for immediate sale without restriction. Of the 200,000 shares of Common Stock reserved for issuance under the Purchase Plan, 31,432 shares had been issued to certain employees as of August 31, 1996. All 31,432 shares are eligible for immediate sale in the public market, subject, in certain instances, to Rule 144 volume restrictions applicable to affiliates. Future sales of Common Stock could have an adverse effect on the market price of the Common Stock. Additionally, the Commission has proposed an amendment to Rule 144 which would reduce the holding period required for shares subject to Rule 144 to become eligible for sale in the public market. This proposal, if adopted, would substantially increase the number of shares of the Company's Common Stock

eligible for immediate sale.

#### PRICE VOLATILITY; DILUTION

The securities markets have from time to time experienced significant price and volume fluctuations that have often been unrelated to the operating performance of particular companies. In addition, the market prices of the common stock of many publicly traded emerging pharmaceutical and biopharmaceutical companies have in the past been, and can in the future be expected to be, especially volatile. Announcements of technological innovations or new products by the Company or its competitors, developments or disputes concerning patents or proprietary rights or collaboration partners, achieving or failing to achieve development milestones, publicity regarding actual or potential medical results relating to products under development by the Company or its competitors, regulatory developments in both U.S. and foreign countries, public concern as to the safety of pharmaceutical products and economic and other external factors, as well as period-to-period fluctuations in the Company's financial results, may have a significant impact on the market price of the Common Stock. Purchasers of Common Stock in this offering will experience an immediate dilution in net tangible book value of their investment of \$10.32 per share (assuming a public offering price of \$13.75 per share). Additional dilution will occur upon exercise of outstanding options and warrants. See "Dilution."

13

#### THE COMPANY

The Company was incorporated under the laws of the State of Nevada on November 17, 1989 as the successor to a partnership formed in 1986, and was reincorporated in the State of Delaware on November 25, 1991. All references to the "Company" or "BioCryst" in this Prospectus include its predecessors, unless the context otherwise requires. The Company's executive offices are located at 2190 Parkway Lake Drive, Birmingham, Alabama, 35244, and its telephone number is (205) 444-4600.

#### USE OF PROCEEDS

The net proceeds to the Company from the sale of the Common Stock being offered hereby are estimated to be approximately \$25.5 million (\$29.4 million assuming the Underwriters' over-allotment option is exercised in full), assuming a public offering price of \$13.75 per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company.

The Company expects to use all of such proceeds to fund research and product development programs, including preclinical studies and clinical trials, and for general corporate purposes. The net proceeds may also be used to acquire technology, products or companies that complement the business of the Company, although no such acquisitions are the subject of any letter of intent or definitive agreement as of the date of this Prospectus.

The amounts and timing of expenditures for each purpose will depend on the progress of the Company's research and development programs; technological, competitive and business developments; determinations as to commercial potential; the terms of any collaborative arrangements entered into by the Company for development and licensing; the receipt and timing of regulatory approvals; the availability and attractiveness of alternative financing; and other factors, many of which are beyond the Company's control. The Company believes that the net proceeds from this offering, together with interest thereon, and the Company's existing capital resources will satisfy its capital requirements through 1998, although this is a forward-looking statement, subject to certain risks and uncertainties including those discussed under "Risk Factors -- Additional Financing Requirements; Uncertainty of Additional Funding" and "Management's Discussion and Analysis of Financial Condition and Results of Operations -- Liquidity and Capital Resources."

Pending such uses, the Company intends to invest the net proceeds in short-term, investment grade instruments, certificates of deposit or direct or guaranteed obligations of the United States or its agencies.

#### DIVIDEND POLICY

The Company has never declared or paid cash dividends on its capital stock. The Company currently anticipates that it will retain all available funds for

use in the operation of its business, and therefore does not anticipate paying any cash dividends in the foreseeable future.

PRICE RANGE OF COMMON STOCK

The Common Stock began trading on the Nasdaq National Market tier of The Nasdaq Stock MarketSM under the symbol "BCRX" effective March 4, 1994. Prior to that date, there was no public market for the Common Stock. The following table sets forth, for the periods indicated, the high and low sales prices of the Common Stock reported on the Nasdaq National Market. These prices do not include retail markups, markdowns or commissions.

	HIGH	LOW
	-----	-----
1994		
First quarter (from March 4).....	\$ 6.75	\$5.50
Second quarter.....	5.88	3.38
Third quarter.....	5.88	3.75
Fourth quarter.....	6.13	4.38
1995		
First quarter.....	7.00	4.63
Second quarter.....	13.75	5.50
Third quarter.....	12.25	7.75
Fourth quarter.....	11.25	8.50
1996		
First quarter.....	10.25	8.63
Second quarter.....	20.75	9.13
Third quarter (through September 23).....	17.13	11.50

On September 23, 1996, the last sale price reported on the Nasdaq National Market tier of The Nasdaq Stock MarketSM for the Common Stock was \$12.38 per share. As of July 31, 1996, there were 561 holders of record of the Common Stock.

DILUTION

As of June 30, 1996, the Company had a net tangible book value of \$17,803,185 or \$1.68 per share. Net tangible book value per share is determined by dividing the net tangible book value (tangible assets less liabilities) of the Company by the number of shares of Common Stock outstanding at that date. Without taking into account any changes in net tangible book value after June 30, 1996, other than to give effect to the sale of the shares of Common Stock offered by the Company hereby (at an assumed public offering price of \$13.75 per share) and the receipt of the net proceeds therefrom, the net tangible book value of the Company as of June 30, 1996 would have been \$43,353,185, or \$3.43 per share. This represents an immediate increase in net tangible book value of \$1.75 per share to existing stockholders and an immediate dilution of \$10.32 per share to new investors. The following table illustrates this dilution per share.

Assumed public offering price per share.....		\$13.75
Net tangible book value per share as of June 30, 1996.....	\$1.68	
Increase in net tangible book value per share attributable to the offering(1).....	1.75	
	-----	
Adjusted net tangible book value per share after the offering.....		3.43
		-----
Dilution per share to new investors(2).....		\$10.32
		-----
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(1) After deduction of underwriting discounts and commissions and estimated



offering expenses.

- (2) Determined by subtracting the adjusted net tangible book value per share after the offering from the amount of cash paid by a new investor for a share of Common Stock.

CAPITALIZATION

The following table sets forth the capitalization of the Company as of June 30, 1996 and as adjusted to reflect the sale of the shares of Common Stock offered hereby (assuming a public offering price of \$13.75 per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company) and the receipt of the estimated net proceeds therefrom.

	JUNE 30, 1996	
	----- ACTUAL	AS ADJUSTED -----
Long-term debt and capital lease obligations, excluding current portions(1).....	\$ 148,112	\$ 148,112
Stockholders' equity:		
Preferred Stock, \$.01 par value; 5,000,000 shares authorized; none issued or outstanding.....		
Common Stock, \$.01 par value; 45,000,000 shares authorized; 10,623,371 shares issued and outstanding, actual; and 12,623,371 shares issued and outstanding, as adjusted(2).....	106,234	126,234
Additional paid-in capital.....	50,887,862	76,417,862
Accumulated deficit.....	(33,190,911)	(33,190,911)
Total stockholders' equity.....	17,803,185	43,353,185
Total capitalization.....	\$17,951,297	\$43,501,297

(1) See Notes 5 and 6 of Notes to Financial Statements for additional information regarding the Company's long-term debt and obligations under capital leases.

(2) Does not include shares of Common Stock issuable upon exercise of (i) the 1,574,616 outstanding options which have been granted pursuant to the Company's amended and restated 1991 Stock Option Plan at a weighted average exercise price of \$5.71 per share; or (ii) the 1,313,541 outstanding warrants issued in connection with certain financing transactions, at a weighted average exercise price of \$4.94 per share. See "Management's Discussion and Analysis of Financial Condition and Results of Operations."

SELECTED FINANCIAL DATA

The following selected financial data set forth below for the fiscal years ended December 31, 1993, 1994 and 1995 were derived from the financial statements of the Company included elsewhere in this Prospectus which have been audited by Ernst & Young LLP, independent auditors. The selected financial data for the fiscal years ended December 31, 1991 and 1992 were derived from the financial statements of the Company audited by Ernst & Young LLP, but not included in this Prospectus. The selected financial data for the six month periods ended June 30, 1995 and 1996 are derived from the unaudited financial statements of the Company, which are included elsewhere in this Prospectus and include all adjustments, consisting of normal recurring adjustments, which the Company considers necessary for a fair presentation of the financial position and results of operations for these periods. Operating results for the six months ended June 30, 1996 are not necessarily indicative of the results that may be expected for the entire year ending December 31, 1996. The selected financial data set forth below should be read in conjunction with Management's Discussion and Analysis of Financial Condition and Results of Operations, the financial statements and related notes thereto included elsewhere in this

Prospectus.

	YEARS ENDED DECEMBER 31,					SIX MONTHS ENDED JUNE 30,	
	1991	1992	1993	1994	1995	1995	1996
STATEMENT OF OPERATIONS DATA:							
Total operating revenues.....	\$ 83,333	\$ 137,614	\$ 302,375	\$ 269,126	\$ 222,329	\$ 94,691	\$ 1,521,279
Operating expenses:							
Research and development.....	706,807	3,018,774	4,195,800	5,551,660	7,107,249	3,752,843	3,414,457
General and administrative.....	641,448	1,085,355	1,098,206	1,904,046	2,209,488	1,041,999	1,562,688
Total operating expenses.....	1,348,255	4,104,129	5,294,006	7,455,706	9,316,737	4,794,842	4,977,145
Interest income.....	28,622	47,468	60,629	464,690	662,259	285,544	387,977
Interest expense.....	(45,792)	(131,927)	(264,994)	(215,985)	(144,115)	(77,501)	(55,629)
Other income (expense), net.....	(17,170)	(84,459)	(204,365)	248,705	518,144	208,043	332,348
Net loss.....	\$ (1,282,092)	\$ (4,050,974)	\$ (5,195,996)	\$ (6,937,875)	\$ (8,576,264)	\$ (4,492,108)	\$ (3,123,518)
Net loss per share(1).....	\$ (1.50)	\$ (1.31)	\$ (1.55)	\$ (1.02)	\$ (.96)	\$ (.54)	\$ (.31)
Weighted average shares outstanding(1).....	855,573	3,100,888	3,352,364	6,787,203	8,905,099	8,305,857	10,095,953

	AS OF DECEMBER 31,					JUNE 30,
	1991	1992	1993	1994	1995	1996
BALANCE SHEET DATA:						
Cash, cash equivalents and securities held-to-maturity.....	\$ 3,163,817	\$ 1,283,681	\$ 2,873,264	\$10,872,861	\$11,414,044	\$ 17,813,084
Working capital.....	2,804,705	356,659	1,889,206	10,364,330	10,564,126	17,022,751
Total assets.....	3,577,911	3,555,257	5,202,511	12,802,831	13,056,213	19,667,319
Long-term debt and capital lease obligations, excluding current portion.....	150,463	930,503	855,389	573,493	300,411	148,112
Accumulated deficit.....	(5,306,284)	(9,357,258)	(14,553,254)	(21,491,129)	(30,067,393)	(33,190,911)
Total stockholders' equity(2).....	2,951,217	1,534,060	2,876,579	11,175,960	11,326,498	17,803,185

(1) See Note 1 of Notes to Financial Statements for information concerning the computation of net loss per share and weighted average shares outstanding.

(2) Includes preferred stock with a liquidation value of \$3.0 million for the year ended December 31, 1991, \$2.9 million for the year ended December 31, 1992 and \$10.2 million for the year ended December 31, 1993.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF  
FINANCIAL CONDITION AND RESULTS OF OPERATIONS

This Prospectus contains, in addition to historical information, forward-looking statements that involve risks and uncertainties. The Company's actual results could differ significantly from the results discussed in the forward-looking statements. Factors that could cause or contribute to such differences include those discussed in "Risk Factors" as well as those discussed elsewhere in this Prospectus.

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 expects to incur significant additional operating losses over the next several years and expects such losses to increase as the Company's research and development and clinical trial efforts expand.

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, including those which are described in "Risk Factors," that the Company must carefully manage in order to be successful.

#### RESULTS OF OPERATIONS

Six Months Ended June 30, 1996 and June 30, 1995

Total operating revenues increased to \$1.5 million in the first six months of 1996 from \$94,691 in the first six months of 1995. The increase was primarily due to the \$1.5 million license fee paid to the Company by Torii pursuant to a license agreement. No assurance can be given as to whether and when Torii may make additional payments under such agreement.

Research and development expenses decreased 9.0% to \$3.4 million in the first six months of 1996 from \$3.8 million in the first six months of 1995. The decrease is primarily attributable to less costs associated with manufacturing compounds for conducting clinical trials and fewer preclinical studies in progress. These costs tend to fluctuate from quarter to quarter depending upon the stage of development and the conduct of clinical trials. This decrease is not necessarily indicative of a decrease in research and development expenses for the full year. The Company expects research and development expenses to increase during the remainder of 1996 due to increased clinical trials and costs associated with manufacturing BCX-34.

General and administrative expenses increased 50.0% to \$1.6 million in the first six months of 1996 from \$1.0 million in the first six months of 1995. The increase is primarily the result of approximately \$574,000 in consulting fees and withholding taxes incurred in connection with the license agreement with Torii.

Other income (expense), net increased 59.7% to \$332,348 in the first six months of 1996 from \$208,043 in the first six months of 1995. This net increase represents an increase in interest and other income and a decrease in interest expenses. The increase in interest income was primarily due to interest earned on funds invested from the proceeds of the Company's private placements in 1995 and 1996. Interest expense decreased 28.2% to \$55,629 in the first six months of 1996 from \$77,501 in the first six months of 1995. The decrease is due to a decline in capitalized lease obligations, along with long-term

18

debt. The Company obtained most of its leases in connection with the move to its new facilities in April 1992.

Years Ended December 31, 1995 and 1994

Total operating revenue decreased 17.4% to \$222,329 in 1995 from \$269,126 in 1994, primarily as a result of \$50,000 of non-recurring contract research in 1994.

Research and development expenses increased 28.0% to \$7.1 million in 1995 from \$5.6 million in 1994. The increase was primarily attributable to expenses associated with conducting clinical trials, preclinical studies and large scale synthesis of BCX-34 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 \$2.2 million in 1995 from \$1.9 million 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 Company's former president's termination in the second quarter of 1994 and contractual

deferred compensation paid to the former president upon the initial public offering in the first quarter of 1994.

Other income (expense), net increased 108.3% to \$518,144 in 1995 from \$248,705 in 1994. This net increase represents an increase in interest and other income and a decrease in interest expense. 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. 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. The Company obtained most of its leases in connection with the move to its new facilities in April 1992.

Years Ended December 31, 1994 and 1993

Total operating revenue decreased 11.0% to \$269,126 in 1994 from \$302,375 in 1993. Revenues in 1994 consisted of \$219,126 from a Phase II Small Business Innovation Research ("SBIR") grant and \$50,000 from contract research. Revenue in 1993 consisted primarily of the proceeds from the exercise of an option for a license by Ciba.

Research and development expenses increased 32.3% to \$5.6 million in 1994 from \$4.2 million 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 \$1.9 million in 1994 from \$1.1 million 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.

Other income (expense), net increased \$453,070 to \$248,705 in 1994 from \$(204,365) in 1993. This net increase represents an increase in interest and other income and a decrease in interest expense. 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. Interest expense decreased 18.5% to \$215,985 in 1994 from \$264,994 in 1993. The decrease was primarily due

19

to a decline in capitalized lease obligations, along with long-term debt. 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 GMP and substantial expenses related to the filing, prosecution, maintenance, defense and enforcement of patent and other intellectual property claims.

At June 30, 1996, the Company's cash, cash equivalents and securities held-to-maturity were \$17.8 million, an increase of \$6.4 million from such

amount at December 31, 1995. The increase was primarily due to the private placement of common stock in March and May 1996 with proceeds of \$9.5 million partially offset by net cash used by operating activities.

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.

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 \$6.0 million over the three-year period ending December 31, 1997 on its influenza neuraminidase project and \$1.0 million over the three-year period ending July 18, 1998 on its complement project in order to maintain a worldwide license from UAB. These two agreements have 25-year terms and are terminable by the Company upon three months' notice. 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. See "Business--Collaborative Arrangements."

In May 1996, the Company entered into an exclusive license agreement with Torii to develop, manufacture and commercialize BCX-34 and certain other PNP inhibitor compounds in Japan for the treatment of rheumatoid arthritis, T-cell cancers (including CTCL) and atopic dermatitis. Upon entering into the agreement, Torii paid the Company \$1.5 million in license fees and made a \$1.5 million equity investment in the Company, purchasing 76,608 shares of Common Stock at a purchase price of \$19.58 per share. The agreement further provides for potential milestone payments of up to \$19.0 million and royalties on future sales of licensed products in Japan. Torii is responsible for all development, regulatory and commercialization expenses in Japan. The agreement is subject to termination by Torii at any time and by the Company in certain circumstances. Pursuant to the agreement, Torii may negotiate a license with the Company to develop BCX-34 and certain other PNP inhibitor compounds for additional indications. See "Business--Collaborative Arrangements."

20

At December 31, 1995, the Company had net operating loss and research and development credit carryforwards of approximately \$25.6 million and \$1.4 million, respectively, which will expire in 2005 through 2010. At June 30, 1996, the Company's net operating loss carryforward was approximately \$28.7 million. 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.

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 after completion of this offering will be sufficient to fund the Company's operations through 1998. However, this is a forward-looking statement, and no assurance can be given that there will be no change that would consume available resources significantly before such time. 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 funds, if any, may possibly be raised through financing arrangements or collaborative relationships and/or the issuance of

preferred or common stock or convertible securities, on terms and prices significantly more favorable than those of the Common Stock in this offering, which could have the effect of diluting or adversely affecting the holdings or rights of existing stockholders of the Company. In addition, collaborative arrangements may require the Company to transfer certain material rights to such corporate partners. If adequate funds are not available, the Company will be required to delay, scale back or eliminate one or more of its research, drug discovery or development programs or attempt to obtain funds through arrangements with collaborative partners or others that may require the Company to relinquish some or all of its rights to certain of its intellectual property, product candidates or products. No assurance can be given that additional financing will be available to the Company on acceptable terms, if at all. 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.

21

## BUSINESS

### OVERVIEW

BioCryst is an emerging 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 believes that structure-based drug design, by precisely designing compounds to fit the active site of target proteins, offers the potential for developing drugs for many indications that have improved efficacy and fewer side effects than currently marketed drugs for the same indications. The Company's development plan focuses on life threatening or significant clinical indications, including T-cell cancers, psoriasis, HIV infection and influenza. The Company is conducting three clinical trials with its most advanced drug, BCX-34: a Phase III trial with a topical formulation for cutaneous T-cell lymphoma ("CTCL"), a Phase I/II trial with an oral formulation for CTCL and a Phase I/II trial with a topical formulation for atopic dermatitis. In addition, the Company expects to initiate by the end of 1996 (assuming satisfactory FDA reviews) a Phase III trial for the topical treatment of psoriasis, a Phase I/II trial for the oral treatment of psoriasis and a Phase I/II trial for the oral treatment of HIV infection. BioCryst has additional research projects underway to develop inhibitors of influenza neuraminidase, an enzyme believed to perform an essential role in the infectious cycle of flu, and enzymes involved in the complement cascade, which is implicated in several major inflammatory conditions. One of the elements of the Company's strategic plan is to leverage its clinical progress by entering into pharmaceutical collaborations with drug companies in major world markets. Recently, BioCryst entered into an exclusive license agreement with Torii, a Japanese pharmaceutical company, for the development and commercialization in Japan of BCX-34 and certain other purine nucleoside phosphorylase ("PNP") inhibitor compounds. PNP is an enzyme believed to be involved in T-cell proliferation.

BioCryst's lead drug program targets T-cell proliferative disorders, which arise when T-cells, immune system cells that 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. Additionally, the Company believes that by suppressing proliferation of the T-cell, the host to the HIV virus, it might be possible to treat HIV-infected patients. BioCryst has designed and synthesized several chemically distinct classes of compounds which inhibit PNP.

The Company has completed six Phase I clinical trials, three Phase I/II clinical trials and three 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 280 subjects, and no significant drug-related adverse side effects have been observed. The completed Phase II trials of topical BCX-34 were double-blinded, placebo-controlled and enrolled 30 CTCL patients and 130 psoriasis patients. A majority of the patients from the Phase II CTCL trial volunteered to roll over into an extended, open-label trial. In addition, the Company has initiated preclinical studies using an ophthalmic formulation of BCX-34 for potential use in treating uveitis and corneal transplant rejection.

In May 1996, BioCryst entered into an exclusive license agreement with Torii to develop, manufacture and commercialize BCX-34 and certain other PNP inhibitor compounds in Japan. Pursuant to the agreement, Torii has made an upfront license fee payment of \$1.5 million and purchased shares of Common Stock for \$1.5 million at a price of \$19.58 per share. The agreement further provides for potential milestone payments of up to \$19.0 million and royalties on future sales of licensed products in Japan. Torii has the right to develop BCX-34 and certain other PNP inhibitor compounds for three indications and can negotiate a license with BioCryst to develop the drug for additional indications.

22

## STRATEGY

BioCryst's objective is to be a leader in the use of structure-based drug design to develop clinically and commercially significant pharmaceutical products. By utilizing structure-based drug design, the Company is able to precisely design compounds that block the active site of certain protein targets associated with particular diseases. BioCryst believes that for many indications small-molecule compounds tailored to block specific biochemical pathways offer the potential to be safer and more effective than drugs that currently exist for the same indications. The key points of the Company's strategy include:

**Target Immunological Mechanisms to Pursue Multiple Indications.** The Company's research efforts focus on inhibiting immunological mechanisms, namely T-cell proliferation and complement activation. While these mechanisms help fight infection and injury, harmful immune responses can damage many types of tissue in the body. By shutting down specific immune responses the Company believes it will be possible to intervene in several major immunological diseases and disorders thereby gaining economies of scale during drug development. The Company intends to focus its immunological development efforts on its PNP and complement enzyme inhibition programs.

**Utilize Advanced Technologies to Design Traditional Pharmaceuticals.** BioCryst utilizes structure-based drug design to precisely engineer novel, small-molecule compounds. The Company believes that this technique may permit it to design traditional pharmaceutical products that have the potential to be safe and effective while having relatively high solubility and bioavailability and relatively low manufacturing costs. BioCryst intends to integrate its technologies with other drug discovery approaches such as screening of combinatorial chemistry libraries. The Company will continue to leverage its drug design capabilities by designing novel lead inhibitors for its research-stage programs.

**Pursue Tiered Clinical Plan for BCX-34.** BioCryst is focusing on drug development programs for indications that will serve as a foundation for initiating other trials for different indications. By initially focusing on dermal indications, the Company was able to begin clinical development with a topical formulation of BCX-34 to suggest proof of principle in humans that blocking PNP inhibits T-cell proliferation. The Company was able to initiate topical trials before other formulations could enter human studies. Having established a broad topical program, the Company has initiated systemic product development focusing on an oral formulation. The initial indication for the oral program is T-cell cancer, a life-threatening disease, which the Company believes will permit it to collect safety and efficacy data to serve as a foundation for initiating additional trials for other systemic indications.

**Establish Additional Research Collaborations and Strategic Partnerships.** By leveraging its drug design capabilities and its relationships with leading scientists at The University of Alabama at Birmingham, the Company generally intends to develop its pharmaceutical products through the preclinical development and initial clinical trial phases and to use strategic alliances to supplement its internal clinical development and regulatory resources. The Company seeks to establish strategic alliances with pharmaceutical companies to conduct late-stage clinical trials, to obtain regulatory approvals, and to market and sell the Company's products, in exchange for license fees, milestone payments, and royalties. The Company also intends to continue to enter into research collaborations with corporate partners and with academic research institutions to enhance and further develop its products.

## PRODUCT RESEARCH AND DEVELOPMENT

Traditional Drug Design. 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 substantial. 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, it is likely that the compound's mode of action will be unknown and the risk of side effects caused by a lack of target specificity will be high. Newer techniques, such as combinatorial chemistry and high throughput screening, have enhanced the range of compounds that can be examined quickly. However, screening-based research has, to date, 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 and to design molecules to perform specific therapeutic tasks. Development of lead compounds is conducted by systematic empirical methods and computer modeling. While this approach is more refined than random screening, it is still 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. Structure-based drug design is a drug discovery approach by which synthetic compounds are designed from detailed structural knowledge of the active site 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, combinatorial chemistry, computer modeling of molecular structures, and protein biophysical chemistry, to focus on the three-dimensional structure and active site characterization of the proteins that control cellular biology. 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.

The initial targets for structure-based drug design are selected based on their involvement in the biological pathways integral to the course of the disease. Once a target is selected, its structure is determined by X-ray crystallography, a method used in determining the precise three-dimensional molecular structure of proteins. This structure is then used as a blueprint for the drug design of a lead compound. 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 changes induced in the target by the binding. These data, in turn, suggest ways to refine the lead compound to improve its binding to the target protein. The refined lead compound is then synthesized and complexed with the target, and further refined in a reiterative process. If lead compounds are available from other studies, such as screening of combinatorial libraries, these compounds may serve as starting points for this optimization cycle using structure-based drug design.

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 at any stage of the biological evaluation, the design team reviews the structural model and uses crystallography to adjust the 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 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.).

This iterative analysis and compound modification is possible because of the structural data obtained by X-ray crystallographic analysis at each stage. This capability renders structure-based drug

design a powerful tool for rapid and efficient development of drugs that are highly specific for particular protein target sites.

Product Development Programs

BioCryst's research and development programs concentrate in the areas of human immunological and infectious diseases and disorders. All of BioCryst's drug discovery programs use structure-based drug design to discover and design novel, small-molecule pharmaceutical products.

The following table summarizes BioCryst's development projects:

PROGRAM/COMPOUND	INDICATION	DELIVERY FORM	STAGE OF DEVELOPMENT (1)
PNP Inhibitors (BCX-34)	CTCL	Topical Oral	Phase III Phase I/II (2)
	Psoriasis	Topical Oral	Phase II Preclinical
	Atopic dermatitis	Topical	Phase I/II
	HIV	Oral	Preclinical
	Rheumatoid arthritis	Oral	Preclinical
	Transplant rejection	Oral	Preclinical
	Ophthalmic diseases and disorders	Ophthalmic	Preclinical
Influenza Neuraminidase Inhibitors	Influenza	Oral	Preclinical
Complement Inhibitors	Immunological diseases and disorders	Intravenous and Oral	Preclinical

(1) See "--Government Regulation" for a description of drug development phases and "Risk Factors" for a discussion of certain factors that can adversely affect the Company's drug development programs.

(2) This trial may also include subjects with T-cell leukemia and other T-cell cancers.

During the years ended December 31, 1993, 1994 and 1995 and the six months ended June 30, 1996 the Company spent an aggregate of \$20.3 million on research and development. Of that amount, \$4.2 million was spent in 1993, \$5.6 million was spent in 1994, \$7.1 million was spent in 1995 and \$3.4 million was spent for the six months ended June 30, 1996. Approximately \$12.4 million of that amount was spent on in-house research and development and approximately \$7.9 million was spent on contract research and development.

PNP INHIBITORS (BCX-34)

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, 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 produce T-cells that multiply uncontrollably. T-cell proliferation in such cases is associated with cancers such as cutaneous T-cell lymphoma. 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.

25

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.

BioCryst has designed and synthesized several chemically distinct groups of small molecule compounds (five of which have been patented and one of which has been allowed 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 group 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 is in the preclinical stage of development of an ophthalmic formulation. Additionally, the Company 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 the 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 effectively with an oral formulation. An ophthalmic formulation in the form of eye droplets may be most suitable for treating certain ophthalmic indications as a result of being able to directly administer the drug to the eye. 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.

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. According to a medical journal, approximately 1,000 new cases of CTCL are diagnosed annually 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. In October 1993, the Company obtained from the FDA orphan drug designation for BCX-34 to treat CTCL and may qualify for accelerated review as a new drug to treat serious and life-threatening illnesses.

The Company is conducting a Phase III trial with topical BCX-34 for the treatment of CTCL. This trial, being conducted at 10 major medical centers, is a randomized, double-blind, placebo-controlled trial designed to include 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. Prior to commencing this trial, the Company completed in 1995 a two-stage Phase II trial, which was conducted at UAB and Washington University in St. Louis. The first stage of the Phase II trial was a randomized, double-blind and placebo-controlled dose-ranging trial that enrolled 30 patients 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 daily for six weeks. This trial did not achieve a statistically significant outcome. Twenty-four of the study patients from the dose-ranging trial continued in an open-label (i.e., non-blinded) trial applying BCX-34 (1%) to all disease

lesions twice daily for six months. The results from the extended trial demonstrated clinical improvement in 75% of the patients. 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.

26

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. To date, nine patients have been enrolled and dosed in this study, and preliminary data indicates biological activity.

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. According to the National Psoriasis Foundation, it is estimated that approximately five million people suffer from some form of psoriasis in the United States, 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 completed a Phase II trial with topical BCX-34 for the treatment of psoriasis in April 1996. This trial, which was conducted at four clinical research centers (two of which were in northern sites and two of which were in sunbelt sites), was a randomized, double-blind, placebo-controlled trial enrolling 90 patients with plaque stage psoriasis. Patients applied either BCX-34 (1% concentration) or placebo cream over their disease lesions twice daily for 12 weeks. Overall, the trial did not demonstrate a statistically significant drug effect relative to the placebo. A subsequent analysis performed by the Company showed that the placebo-treated patients at the sunbelt sites had a statistically significant greater therapeutic response than those at the northern sites. The Company believes that the response in placebo-treated patients at sunbelt sites may have been increased by the recognized therapeutic effect sun exposure has on psoriasis. The Company designed its Phase III trial protocol to take into consideration this factor. The Company believes that the outcome of this trial is sufficient to justify proceeding to a Phase III trial. Preceding this trial was 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 daily for six weeks. While there were no significant drug-related adverse events, this trial did not achieve a statistically significant outcome. 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 intends to initiate a Phase III topical trial by the end of 1996, subject to satisfactory review by the FDA. The Company filed in July 1996 an IND for the oral treatment of psoriasis and, assuming satisfactory FDA review, expects to initiate a Phase I/II Clinical Trial by the end of 1996.

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. Recent market reviews have suggested that over 1.8 million individuals suffer from 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 used in treating atopic dermatitis. These

other agents have limited therapeutic benefit or generally cause adverse side effects which can be severe. In June 1996, the Company initiated a Phase I/II clinical trial with topical BCX-34 for atopic dermatitis.

HIV. Due to the increasing number of HIV-infected people, HIV infection is a major health concern. Despite extensive research and development, the treatment of HIV infection remains unsatisfactory due to the toxicity or limited therapeutic benefit of currently approved therapies. The Centers for Disease Control and Prevention ("CDC") estimates that there are approximately one million people

27

in the United States infected with HIV. HIV drug research has focused primarily on developing inhibitors of the enzymes reverse transcriptase ("RT") and HIV protease. Initially, scientists thought blocking the HIV essential RT enzyme would shutdown replication of HIV and curb the progression of HIV infection to AIDS. Several RT inhibitors are now approved, but the clinical usefulness of these drugs has been limited by their toxicity and by the ability of HIV to mutate into forms that are resistant to them. A second approach of HIV drug research has targeted the HIV protease enzyme. HIV protease is an enzyme that performs an essential role in the infectious cycle of HIV. It is believed that blocking HIV protease renders HIV unable to form a new infectious virus. Although numerous companies are developing protease inhibitors, the long-term therapeutic potential of these drugs is uncertain.

A new approach to HIV drug research focuses on the T-cell host rather than the virus. It is believed that while resting, nondividing CD4 T-cells can be infected by the virus, the virus does not multiply. Since T-cell activation and growth appear to be essential for virus replication, a treatment which inhibits T-cell growth might decrease the overall viral burden. The Company believes, based in part upon preliminary preclinical in vitro tests, that BCX-34 could potentially be useful in treating HIV-infected patients by reversibly inhibiting the growth of infected T-cells. The Company is collaborating with researchers at the UAB Center for AIDS Research on the design of an oral Phase I/II study which will be initiated following satisfactory FDA review.

Rheumatoid Arthritis. Rheumatoid arthritis is an autoimmune disease that involves inflammation of the membranes lining joints, causing joint pain, swelling, and deformities. According to a scientific journal, it is estimated that approximately 1% to 2% of the U.S. adult population, or approximately 2.6 million to 5.2 million adults, 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 has rights to develop a group of PNP inhibitors excluding BCX-34, licensed from BioCryst, with potential application in the treatment of rheumatoid arthritis.

Transplant Rejection. Risk of rejection is one of the most frequent concerns 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. 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 preclinical stage of development of the oral formulation of BCX-34 for treatment of transplant rejection.

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, may result in blindness. Clinical studies conducted by third parties 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 is particularly dangerous to the very young, the elderly and debilitated patients and those who have suppressed immune systems. The CDC estimates that approximately 10% to 20% of the U.S. population is infected with influenza during most influenza seasons. 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.

28

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. 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. The Company believes that a neuraminidase inhibitor may be useful as a treatment for influenza and is in the preclinical stage of development of neuraminidase inhibitors. Funded in part by a National Institutes of Health ("NIH") Phase I 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. At least one major pharmaceutical company is engaged in clinical studies of an influenza neuraminidase inhibitor compound intended to treat influenza, and the Company believes 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." Once an activator of the system converts an inactive enzyme to an active enzyme, the activated enzyme activates more proteins at the next stage, which in turn activate other proteins. This mechanism, if inappropriately activated, can cause acute medical reactions, including 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.

Due to the biochemical mechanism of the complement cascade, BioCryst believes complement inhibitors may have therapeutic applications in numerous acute and chronic immunological disorders. 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. The Company is performing preclinical studies with certain inhibitors it has designed and synthesized. The Company continues to design additional inhibitors.

## COLLABORATIVE ARRANGEMENTS

Torii

In May 1996, the Company entered into an agreement pursuant to which it granted Torii an exclusive license, with the right to sublicense, to develop, manufacture and commercialize BCX-34 and certain other PNP inhibitor compounds in Japan for the treatment of rheumatoid arthritis, T-cell cancers (including CTCL) and atopic dermatitis. Upon entering into the agreement, Torii paid the Company \$1.5 million in license fees and made a \$1.5 million equity investment in the Company, purchasing 76,608 shares of Common Stock at a purchase price of \$19.58 per share. In order for Torii to maintain its licensing rights, it is obligated to make payments to the Company of up to \$19.0 million upon the

achievement of specified development milestones. Torii is responsible for all development, regulatory and commercialization expenses in Japan and is obligated to pay royalties to the Company on sales of licensed products in Japan. The agreement will remain in effect, unless earlier terminated, until the last to expire of any patent rights licensed under the agreement, or in the event no patents issue, for twenty years from May 31, 1996. The agreement is subject to termination by Torii at any time and by the Company in certain circumstances, including any material breaches of the agreement by Torii. Pursuant to the agreement, Torii may negotiate a license with the Company to develop BCX-34 and certain other PNP inhibitor compounds for additional indications.

29

#### UAB Collaborative Arrangements

UAB has one of the leading X-ray crystallography centers in the world, with approximately 100 full-time staff members and approximately \$9.0 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.

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 joint research and development relating to development of an influenza neuraminidase inhibitor. UAB has granted the Company certain rights to any discoveries in this area resulting from research previously developed by UAB or jointly developed with BioCryst. The Company has agreed to fund certain UAB research laboratories, to expend at least \$6.0 million for the project over the 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 joint research and development relating to factor D inhibitors. UAB has also granted the Company certain rights to any discoveries in this area resulting from research previously developed by UAB or jointly developed with BioCryst. The Company has agreed to fund certain UAB research laboratories, to expend at least \$1.0 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 initial 25-year terms, (automatically renewable for five year terms throughout the life of the last patent or extension thereof incorporating the licensed rights) and are terminable by the Company upon three months' notice and by UAB under certain circumstances.

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. See Note 10 to Notes to Financial Statements.

#### Grants and Technology Agreements

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 of the Company's PNP inhibitor compounds. 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. See Note 10 to Notes to Financial Statements.

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. See Note 10 to Notes to Financial Statements.

30

#### PATENTS AND PROPRIETARY INFORMATION

The Company owns or has rights to certain proprietary information, issued and allowed 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 in 2009 or 2010 and relate to its PNP inhibitor compounds. The Company's current lead compound, BCX-34, is covered by one of the composition of matter patents. Two patent applications relating to other of the Company's PNP inhibitor compounds are pending at the PTO. The Company's patent application relating to two additional PNP inhibitor compounds has been allowed. The compound under a disputed option to Warner-Lambert is included in this group. The Company may require a license from Warner-Lambert to market a product containing this compound. No assurance can be given that such a license would be available or obtainable on terms acceptable to BioCryst. 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, two patent applications relating to inhibitors of influenza neuraminidase have been filed at the PTO, one of which has been allowed. 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's success will depend in part on its ability to obtain and enforce patent protection for products developed by it, preserve its trade secrets, and operate without infringing on the proprietary rights of third parties, both in the United States and other countries. In the absence of patent protection, the Company's business may be adversely affected by competitors who develop substantially equivalent technology. Because of the substantial length of time and expense associated with bringing new products through development and regulatory approval to the marketplace, the pharmaceutical and biotechnology industries place considerable importance on obtaining and maintaining patent and trade secret protection for new technologies, products and processes. There can be no assurance that patents will be issued from such applications, that the Company will develop additional products that are patentable or that present or future patents will provide sufficient protection to the Company's present or future technologies, products and processes. In addition, there can be no assurance that others will not independently develop substantially equivalent proprietary information, design around the Company's patents or obtain access to the Company's know-how or that others will not successfully challenge the validity of the Company's patents or be issued patents which may prevent the sale of one or more of the Company's product candidates, or require licensing and the payment of significant fees or royalties by the Company to third parties in order to enable the Company to conduct its business. Legal standards relating to the scope of claims and the validity of patents in the fields in which the Company is pursuing research and development are still evolving, are highly uncertain and involve complex legal and factual issues. No assurance can be given as to the degree of protection or competitive advantage any patents issued to the Company will afford, the validity of any such patents or the Company's ability to avoid violating or infringing any patents issued to others. Further, there can be no guarantee that any patents issued to or licensed by the Company will not be infringed by the products of others. Litigation and other proceedings involving the defense and prosecution of patent claims can be expensive and time consuming, even in those instances in which the outcome is favorable to the Company, and can result in the diversion of resources from the Company's other activities. An adverse outcome could subject the Company to significant liabilities to third parties, require the Company to obtain licenses from third parties or require the Company to cease any related research and development activities or sales.

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.

31

The Company's research has been or is being funded in part by Small Business Innovation Research or National Institutes of Health grants. See "Business -- Collaborative Arrangements." As a result of such funding, the United States Government has or will have certain rights in the inventions developed with the funding. These rights include a non-exclusive, paid-up, worldwide license under such inventions for any governmental purpose. In addition, the government has the right to require the Company to grant an exclusive license under any of such inventions to a third party if the government determines that (i) adequate steps have not been taken to commercialize such inventions, (ii) such action is necessary to meet public health or safety needs or (iii) such action is necessary to meet requirements for public use under federal regulations. Federal law requires that any exclusive licensor of an invention that was partially funded by federal grants (which is the case with the subject matter of certain patents issued in the Company's name) agree that it will not grant exclusive rights to use or sell the invention in the United States unless the grantee agrees that any products embodying the invention will be manufactured substantially in the United States, although such requirement is subject to a discretionary waiver by the government. It is not expected that the government will exercise any such rights.

#### MARKETING, DISTRIBUTION AND SALES

The Company lacks experience in marketing, distributing or selling pharmaceutical products and will have to develop a pharmaceutical sales force and/or rely on collaborators, licensees or 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.

#### MANUFACTURING

The Company has not yet manufactured or marketed any products and currently does not have the facilities to manufacture its product candidates in commercial quantities under GMP as prescribed and required by the FDA. To be successful, the Company's products must be manufactured in commercial quantities under GMP and at acceptable costs. Although the Company is formulating and packaging under GMP conditions small amounts of certain drug formulations which are the subject of preclinical studies and clinical trials, the current facilities of the Company are not adequate for commercial scale production. Therefore, the Company will need to develop its own GMP manufacturing facility and/or depend on its collaborators, licensees or contract manufacturers for the commercial manufacture of its products. The Company has no experience in such commercial manufacturing and no assurance can be given that the Company will be able to make the transition to commercial production successfully or at an acceptable cost. In addition, no assurance can be given that the Company will be able to make arrangements with third parties to manufacture its products on acceptable terms, if at all. See "Risk Factors -- Lack of Manufacturing, Marketing or Sales Capability."

#### 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 investigational new drug ("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 a new drug application ("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

32

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 to 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 are also intended to elicit additional safety data on the drug, including evidence of the short-term side effects and other 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 benefit-risk 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 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

33

submitting an NDA. 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 rights for seven years to the first company to receive FDA approval to market such designated drug, subject to certain limitations. A product that is considered by the FDA to be different from a particular orphan drug or is approved for different indications is not barred from sale in the United States during the seven year exclusivity period. 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. 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.

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 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.

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.

In June 1996, the FDA inspected the Company and one of its clinical sites in relation to Phase II dose-ranging studies of BCX-34 for CTCL and psoriasis, each of which was concluded in early 1995. At the conclusion of the inspection, the FDA issued to the Company a Form FDA 483 citing deficiencies relating to the

monitoring of the studies and the Company's procedures for generating, archiving, and safeguarding the randomization tables used in the studies. The deficient procedures failed to prevent the use of an incorrect randomization table which ultimately resulted in the initial submission to the FDA of data which reported false statistical significance. The FDA issued a Form FDA 483 to the principal investigator at one of the Company's clinical sites, citing numerous significant deficiencies in the conduct of the Phase II dose-ranging study of BCX-34 for CTCL and psoriasis. These deficiencies

34

included improper delegations of authority by the principal investigator, failures to follow the protocols, institutional review board deviations, and discrepancies or deficiencies in documentation and reporting. As a result of the FDA inspections the FDA may not accept data from these studies. As a consequence of the FDA inspections and such resulting Form 483s, the Company's ongoing clinical studies, and in particular, the Phase III trial with topical BCX-34 for CTCL, are likely to receive increased scrutiny since the same clinical site which received the 483 is involved in that trial; this may delay the regulatory review process or require the Company to increase the number of patients at other sites to obtain approval (which can not be assured on a timely basis or at all).

The Company believes that its procedures and monitoring practices are now in compliance with the FDA's requirements governing GCP. There can be no assurance, however, that the FDA will agree or that, even if it does agree, it will not seek to impose administrative, civil, or other sanctions in connection with the earlier studies and submission. Administrative sanctions could include refusing to accept earlier studies and requiring the Company to repeat one or more clinical studies, which would be the only studies the FDA would accept for purposes of substantive scientific review of any NDA by the agency.

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 in all material respects 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.

#### COMPETITION

The pharmaceutical industry is intensely competitive. Many companies, including other pharmaceutical companies and biotechnology 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 such companies 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, and the Company is aware that other companies or

institutions are pursuing development of new drugs and technologies directly targeted at applications for which the Company is developing its drug compounds. 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. See "Risk Factors -- Competition."

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 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 71,000 shares of Common Stock at a weighted average exercise price of \$5.99 per share. Consultants have also been granted stock options to purchase a total of 52,500 shares at a weighted average exercise price of \$4.92 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 expertise of the Scientific Advisors and Consultants. 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.

The Scientific Advisory Board presently consists of the following individuals:

NAME	POSITION
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Albert F. LoBuglio, M.D. (Chairman).....	Professor of Medicine and the Director of the Comprehensive Cancer Center of UAB
J. Claude Bennett, M.D. ....	President of UAB and formerly the Spencer Professor of Medicine and Chairman of the Department of Medicine of UAB, as well as Physician-in-Chief of the University of Alabama Hospital
Gordon N. Gill, M.D. ....	Professor of Medicine and Chair of the Faculty of Basic Biomedical Sciences at the University of California, San Diego School of Medicine
Robert E. Handschumacher, Ph.D. ....	Professor and former Chairman of the

Herbert A. Hauptman, Ph.D. ....	Department of Pharmacology at Yale University School of Medicine Research Professor in Biophysical Science at the State University of New York (Buffalo), the President of the Hauptman-Woodward Medical Research Institute, Inc. (formerly the Medical Foundation (Buffalo), Inc.), and Research Professor in Biophysical Sciences at the State University of New York (Buffalo), recipient of the Nobel Prize in Chemistry (1985)
Yuichi Iwaki, M.D., Ph.D. ....	Professor of Urology and Pathology, University of Southern California School of Medicine
Hamilton O. Smith, M.D. ....	Professor, Molecular Biology and Genetics Department at The Johns Hopkins University School of Medicine, recipient of the Nobel Prize in Medicine (1978)

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.

HUMAN RESOURCES

As of July 31, 1996, the Company had 45 employees, of whom 37 were engaged in research and development and eight were in general and administrative functions. The Company's scientific staff (16 of whom hold Ph.D. degrees and one of whom holds an M.D. degree) 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 good.

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 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 fiscal year), and a pro rata share of operating expenses and real estate taxes in excess of base year amounts. 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.

LEGAL PROCEEDINGS

In October 1991, the Company granted an option to Warner-Lambert to license BioCryst's group 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 the earlier of September 1994 or completion of Warner-Lambert's clinical trials, while being restricted to only BCX-5, one PNP inhibitor compound in BioCryst's group one inhibitors. The Company's patent application for two compounds in this group of PNP inhibitor compounds, including BCX-5, has been allowed by the PTO. 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 July 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. Warner-Lambert claims compensatory damages for the alleged breach, including the amounts it has paid to date to BioCryst, its costs in testing BCX-5 and for profits lost because it will not have certain patent rights to BCX-5 that might have been granted by a license. In May 1996, BioCryst amended its complaint to assert certain damage claims.

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. The proceedings are ongoing, and there can be no assurance that the Company will prevail or that Warner-Lambert will not prevail on its counter-claims. No assurance can be given that this litigation will not have a material adverse effect on the Company.

MANAGEMENT

DIRECTORS AND EXECUTIVE OFFICERS

The following table sets forth certain information with respect to the directors and executive officers of the Company:

NAME	AGE	POSITION
Charles E. Bugg, Ph.D.....	55	Chairman, President, Chief Executive Officer and Director
John A. Montgomery, Ph.D.....	72	Executive Vice President, Secretary, Chief Scientific Officer and Director
Ronald E. Gray.....	55	Chief Financial Officer, Assistant Secretary and Treasurer
John L. Higgins.....	26	Vice President, Corporate Development
William W. Featheringill (1).....	53	Director
Edwin A. Gee, Ph.D. (1).....	76	Director
Zola P. Horovitz, Ph.D.....	61	Director
Lindsay A. Rosenwald, M.D.....	41	Director
Joseph H. Sherrill, Jr. ....	55	Director
William M. Spencer, III (1).....	75	Director
Randolph C. Steer, M.D., Ph.D.....	46	Director

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

Charles E. Bugg, Ph.D. was named Chairman of the Board and Director in November 1993, Chief Executive Officer in January 1994 and President in early 1995. Prior to joining the Company, Dr. Bugg had served as 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 Crystallo-

graphy 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.

39

John L. Higgins joined BioCryst in August 1994 as the Director of Corporate Development. In July 1995 he was promoted to Vice President, Corporate Development. From June 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 has served since 1975 as President and Director of Private Capital Corporation, a venture capital management company, 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, and as a director of Buck Hill Falls Company, a golf course management firm. 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.

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.

40

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.

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In accordance with the terms of the 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. Dr. Horovitz's, Mr. Spencer's and Dr. Steer's terms expire at the 1997 annual meeting, Dr. Bugg's, Dr. Montgomery's and Dr. Gee's terms expire at the 1998 annual meeting and Dr. Rosenwald's term expire at the 1999 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 were elected at the 1996 annual meeting of stockholders, along with Dr. Rosenwald, 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 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 a Compensation Committee consisting of Messrs. Featheringill, Gee and Spencer. 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.

The Company also has an Audit Committee, consisting of Messrs. Featheringill, Gee 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.

41

CERTAIN 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 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.

In March 1996, the Company sold an aggregate of 1,000,000 shares of Common Stock at a purchase price of \$8.00 per share to a group of investors including William W. Featheringill (235,000 shares), William M. Spencer, III (80,000 shares) and Joseph H. Sherrill, Jr. (25,000 shares), Directors of the Company, and John P.K. Featheringill (77,500 shares), the brother of William W. Featheringill. William W. Featheringill is the beneficial owner of 65,000 of the shares purchased by John P.K. Featheringill.

UNDERWRITING

Under the terms and subject to the conditions contained in the Underwriting Agreement dated the date hereof, each Underwriter named below has severally agreed to purchase, and the Company has agreed to sell to such Underwriter, shares of Common Stock which equal the number of shares set forth opposite the name of such Underwriter below:

UNDERWRITER	NUMBER OF SHARES
-----	
Smith Barney Inc.....	
Needham & Company, Inc.....	
Total.....	2,000,000
	-----

The Underwriters are obligated to take and pay for all shares of Common Stock offered hereby (other than those covered by the over-allotment option described below) if any such shares are taken.

The Underwriters propose initially to offer part of the shares of Common Stock directly to the public at the public offering price set forth on the cover page hereof and part to certain dealers at a price that represents a concession not in excess of \$ per share under the public offering price. The Underwriters may allow, and such dealers may re-allow, a concession not in excess of \$ per share to other Underwriters or to certain other dealers. After the offering of the shares of Common Stock offered hereby, the public offering price and such concessions may be changed by the Underwriters.

The Company has granted to the Underwriters an option, exercisable for 30 days from the date of this Prospectus, to purchase up to 300,000 additional shares of Common Stock at the public offering price set forth on the cover page hereof less underwriting discounts and commissions. The Underwriters may exercise such option to purchase additional shares solely for the purpose of covering over-allotments, if any, incurred in connection with the sale of the shares offered hereby. To the extent such option is exercised, each Underwriter will be obligated, subject to certain conditions, to purchase approximately the same percentage of such additional shares as the number of shares set forth opposite such Underwriter's name in the preceding table bears to the total number of shares in such table.

The Company and the Underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

The Company, its directors and officers, and certain other stockholders of the Company, holding in the aggregate approximately 3,172,767 shares of Common Stock, have agreed not to offer, sell, contract to sell, or otherwise dispose of any shares of Common Stock or any securities convertible into or exercisable or exchangeable for Common Stock, other than the shares subject to the Underwriters' over-allotment option, without the prior written consent of Smith Barney Inc., for a period of 90 days after the date of this Prospectus.

The Underwriters and certain selling group members that currently act as market makers for the Common Stock may engage in "passive market making" in the Common Stock in accordance with Rule 10b-6A under the Exchange Act. Rule 10b-6A permits, upon the satisfaction of certain conditions, underwriters and selling group members participating in a distribution that are also market makers in the security being distributed to engage in limited market making transactions during the period when Rule 10b-6 under the Securities Exchange Act of 1934, as amended (the "Exchange Act") would otherwise prohibit such activity. In general, under Rule 10b-6A, any Underwriter or selling group member engaged in passive market making in the Common Stock (i) may not effect transactions in, or display bids for, the Common Stock at a price that exceeds the highest bid for the Common Stock displayed by a market maker that is not participating in the distribution of the Common Stock, (ii) may not have net daily purchases of the Common Stock that exceed 30% of its average daily trading volume in such stock for the two full consecutive calendar months immediately preceding the filing date of the

43

registration statement of which this Prospectus forms a part and (iii) must identify its bids as bids made by a passive market maker.

#### LEGAL MATTERS

The validity of the shares of Common Stock being offered hereby will be passed upon for the Company by Brobeck, Phleger & Harrison LLP, New York, New York. A member of Brobeck, Phleger & Harrison LLP owns 5,000 shares of Common Stock of the Company. Certain legal matters in connection with this offering will be passed upon for the Underwriters by Dewey Ballantine, New York, New York.

#### EXPERTS

The financial statements of BioCryst at December 31, 1994 and 1995, and for each of the three years in the period ended December 31, 1995, appearing and incorporated by reference in this Prospectus and Registration Statement, have been audited by Ernst & Young LLP, independent auditors, as set forth in their report thereon appearing elsewhere herein, and are included and incorporated by reference in reliance upon such report given upon the authority of such firm as experts in accounting and auditing.

The statements in this Prospectus under the captions "Risk Factors -- Uncertainty of Protection of Patents and Proprietary Rights" and "Business -- Patents and Proprietary Information" and other references herein to U.S. patent matters have been reviewed and approved by Pollock, Vande Sande & Priddy, R.L.L.P., patent counsel for the Company, as experts on such matters and are included herein in reliance upon that review and approval.

#### INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The following documents filed with the Commission are hereby incorporated by reference in this Prospectus: (i) the Annual Report of the Company on Form 10-K/A for the fiscal year ended December 31, 1995, (ii) current reports of the Company on Form 8-K, filed April 5, 1996 and Form 8-K/A filed July 26, 1996, (iii) the Quarterly Reports of the Company on Form 10-Q for the quarters ended March 31, 1996 and June 30, 1996, (iv) the 1996 Proxy Statement, dated April 1, 1996 and (v) the description of the Common Stock contained in the Company's Registration Statement on Form 8-A as filed with the Commission on January 8, 1994.

All reports and other documents subsequently filed by the Company pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this Prospectus and prior to the termination of this offering shall be deemed to be

incorporated by reference herein and to be a part hereof from the date of filing of such reports and documents. Any statement incorporated herein shall be deemed to be modified or superseded for purposes of this Prospectus to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this Prospectus.

The Company will provide without charge to each person to whom this Prospectus is delivered, upon written or oral request of such person, a copy of any or all of the foregoing documents incorporated herein by reference (other than exhibits to such documents, unless such exhibits are specifically incorporated by reference into such document). Requests for such documents should be submitted in writing to Mr. Ronald E. Gray, Chief Financial Officer, BioCryst Pharmaceuticals, Inc., 2190 Parkway Lake Drive, Birmingham, Alabama 35244.

AVAILABLE INFORMATION

The Company has filed with the Securities and Exchange Commission (the "Commission") a Registration Statement on Form S-3 under the Securities Act with respect to the Common Stock offered hereby. This Prospectus does not contain all of the information set forth in the Registration Statement and the exhibits and the schedules thereto. For further information with respect to the Company and such Common Stock, reference is made to the Registration Statement and exhibits and schedules thereto. Statements contained in this Prospectus as to the contents of any contract or other document referred to are not necessarily complete, and, with respect to any contract or other document filed as an exhibit to the Registration Statement, each such statement is qualified in all respects by reference to such exhibit. Copies of the Registration Statement and the exhibits thereto are on file at the offices of the Commission and may be obtained upon payment of the prescribed fee or may be examined without charge at the public reference facilities of the Commission described below.

The Company is subject to the reporting requirements of the Exchange Act, and in accordance therewith files annual and quarterly reports, proxy statements and other information with the Commission. Such reports, proxy statements and other information may be inspected, and copies of such material may be obtained upon payment of the prescribed fees, at the Commission's Public Reference Section, Room 1024, 450 Fifth Street, N.W., Washington, D.C. 20549, as well as at the Commission's Regional Offices at Seven World Trade Center, New York, New York 10048, and Citicorp Center, 500 West Madison Street, Suite 1400, Chicago, Illinois 60661-2511. Copies of such material can be obtained in person from the Public Reference Section of the Commission at its principal office located at 450 Fifth Street, N.W., Washington, D.C. 20549, upon payment of the prescribed fees. The Commission maintains a web site (with the address <http://www.sec.gov>) that contains reports, proxy and information statements and other information regarding the registrant.

The Common Stock is traded on the Nasdaq National Market tier of The Nasdaq Stock MarketSM, and in accordance therewith, annual and quarterly reports, proxy statements and other information concerning the Company may be inspected at the National Association of Securities Dealers, Inc., at 1735 K Street, N.W., Washington, D.C. 20006.

BIOCRYST PHARMACEUTICALS, INC.  
INDEX TO FINANCIAL STATEMENTS

	PAGE
Audited Financial Statements:	
Report of Independent Auditors.....	F-2
Balance Sheets.....	F-3
Statements of Operations.....	F-4
Statements of Stockholders' Equity.....	F-5
Statements of Cash Flows.....	F-6
Notes to Financial Statements.....	F-7

## 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, 1994 and 1995, 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, 1994 and 1995, 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.

ERNST & YOUNG LLP

Birmingham, Alabama  
January 24, 1996

BIOCRYST PHARMACEUTICALS, INC.  
BALANCE SHEETS

	DECEMBER 31,		JUNE 30,
	1994	1995	1996
	-----	-----	-----
			(UNAUDITED)
<b>ASSETS:</b>			
Cash and cash equivalents (Note 4).....	\$ 2,678,059	\$ 6,134,968	\$ 6,272,730
Securities held-to-maturity (Note 4).....	8,194,802	5,279,076	11,540,354
Prepaid expenses and other current assets.....	244,847	279,386	625,689
	-----	-----	-----
Total current assets.....	11,117,708	11,693,430	18,438,773
Furniture and equipment, net (Note 2).....	1,685,123	1,362,783	1,228,546
	-----	-----	-----
Total assets.....	\$12,802,831	\$13,056,213	\$19,667,319
	-----	-----	-----
<b>LIABILITIES AND STOCKHOLDERS' EQUITY:</b>			
Accounts payable.....	\$ 148,114	\$ 210,177	\$ 460,312
Accrued expenses.....	171,012	187,673	378,275
Accrued taxes, other than income.....	23,726	350,223	155,223
Accrued vacation.....	134,727	110,704	131,140
Current maturities of long-term debt (Note 5).....	25,416	28,782	30,629
Current maturities of capital lease obligations (Note 6).....	250,383	241,745	260,443
	-----	-----	-----
Total current liabilities.....	753,378	1,129,304	1,416,022
	-----	-----	-----
Long-term debt (Note 5).....	47,342	18,560	2,770
	-----	-----	-----
Capital lease obligations (Note 6).....	526,151	281,851	145,342
	-----	-----	-----
Deferred license fee (Note 10).....	300,000	300,000	300,000
	-----	-----	-----
Stockholders' equity (Notes 8 and 9):			
Preferred stock, \$.01 par value; shares authorized			

5,000,000--none issued or outstanding			
Common stock, \$.01 par value; shares authorized--			
45,000,000; shares issued and outstanding--			
7,907,166--1994; 9,504,331--1995 and			
10,623,371--1996.....	79,072	95,043	106,234
Additional paid-in capital.....	32,588,017	41,298,848	50,887,862
Accumulated deficit.....	(21,491,129)	(30,067,393)	(33,190,911)
Total stockholders' equity.....	11,175,960	11,326,498	17,803,185
Commitments and contingency (Notes 6 and 10).....			
Total liabilities and stockholders' equity.....	\$12,802,831	\$13,056,213	\$19,667,319

See accompanying notes to financial statements.

F-3

BIOCRYST PHARMACEUTICALS, INC.  
STATEMENTS OF OPERATIONS

	YEARS ENDED DECEMBER 31,			SIX MONTHS ENDED JUNE 30,	
	1993	1994	1995	1995	1996
				(UNAUDITED)	
Total operating revenues (Notes 1 and 10).....	\$ 302,375	\$ 269,126	\$ 222,329	\$ 94,691	\$ 1,521,279
Expenses:					
Research and development.....	4,195,800	5,551,660	7,107,249	3,752,843	3,414,457
General and administrative.....	1,098,206	1,904,046	2,209,488	1,041,999	1,562,688
Total operating expenses.....	5,294,006	7,455,706	9,316,737	4,794,842	4,977,145
Interest income.....	60,629	464,690	662,259	285,544	387,977
Interest expense.....	(264,994)	(215,985)	(144,115)	(77,501)	(55,629)
Other income (expense), net.....	(204,365)	248,705	518,144	208,043	332,348
Net loss.....	\$ (5,195,996)	\$ (6,937,875)	\$ (8,576,264)	\$ (4,492,108)	\$ (3,123,518)
Net loss per share (Note 1).....	\$ (1.55)	\$ (1.02)	\$ (.96)	\$ (.54)	\$ (.31)
Weighted average shares outstanding (Note 1).....	3,352,364	6,787,203	8,905,099	8,305,857	10,095,953

See accompanying notes to financial statements.

F-4

BIOCRYST PHARMACEUTICALS, INC.  
STATEMENTS OF STOCKHOLDERS' EQUITY  
(AMOUNTS PRESENTED FOR THE SIX MONTHS  
ENDED JUNE 30, 1996 ARE UNAUDITED)

	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
Sale of 1,000,000 shares of common stock at \$8.00 per share, less issuance cost.....		10,000	7,957,000		7,967,000
Exercise of 33,887 shares of common stock under the stock option plan.....		340	146,252		146,592
Exercise of 800 shares of common stock under warrants.....		8	6,392		6,400
Sale of 76,608 shares of common stock at \$19.58 per share, less issuance cost.....		766	1,417,734		1,418,500
Sale of 7,745 shares of common stock under the employee stock purchase plan at \$7.97 per share.....		77	61,636		61,713
Net loss.....				(3,123,518)	(3,123,518)
BALANCE AT JUNE 30, 1996 (UNAUDITED).....	\$	\$ 106,234	\$50,887,862	\$ (33,190,911)	\$ 17,803,185

\* 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.

F-5

BIOCRYST PHARMACEUTICALS, INC.  
STATEMENTS OF CASH FLOWS

	YEARS ENDED DECEMBER 31,			SIX MONTHS ENDED JUNE 30,	
	1993	1994	1995	1995	1996
				(UNAUDITED)	
OPERATING ACTIVITIES:					
Net loss.....	\$ (5,195,996)	\$ (6,937,875)	\$ (8,576,264)	\$ (4,492,108)	\$ (3,123,518)
Adjustments to reconcile net loss to net cash used in operating activities:					
Depreciation and amortization.....	603,532	607,399	554,025	295,880	264,631

Changes in operating assets and liabilities:					
Prepaid expenses and other assets.....	(230,813)	149,638	(34,539)	(214,625)	(346,303)
Accounts payable.....	(232,266)	80,541	62,063	65,787	250,135
Accrued expenses.....	204,263	(452,038)	16,661	(17,711)	190,602
Accrued taxes, other than income.....	(24,813)	(1,461)	326,497	11,079	(195,000)
Vacation accrual.....	78,774	38,439	(24,023)	23,213	20,436
	-----	-----	-----	-----	-----
Net cash used in operating activities.....	(4,797,319)	(6,515,357)	(7,675,580)	(4,328,485)	(2,939,017)
	-----	-----	-----	-----	-----
INVESTING ACTIVITIES:					
Purchases of furniture and equipment.....	(327,216)	(357,760)	(231,685)	(113,253)	(130,396)
Purchase of marketable securities.....		(13,433,567)	(11,397,640)	(4,917,517)	(10,578,817)
Maturities of marketable securities.....		5,238,765	14,313,366	12,706,883	4,317,540
	-----	-----	-----	-----	-----
Net cash (used in)/provided by investing activities....	(327,216)	(8,552,562)	2,684,041	7,676,113	(6,391,673)
	-----	-----	-----	-----	-----
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.....	(2,108,225)	(364,542)	(278,354)	(157,586)	(131,753)
Deferred license.....	300,000				
Sale of preferred stock, net of issuance costs....	6,521,015				
Exercise of stock options.....	17,500	6,747	50,694	7,405	146,592
Exercise of warrants.....					6,400
Sale of common stock under the Employee Stock Purchase Plan.....			65,858		61,713
Sale of common stock, net of issuance costs.....		15,230,509	8,610,250	8,610,250	9,385,500
	-----	-----	-----	-----	-----
Net cash provided by financing activities.....	6,714,118	14,872,714	8,448,448	8,460,069	9,468,452
	-----	-----	-----	-----	-----
Increase (decrease) in cash and cash equivalents.....	1,589,583	(195,205)	3,456,909	11,807,697	137,762
Cash and cash equivalents at beginning of period...	1,283,681	2,873,264	2,678,059	2,678,059	6,134,968
	-----	-----	-----	-----	-----
Cash and cash equivalents at end of period.....	\$ 2,873,264	\$ 2,678,059	\$ 6,134,968	\$14,485,756	\$ 6,272,730
	-----	-----	-----	-----	-----

See accompanying notes to financial statements.

F-6

BIOCRYST PHARMACEUTICALS, INC.  
 NOTES TO FINANCIAL STATEMENTS  
 (INFORMATION AS OF JUNE 30, 1996 AND FOR THE SIX MONTHS  
 ENDED JUNE 30, 1996 IS UNAUDITED)

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 and June 30, 1996, securities held-to-maturity, all current, consisted of \$2,714,385 and \$1,710,524, respectively, of U.S. Treasury and Agency securities and \$2,564,691 and \$9,829,830, respectively, of high-grade domestic corporate debt carried at amortized cost. The amortized cost of these securities at December 31, 1995 and June 30, 1996 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.

F-7

### BIOCRYST PHARMACEUTICALS, INC. NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

#### NOTE 1 -- ACCOUNTING POLICIES--(CONTINUED)

##### 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.

##### 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:

	DECEMBER 31,		JUNE 30,
	1994	1995	1996 (UNAUDITED)
Furniture and fixtures.....	\$ 61,845	\$ 78,560	\$ 89,754
Office equipment.....	128,936	197,389	217,238
Laboratory equipment.....	639,225	765,873	860,174
Leased laboratory equipment.....	1,670,651	1,220,778	1,220,778
Leasehold improvements.....	783,122	802,987	808,038
	-----	-----	-----
	3,283,779	3,065,587	3,195,982
Less accumulated depreciation and amortization.....	1,598,656	1,702,804	1,967,436
	-----	-----	-----
Furniture and equipment, net.....	\$1,685,123	\$1,362,783	\$ 1,228,546
	-----	-----	-----

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.

F-8

BIOCRYST PHARMACEUTICALS, INC.  
NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

NOTE 3 -- LINE OF CREDIT

The Company had an unused line of credit of \$500,000 at December 31, 1995 and June 30, 1996.

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. At December 31, 1995 and June 30, 1996, approximately \$4,868,045 and \$6,311,226, respectively, 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.

NOTE 5 -- LONG-TERM DEBT

Long-term debt consisted of the following:

	DECEMBER 31,		JUNE 30,
	1994	1995	1996
			(UNAUDITED)
Installment note, payable \$2,757 monthly, including interest at 12.9% through May 1997.....	\$72,758	\$47,342	\$33,399
Less current maturities.....	25,416	28,782	30,629
Long-term debt, non-current portion.....	\$47,342	\$18,560	\$ 2,770

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 \$132,484, \$215,985, \$144,115 and \$55,629 in interest on debt and lease obligations for the years ended December 31, 1993, 1994, 1995 and the six months ended June 30, 1996, 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

F-9

BIOCRYST PHARMACEUTICALS, INC.  
NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

NOTE 6 -- LEASES--(CONTINUED)

\$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 \$95,343, \$151,914, \$183,522 and \$95,083 in 1993, 1994, 1995 and the six months ended June 30, 1996, 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 \$7,100,000, \$11,250,000 and \$12,500,000 at December 31, 1994 and 1995 and June 30, 1996, 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 \$7,100,000, \$11,250,000 and \$12,500,000 at December 31, 1994 and 1995 and June 30, 1996, respectively, which will remain until it is more likely than not that the related tax benefits will be realized.

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. At June 30, 1996, the Company had a net operating loss carryforward of approximately \$28,700,000. 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, the Company 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

F-10

#### BIOCRYST PHARMACEUTICALS, INC. NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

#### NOTE 8 -- STOCKHOLDERS' EQUITY--(CONTINUED)

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. At June 30, 1996, 1,313,541 shares of the Company's common stock were reserved for issuance under warrant agreements and the weighted average per share exercise price was \$4.94.

#### 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 and 3,336,454 shares reserved for future issuance for the options and warrants discussed above and the Stock Purchase Plan discussed in Note 9 as of December 31, 1995 and June 30, 1996, respectively.

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, 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

F-11

BIOCRYST PHARMACEUTICALS, INC.  
NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

NOTE 8 -- STOCKHOLDERS' EQUITY--(CONTINUED)

stock reserved for issuance to 2,000,000 shares. The following is an analysis of stock options for the three years and six months ending June 30, 1996.

	OPTIONS AVAILABLE	OPTIONS OUTSTANDING	AVERAGE EXERCISE PRICE
	-----	-----	-----
BALANCE 12/31/92.....	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 12/31/93.....	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 12/31/94.....	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 12/31/95.....	247,814	1,630,062	5.49
Options granted.....	(38,650)	38,650	10.36
Options exercised.....		(33,887)	4.33
Options canceled.....	60,209	(60,209)	4.29
	-----	-----	
BALANCE JUNE 30, 1996.....	269,373	1,574,616	5.71
	-----	-----	

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 Stock Purchase Plan

qualifies under Section 423 of the Internal Revenue Code and thus is non-compensatory. 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 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. On January 31, 1996, 7,745 shares of common stock were purchased under the Stock Purchase Plan at a price of \$7.97 per share.

F-12

BIOCRYST PHARMACEUTICALS, INC.  
NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

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.

In May 1996, the Company entered into an exclusive license agreement with Torii Pharmaceutical Co., Ltd. ("Torii") to develop, manufacture and commercialize BCX-34 and certain other PNP inhibitor compounds in Japan for the treatment of rheumatoid arthritis, T-cell cancers and atopic dermatitis. Upon entering into the agreement, Torii paid the Company \$1.5 million in license fees and made a \$1.5 million equity investment in the Company, purchasing 76,608 shares of Common Stock at a purchase price of \$19.58 per share. The agreement further provides for potential milestone payments of up to \$19.0 million and royalties on future sales of licensed products in Japan. Torii is responsible for all development, regulatory and commercialization expenses in Japan. The agreement is subject to termination by Torii at any time and by the Company in certain circumstances. Pursuant to the agreement, Torii may negotiate a license with the Company to develop BCX-34 and certain other PNP inhibitor compounds for additional indications.

F-13

NOTES TO FINANCIAL STATEMENTS--(CONTINUED)

NOTE 11 -- QUARTERLY FINANCIAL INFORMATION (UNAUDITED)  
(In thousands, except per share)

	FIRST	SECOND	THIRD	FOURTH
	-----	-----	-----	-----
1994 QUARTERS:				
Revenues.....	\$ 42	\$ 52	\$ 113	\$ 62
Net loss.....	(1,564)	(1,866)	(1,633)	(1,875)
Net loss per share.....	(.35)	(.25)	(.22)	(.24)
1995 QUARTERS:				
Revenues.....	\$ 31	\$ 64	\$ 64	\$ 63
Net loss.....	(2,908)	(1,584)	(1,915)	(2,169)
Net loss per share.....	(.37)	(.18)	(.20)	(.23)
1996 QUARTERS:				
Revenues.....	\$ 21	\$ 1,500		
Net loss.....	(1,913)	(1,211)		
Net loss per share.....	(.20)	(.11)		

F-14

NO PERSON IS AUTHORIZED IN CONNECTION WITH ANY OFFERING MADE HEREBY TO GIVE ANY INFORMATION OR TO MAKE ANY REPRESENTATION NOT CONTAINED IN THIS PROSPECTUS, AND, IF GIVEN OR MADE, SUCH INFORMATION OR REPRESENTATION MUST NOT BE RELIED UPON AS HAVING BEEN AUTHORIZED BY THE COMPANY OR ANY UNDERWRITER. THIS PROSPECTUS DOES NOT CONSTITUTE AN OFFER TO SELL OR A SOLICITATION OF AN OFFER TO BUY ANY SECURITY OTHER THAN THE SHARES OF COMMON STOCK OFFERED HEREBY, NOR DOES IT CONSTITUTE AN OFFER TO SELL OR A SOLICITATION OF AN OFFER TO BUY ANY OF THE SECURITIES OFFERED HEREBY TO ANY PERSON IN ANY JURISDICTION IN WHICH IT IS UNLAWFUL TO MAKE SUCH AN OFFER OR SOLICITATION. NEITHER THE DELIVERY OF THIS PROSPECTUS NOR ANY SALE MADE HEREUNDER SHALL UNDER ANY CIRCUMSTANCES CREATE ANY IMPLICATION THAT THE INFORMATION CONTAINED HEREIN IS CORRECT AS OF ANY DATE SUBSEQUENT TO THE DATE HEREOF.

2,000,000 SHARES

[BIOCRYST PHARMACEUTICALS, INC. LOGO]

COMMON STOCK

TABLE OF CONTENTS

	PAGE
	----
Prospectus Summary.....	3
Risk Factors.....	5
The Company.....	14
Use of Proceeds.....	14
Dividend Policy.....	14
Price Range of Common Stock.....	15
Dilution.....	15
Capitalization.....	16
Selected Financial Data.....	17
Management's Discussion and Analysis of Financial Condition and Results of Operations.....	18
Business.....	22
Management.....	39
Certain Transactions.....	42
Underwriting.....	43

PROSPECTUS

, 1996

SMITH BARNEY INC.

NEEDHAM & COMPANY, INC.

Legal Matters.....	44
Experts.....	44
Incorporation of Certain Information by Reference.....	44
Available Information.....	45
Index to Financial Statements.....	F-1

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PART II  
INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

The following table sets forth an estimate of the expenses to be incurred by the Company in connection with the issuance and distribution of the securities being registered:

	AMOUNT TO BE PAID
Securities and Exchange Commission Registration Fee.....	\$ 13,384
National Association of Securities Dealers, Inc. Filing Fee.....	4,381
Nasdaq National Market Listing Fee.....	17,500
Legal Fees and Expenses.....	125,000
Accounting Fees and Expenses.....	50,000
Printing and Engraving.....	50,000
Blue Sky Fees and Expenses.....	20,000
Miscellaneous.....	19,735
	-----
Total.....	\$ 300,000
	----- -----

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS

Section 145 of the Delaware General Corporation Law authorizes a court to award, or a corporation's Board of Directors to grant, indemnification to directors and officers in terms sufficiently broad to permit such indemnification under certain circumstances for liabilities (including reimbursement for expenses incurred) arising under the Securities Act of 1933, as amended (the "Act"). Article Eight of the Registrant's Composite Certificate of Incorporation provides for indemnification of its directors and officers and permissible indemnification of employees and other agents to the maximum extent permitted by the Delaware General Corporation Law. The Selling Stockholders have agreed to indemnify officers, directors and controlling persons of the Registrant against certain liabilities, including liabilities under the Securities Act under certain circumstances. The Company has liability insurance for its Directors and Officers.

ITEM 16. EXHIBITS

The following is a list of Exhibits filed as part of the Registration Statement:

- 1.1 Form of Underwriting Agreement.
- 4.1 Specimen certificate for shares of the Registrant's Common Stock, incorporated herein by reference to Exhibit 4.1 to Registration Statement No. 33-73868.
- 4.2 Provisions of the Composite Certificate of Incorporation and By-Laws of the Registrant defining rights of holders of Common Stock of the Registrant, incorporated herein by reference to Exhibits 3.1 and 3.2 to the Company's Form 10-Q for the second quarter ending June 30, 1995 dated August 11, 1995.
- 5. Opinion and Consent of Brobeck, Phleger & Harrison LLP.
- 23.1 Consent of Ernst & Young LLP, independent auditors.
- 23.2 Consent of Pollock, Vande Sande & Priddy, R.L.L.P.

Consent of Brobeck, Phleger & Harrison LLP (included in the opinion filed as Exhibit 5).

24.\*\* Powers of Attorney.

27.1\*\* Financial Data Schedule.

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\*\* Previously filed.

II-1

ITEM 17. UNDERTAKINGS

Insofar as indemnification for liabilities arising under the Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the Delaware General Corporation Law, the Composite Certificate of Incorporation of the Registrant, the Bylaws of the Registrant, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act, and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered hereunder, the Registrant will, unless in the opinion of counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities and Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

The undersigned Registrant hereby undertakes that:

- (1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this Registration Statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this Registration Statement as of the time it was declared effective.
- (2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

II-2

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Amendment No. 2 to the Registration Statement 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.

BIOCRYST PHARMACEUTICALS, INC.

By:

\*

.....



Charles E. Bugg  
 Chairman, President and Chief  
 Executive Officer

Pursuant to the requirements of the Securities Act of 1933, as amended, this Amendment No. 2 to the Registration Statement has been signed by the following persons in the capacities indicated on September 24, 1996:

SIGNATURE	TITLE(S)
..... * ..... (Charles E. Bugg)	Chairman, President, Chief Executive Officer and Director
..... * ..... (John A. Montgomery)	Executive Vice President, Secretary, Chief Scientific Officer and Director
..... /s/ RONALD E. GRAY ..... (Ronald E. Gray)	Chief Financial Officer (Principal Financial and Accounting Officer)
..... * ..... (William W. Featheringill)	Director
..... * ..... (Edwin A. Gee)	Director
..... * ..... (Zola P. Horovitz)	Director
..... * ..... (Lindsay A. Rosenwald)	Director
..... * ..... (Joseph H. Sherrill, Jr.)	Director
..... * ..... (William M. Spencer, III)	Director
..... * ..... (Randolph C. Steer)	Director
..... *By /s/ RONALD E. GRAY ..... Ronald E. Gray Attorney-in-Fact	

II-3

EXHIBIT INDEX

EXHIBIT NO.	DESCRIPTION	PAGE
1.1	Form of Underwriting Agreement	
4.1	Specimen certificate for shares of the Registrant's Common Stock, incorporated herein by reference to Exhibit 4.1 to Registration Statement No. 33-73868	
4.2	Provisions of the Certificate of Incorporation and By-Laws of the Registrant defining rights of holders of Common Stock of the Registrant, incorporated	

herein by reference to Exhibits 3.1 and 3.2 to the Company's Form 10-Q for the second quarter ending June 30, 1995 dated August 11, 1995

- 5. Opinion and Consent of Brobeck, Phleger & Harrison LLP
- 23.1 Consent of Ernst & Young LLP, independent auditors
- 23.2 Consent of Pollock, Vande Sande & Priddy, R.L.L.P.
- 23.3 Consent of Brobeck, Phleger & Harrison LLP (included in the opinion filed as Exhibit 5)
- 24. \*\* Powers of Attorney
- 27.1\*\* Financial Data Schedule

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\*\* Previously filed.

Draft of 9/20/96

2,000,000 Shares

BIOCRYST PHARMACEUTICALS, INC.

Common Stock

UNDERWRITING AGREEMENT  
-----

, 1996

SMITH BARNEY INC.  
NEEDHAM & COMPANY, INC.  
c/o SMITH BARNEY INC.  
388 Greenwich Street  
New York, New York 10013

Dear Sirs:

BioCryst Pharmaceuticals, Inc., a Delaware corporation (the "Company"), proposes to issue and sell an aggregate of 2,000,000 shares (the "Firm Shares") of its common stock, par value \$0.01 per share (the "Common Stock"), to the several Underwriters named in Schedule I hereto (the "Underwriters"). In addition, solely for the purpose of covering over-allotments, the Company proposes to sell to the Underwriters, upon the terms and conditions set forth in Section 2 hereof, up to an additional 300,000 shares (the "Additional Shares") of Common Stock. The Firm Shares and the Additional Shares are hereinafter collectively referred to as the "Shares."

The Company wishes to confirm as follows its agreement with you, in connection with the several purchases of the Shares by the Underwriters.

1. REGISTRATION STATEMENT AND PROSPECTUS. The Company has prepared and filed with the Securities and Exchange Commission (the "Commission") in accordance with the provisions of the Securities Act of 1933, as amended, and the rules and regulations of the Commission thereunder (collectively, the "Act"), a registration statement on Form S-3 under the Act (the "registration statement"), including a prospectus subject to completion, relating to the Shares. The term "Registration Statement" as used in this Agreement means the registration statement (including all financial schedules and exhibits) as amended at the time it becomes effective or, if the registration statement became effective prior to the execution of this Agreement, as supplemented or amended prior to the execution of this Agreement. If it is contemplated, at the time this Agreement is executed, that a post-effective amendment to the registration statement will be filed and must be declared effective before the offering of the Shares may commence, the term "Registration Statement" as used in this Agreement means the registration statement as amended

by said post-effective amendment. If an abbreviated registration statement relating to the offering of the Shares is prepared and filed with the Commission in accordance with Rule 462(b) under the Act (an "Abbreviated Registration Statement"), the term "Registration Statement" as used in this Agreement includes the Abbreviated Registration Statement. The term "Prospectus" as used in this Agreement means the prospectus in the form included in the Registration Statement, or, if the prospectus included in the Registration Statement omits information in reliance on Rule 430A under the Act and such information is included in a prospectus filed with the Commission pursuant to Rule 424(b) under the Act, the term "Prospectus" as used in this Agreement means the prospectus in the form included in the Registration Statement as supplemented by the addition of the Rule 430A information contained in the prospectus filed with the Commission pursuant to Rule 424(b). The term "Prepricing Prospectus" as used in this Agreement means the prospectus subject to completion in the form included in the registration statement at the time of the initial filing of the registration statement with the Commission and as such prospectus shall have been amended from time to time prior to the date of the Prospectus. Any reference herein to the registration statement, the Registration Statement, any Prepricing Prospectus or the Prospectus shall be deemed to refer to and include the documents incorporated by reference therein pursuant to Form S-3 under the Act, as of the date of the registration statement, the Registration Statement, such Prepricing Prospectus or the Prospectus, as the case may be, and any reference to any amendment or supplement to the registration statement, the Registration Statement, any Prepricing Prospectus or the Prospectus shall be deemed to refer to and include any documents filed after such date under the Securities Exchange Act of 1934, as amended, and the rules and regulations of the Commission thereunder (collectively, the "Exchange Act") and deemed incorporated by reference pursuant to Form S-3 under the Act. As used herein, the term "Incorporated Documents" means the documents which at the time are incorporated by reference in the registration statement, the Registration Statement, any Prepricing Prospectus, the Prospectus or any amendment or supplement thereto.

2. AGREEMENTS TO SELL AND PURCHASE. The Company hereby agrees, subject to all the terms and conditions set forth herein, to issue and sell to each Underwriter and, upon the basis of the representations, warranties and agreements of the Company herein contained and subject to all the terms and conditions set forth herein, each Underwriter agrees, severally and not jointly, to purchase from the Company, at a purchase price of \$            per share (the "purchase price per share"), the number of Firm Shares set forth opposite the name of such Underwriter in Schedule I hereto (or such number of Firm Shares increased as set forth in Section 10 hereof).

The Company also agrees, subject to all the terms and conditions set forth herein, to sell to the Underwriters, and, upon the basis of the representations, warranties and agreements of the Company herein contained and subject to all the terms and conditions set forth herein, the Underwriters shall have the right to purchase from the Company, at the purchase price per share, pursuant to an option (the "over-allotment option") which may be exercised at any time and from time to time prior to 9:00 p.m., New York City time, on the 30th day after the date of the Prospectus (or, if such 30th day shall be a Saturday or Sunday or a holiday, on the next business day thereafter when the

New York Stock Exchange is open for trading), up to an aggregate of 300,000 Additional Shares from the Company. Additional Shares may be purchased solely to cover over-allotments made in connection with the offering of the Firm Shares. Upon any exercise of the over-allotment option, each Underwriter, severally and not jointly, agrees to purchase from the Company the number of Additional Shares (subject to such adjustments as you may determine in order to avoid fractional shares) which bears the same proportion to the number of Additional Shares to be purchased by the Underwriters as the number of Firm Shares set forth opposite the name of such Underwriter in Schedule I hereto (or such number of Firm Shares increased as set forth in Section 10 hereof) bears to the aggregate number of Firm Shares.

2

3. TERMS OF PUBLIC OFFERING. The Company has been advised by you that the Underwriters propose to make a public offering of their respective portions of the Shares as soon after the Registration Statement and this Agreement have become effective as in your judgment is advisable and initially to offer the Shares upon the terms set forth in the Prospectus.

4. DELIVERY OF THE SHARES AND PAYMENT THEREFOR. Delivery to the Underwriters of and payment for the Firm Shares shall be made at the office of Smith Barney Inc., 388 Greenwich Street, New York, New York 10013, at 10:00 A.M., New York City time, on \_\_\_\_\_, 1996 (the "Closing Date"). The place of closing for the Firm Shares and the Closing Date may be varied by agreement among you and the Company.

Delivery to the Underwriters of and payment for any Additional Shares to be purchased by the Underwriters shall be made at the aforementioned office of Smith Barney Inc. at such time on such date (the "Option Closing Date"), which may be the same as the Closing Date but shall in no event be earlier than the Closing Date nor earlier than two nor later than ten business days after the giving of the notice hereinafter referred to, as shall be specified in a written notice from you on behalf of the Underwriters to the Company of the Underwriters' determination to purchase a number, specified in such notice, of Additional Shares. The place of closing for any Additional Shares and the Option Closing Date for such Shares may be varied by agreement among you and the Company.

Certificates for the Firm Shares and for any Additional Shares to be purchased hereunder shall be registered in such names and in such denominations as you shall request by written notice, it being understood that a facsimile transmission shall be deemed written notice, prior to 9:30 A.M., New York City time, on the second business day preceding the Closing Date or any Option Closing Date, as the case may be. Such certificates shall be made available to you in New York City for inspection and packaging not later than 9:30 A.M., New York City time, on the business day next preceding the Closing Date or the Option Closing Date, as the case may be. The certificates evidencing the Firm Shares and any Additional Shares to be purchased hereunder shall be delivered to you on the Closing Date or the Option Closing Date, as the case may be, against payment of the purchase price therefor in immediately available funds.

5. AGREEMENTS OF THE COMPANY. The Company agrees with the several Underwriters as follows:

(a) If, at the time this Agreement is executed and delivered, it is necessary for the registration statement or a post-effective amendment thereto or any Abbreviated Registration Statement to be declared or, in the case of an Abbreviated Registration Statement, to become effective before the offering of the Shares may commence, the Company will endeavor to cause the Registration Statement or such post-effective amendment or Abbreviated Registration Statement to become effective as soon as possible and will advise you promptly and, if requested by you, will confirm such advice in writing, when the Registration Statement or such post-effective amendment or Abbreviated Registration Statement has become effective.

(b) The Company will advise you promptly and, if requested by you, will confirm such advice in writing: (i) of any request by the Commission for amendment of or a supplement to the Registration Statement, any Prepricing Prospectus or the Prospectus or for additional information; (ii) of the issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement or of the suspension of qualification of the Shares for offering or sale in any jurisdiction or the initiation of any proceeding for such purpose; and (iii) within the period of time referred to in paragraph (f) below, of any change in the Company's condition (financial or other), business, prospects, properties, net worth or results of operations, or of the happening of any event, of which the Company has or should reasonably be expected to have knowledge, which makes any statement of a material fact made in the Registration Statement (as then amended) untrue or which requires the making of any additions to or changes in the Registration Statement or the Prospectus (as then amended) in order to state a material fact required by the Act or the regulations thereunder to be stated therein or necessary in order to make the statements therein not misleading, or which makes any statement of a material fact made in the Prospectus (as then amended or supplemented) untrue or which requires the making of any additions to or changes in the Prospectus (as then amended or supplemented) in order to state a material fact required by the Act to be stated therein or necessary in order to make the statements therein, in light of the circumstances under which they were made, not misleading, or of the necessity to amend or supplement the Prospectus (as then amended or supplemented) to comply with the Act or any other law. If at any time the Commission shall issue any stop order suspending the effectiveness of the Registration Statement, the Company will make every reasonable effort to obtain the withdrawal of such order at the earliest possible time.

(c) The Company will furnish to you, without charge, four signed

copies of the registration statement as originally filed with the Commission and of each amendment thereto, including financial statements and all exhibits and Incorporated Documents thereto and will also furnish to you, without charge, such number of conformed copies of the registration statement as originally filed and of each amendment thereto, but without exhibits, and Incorporated Documents thereto as you may reasonably request.

(d) The Company will not (i) file any amendment to the Registration Statement or make any amendment or supplement to the Prospectus of which you shall not previously have been advised or to which you shall reasonably object after being so advised or (ii) so long as, in the reasonable opinion of counsel for the Underwriters, a prospectus is required to be delivered in connection with sales by any Underwriter or dealer, file any information, documents or reports pursuant to the Exchange Act which upon filing becomes an Incorporated Document, without delivering a copy of such information, documents or reports to you, prior to or concurrently with such filing.

(e) Prior to the execution and delivery of this Agreement, the Company has delivered or will deliver to you, without charge, in such quantities as you have reasonably requested or may hereafter reasonably request, copies of each form of the Prepricing Prospectus. The Company consents to the use, in accordance with the provisions of the Act and with the securities or Blue Sky laws of the jurisdictions in which the Shares are offered by the several Underwriters and by dealers, prior to the date of the Prospectus, of each Prepricing Prospectus so furnished by the Company.

(f) As soon after the execution and delivery of this Agreement as possible and thereafter from time to time for such period as in the opinion of counsel for the Underwriters a prospectus is required by the Act to be delivered in connection with sales by any Underwriter or dealer, the Company will expeditiously deliver to each Underwriter and each dealer, without charge, as many copies of the Prospectus (and of any amendment or supplement thereto) as you may reasonably request. The Company

consents to the use of the Prospectus (and of any amendment or supplement thereto) in accordance with the provisions of the Act and with the securities or Blue Sky laws of the jurisdictions in which the Shares are offered by the several Underwriters and by all dealers to whom Shares may be sold, both in connection with the offering and sale of the Shares and for such period of time thereafter as the Prospectus is required by the Act to be delivered in connection with sales by any Underwriter or dealer. If during such period of time any event shall occur that in the judgment of the Company or in the opinion of counsel for the Underwriters is required to be set forth in the Prospectus (as then amended or supplemented) or should be set forth therein in order to make the statements therein, in the light of the circumstances under which they were made, not misleading, or if it is necessary to supplement or amend the Prospectus, or to file under the Exchange Act any document which upon filing becomes an Incorporated Document, to comply with the Act, the Exchange Act or any other law, the Company will forthwith prepare and, subject to the provisions of paragraph (d) above, file with the Commission an appropriate supplement or amendment thereto or Incorporated Document and will expeditiously furnish copies thereof to the Underwriters and dealers in such quantities as you shall request. In the event that the Company and you agree that the Prospectus should be

amended or supplemented, or that a document should be filed under the Exchange Act which upon filing becomes an Incorporated Document, the Company, if requested by you, will promptly issue a press release announcing or disclosing the matters to be covered by the proposed amendment or supplement.

(g) The Company will cooperate with you and with counsel for the Underwriters in connection with the registration or qualification of the Shares for offering and sale by the several Underwriters and by dealers under the securities or Blue Sky laws of such jurisdictions as you may designate and will file such consents to service of process or other documents necessary or appropriate in order to effect such registration or qualification; provided that in no event shall the Company be obligated to qualify to do business in any jurisdiction where it is not now so qualified or to take any action that would subject it to service of process in suits, other than those arising out of the offering or sale of the Shares, in any jurisdiction where it is not now so subject.

(h) The Company will make generally available to its security holders a consolidated earnings statement, which need not be audited, covering a twelve-month period commencing after the effective date of the Registration Statement and ending not later than 15 months thereafter, as soon as practicable after the end of such period, which consolidated earnings statement shall satisfy the provisions of Section 11(a) of the Act.

(i) During the period of five years hereafter, the Company will furnish to you (i) as soon as available, a copy of each report of the Company mailed to stockholders or filed with the Commission and (ii) from time to time such other information concerning the Company as you may reasonably request, provided, however, that the Company shall not be required to furnish any information deemed confidential by the Company.

(j) If this Agreement shall terminate or shall be terminated after execution pursuant to any provisions hereof (otherwise than pursuant to the second paragraph of Section 10 hereof or by notice given by you terminating this Agreement pursuant to Section 10 or Section 11 hereof), or if this Agreement shall be terminated by the Underwriters because of any failure or refusal on the part of the Company to comply with the terms or fulfill any of the conditions of this Agreement, the Company agrees to reimburse the Underwriters for all out-of-pocket expenses (including fees and expenses of counsel for the Underwriters) incurred by you in connection herewith.

(k) The Company will apply the net proceeds from the sale of the Shares substantially in accordance with the description set forth in the Prospectus under "Use of Proceeds."

(l) If Rule 430A of the Act is employed, the Company will timely file the Prospectus pursuant to Rule 424(b) under the Act and will advise you of the time and manner of such filing.



(m) Except as provided in this Agreement, the Company will not (and will not announce or disclose any intention to) sell, offer to sell, contract to sell or otherwise transfer or dispose of any Common Stock (or any securities convertible into or exercisable or exchangeable for Common Stock), other than upon the exercise of options or warrants outstanding on the date hereof and disclosed in the Prospectus, or grant any options or warrants to purchase Common Stock, other than to purchase shares of Common Stock pursuant to option plans existing on the date hereof and disclosed in the Prospectus, for a period of 90 days after the date of the Prospectus, without the prior written consent of Smith Barney Inc.; provided, however, that the Company may sell shares of its

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Common Stock in connection with corporate partnering or collaboration arrangements where such purchaser agrees not to sell, offer to sell or otherwise transfer or dispose of such Common Stock for a period of 90 days after the date of the Prospectus.

(n) The Company has furnished or will furnish to you "lock-up" letters, in form and substance satisfactory to you, signed by each of its current officers and directors and each of its stockholders designated by you.

(o) Except as stated in this Agreement and in the Prepricing Prospectus and Prospectus, the Company has not taken, nor will it take, directly or indirectly, any action designed to or that might reasonably be expected to cause or result in stabilization or manipulation of the price of the Common Stock to facilitate the sale or resale of the Shares.

(p) The Company will timely file with The Nasdaq Stock Market a notification form for listing of additional shares on The Nasdaq National Market with respect to the Shares.

(q) Any Incorporated Documents filed subsequent to the date hereof will, when so filed, be filed in a timely manner and conform with the requirements of the Exchange Act and will not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading.

6. REPRESENTATIONS AND WARRANTIES OF THE COMPANY. The Company represents and warrants to each Underwriter that:

(a) Each Prepricing Prospectus included as part of the registration statement as originally filed or as part of any amendment or supplement thereto, or filed pursuant to Rule 424 under the Act, complied when so filed in all material respects with the provisions of the Act. The Commission has not issued any order preventing or suspending the use of any Prepricing Prospectus.

(b) The Company meets the requirements for use of Form S-3 under the Act. The registration statement in the form in which it became or becomes effective and also in such form as it may be when any post-effective amendment thereto or any Abbreviated Registration Statement shall become effective complied or will comply in all material respects with the provisions of the Act and did not or will not at any such times contain an untrue statement of a material fact or omit to state a material fact required

to be stated therein or necessary to make the statements therein not misleading, and the Prospectus and any supplement or amendment thereto when filed with the Commission under Rule 424(b) under the Act complied or will comply in all material respects with the provisions of the Act and did not or will not at any such times contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein, in light of the circumstances under which they were made, not misleading, except that this representation and warranty does not apply to statements in or omissions from the registration statement or the Prospectus made in reliance upon and in conformity with information relating to any Underwriter furnished to the Company in writing by or on behalf of any Underwriter through you expressly for use therein.

(c) All the outstanding shares of capital stock of the Company have been duly authorized and validly issued, are fully paid and nonassessable, are free of any preemptive or similar rights (other than such rights as shall terminate upon completion of the offering contemplated hereby, as set forth in the Registration Statement and the Prospectus) and have been issued and sold in compliance with all Federal and state securities laws; the Shares have been duly authorized and, when issued and delivered to the Underwriters against payment therefor in accordance with the terms hereof, will be validly issued, fully paid and nonassessable and free of any preemptive or similar rights; and the capital stock of the Company conforms in all material respects to the description thereof in the Registration Statement and the Prospectus.

(d) The Company is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware with full corporate power and authority to own, lease and operate its properties and to conduct its business as described in the Registration Statement and the Prospectus, and is duly registered and qualified to conduct its business and is in good standing in each jurisdiction or place where the nature of its properties or the conduct of its business requires such registration or qualification, except where the failure to so register or qualify does not have a material adverse effect on the condition (financial or other), business, prospects, properties, net worth or results of operations of the Company (a "Material Adverse Effect"). The Company has no subsidiaries (as defined in the Act).

(e) There are no legal or governmental proceedings pending or, to the knowledge of the Company, threatened, against the Company, or to which the Company or any of its properties is subject, that are required to be described in the Registration Statement or the Prospectus but are not described as required. There are no agreements, contracts, indentures, leases or other instruments that are required to be described in the Registration Statement or the Prospectus or to be filed as an exhibit to the Registration Statement that are not described or filed as required by the Act. The Company is not involved in any strike, job action or labor dispute, and to the Company's knowledge no such action or dispute is threatened.

(f) The Company is not (i) in violation of its certificate of incorporation or by-laws, or of any law, ordinance, administrative or governmental rule or regulation applicable to the Company or of any decree of any court or governmental agency or body having jurisdiction over the Company, which violation would have a Material Adverse Effect, or (ii) in default in any material respect in the performance of any obligation, agreement or condition contained in any bond, debenture, note or any other evidence of indebtedness or in any material agreement, indenture, lease or other instrument to which the Company is a party or by which it or any of its properties may be bound.

(g) Neither the issuance and sale of the Shares, the execution, delivery or performance of this Agreement by the Company nor the consummation by the Company of the transactions contemplated hereby (i) requires any consent, approval, authorization or other order of, or registration or filing with, any court, regulatory body, administrative agency or other governmental body, agency or official (except

such as may be required for the registration of the Shares under the Act, which has been or will be effected in accordance with this Agreement, and compliance with the securities or Blue Sky laws of various jurisdictions) or conflicts or will conflict with or constitutes or will constitute a breach of, or a default under, the certificate of incorporation or bylaws, or other organizational documents, of the Company or (ii) conflicts or will conflict with or constitutes or will constitute a breach of, or a default under, any agreement, indenture, lease or other instrument to which the Company is a party or by which the Company or any of its properties may be bound, or violates or will violate any statute, law, regulation or filing or judgment, injunction, order or decree applicable to the Company or any of its properties and which would have a Material Adverse Effect, or will result in the creation or imposition of any lien, charge or encumbrance upon any property or assets of the Company pursuant to the terms of any agreement or instrument to which it is a party or by which it may be bound or to which any of the property or assets of it is subject.

(h) The accountants, Ernst & Young LLP, who have certified or shall certify the financial statements filed or to be filed as part of the Registration Statement or the Prospectus (or any amendment or supplement thereto), or incorporated by reference therein are independent public accountants as required by the Act and the Exchange Act.

(i) The financial statements, together with related schedules and notes forming part of the Registration Statement and the Prospectus (and any amendment or supplement thereto), comply in all material respects with the requirements of the Act and present fairly the financial position, results of operations and changes in stockholders' equity and cash flows of the Company on the basis stated in the Registration Statement at the respective dates or for the respective periods to which they apply; such statements and related schedules and notes have been prepared in accordance with generally accepted accounting principles consistently applied throughout the periods involved, except as disclosed therein; and the other financial data set forth in the Registration Statement and the Prospectus (and any amendment or supplement thereto) are accurately presented and prepared on a basis consistent with such financial statements and the books and records of the Company.

(j) The Company has all requisite power and authority to execute, deliver and perform its obligations under this Agreement; the execution and delivery of, and the performance by the Company of its obligations under, this Agreement have been duly and validly authorized by the Company, and this Agreement has been duly executed and delivered by the Company and constitutes the valid and legally binding agreement of the Company, enforceable against the Company in accordance with its terms, except as rights to indemnity and contribution hereunder may be limited by federal or state securities laws or principles of public policy and subject to the qualification that the enforceability of the Company's obligations hereunder may be limited by bankruptcy, fraudulent conveyance, insolvency, reorganization, moratorium and other laws relating to or affecting creditors' rights generally and by general equitable principles.

(k) Except as disclosed in or contemplated by the Registration Statement and the Prospectus (or any amendment or supplement thereto), subsequent to the respective dates as of which such information is given in the Registration Statement and the Prospectus (or any amendment or supplement thereto), the Company has not incurred any liability or obligation, direct or contingent, or entered into any transaction that is material to the Company, and there has not been any change in the capital stock, or material increase in the short-term or long-term debt, of the Company, or any material adverse change, or any development involving or which may reasonably be expected to involve a prospective material

adverse change, in the condition (financial or otherwise), business, prospects, properties, net worth or results of operations of the Company.

(l) The Company has good and marketable title to all property (real and personal) described in the Prospectus as being owned by it, free and clear of all liens, claims, security interests or other encumbrances except such as are described in the Registration Statement and the Prospectus or in a document filed as an exhibit to the Registration Statement, and all the property described in the Prospectus as being held under lease by the Company is held by it, to the extent material, under valid, subsisting and enforceable leases.

(m) The Company has not distributed and, prior to the later to occur of the Closing Date and completion of the distribution of the Shares, will not distribute any offering material in connection with the offering and sale of the Shares other than the Registration Statement, the Prepricing Prospectus, the Prospectus or other materials, if any, permitted by the Act; provided, however, that nothing contained herein is intended to prohibit the Company from making required or permitted filings with the Commission pursuant to the Exchange Act.

(n) The Company has such permits, licenses, franchises, authorizations and clearances ("Permits") of governmental or regulatory authorities, including, without limitation, the Food and Drug Administration (the "FDA") of the U.S. Department of Health and Human Services and/or any committee thereof, as are necessary to own, lease and operate its properties and to conduct its business in the manner described in the Prospectus, subject to such qualifications as may be set forth in the Prospectus; subject to such qualifications as may be set forth in the Prospectus, the Company has fulfilled and performed all its material obligations with respect to the Permits, and no event has occurred which allows, or after notice or lapse of time would allow, revocation or termination thereof or results in any other material impairment of the rights of the holder of any Permit, subject in each case to such qualification as may be set forth in the Prospectus. Except as described in the Prospectus, none of the Permits contains any restriction that is materially burdensome to the Company.

(o) Except to the extent disclosed in the Registration Statement and the Prospectus (or any amendment or supplement thereto), the clinical, pre-clinical and other studies and tests conducted by or on behalf of or sponsored by the Company or in which the Company or the Company's products under development have participated that are described in the Prospectus or the results of which are referred to in the Prospectus were and, if still pending, are being conducted in accordance with standard medical and scientific research procedures. The descriptions of the results of such studies and tests are accurate and complete in all material respects and fairly present the data derived from such studies and tests, and the Company has no knowledge of any other studies or tests the results of which are inconsistent with or otherwise call into question the results described or referred to in the Prospectus. Except to the extent disclosed in the Registration Statement and the Prospectus (or any amendment or supplement thereto), the Company has operated and currently

is in compliance in all material respects with all applicable FDA rules, regulations and policies. Except to the extent disclosed in the Registration Statement and the Prospectus (or any amendment or supplement thereto), the Company has not received any notices or other correspondence from the FDA or any other governmental agency requiring the termination, suspension or modification of any clinical or pre-clinical studies or tests that are described in the Prospectus or the results of which are referred to in the Prospectus.

(p) The Company has not received nor is it aware of any communication (written or oral) relating to the termination or modification or threatened termination or modification of any of the

9

agreements described or referred to in the Prospectus under the captions "Risk Factors-Dependence on Collaborative Partner; Relationship with the University of Alabama at Birmingham" and "Business--Collaborative Arrangements," nor is it aware of any communication (written or oral) relating to any determination or threatened determination not to renew or extend any agreement described or referred to under such captions at the end of the current term of any such agreement.

(q) The property, assets and operations of the Company comply in all material respects with all applicable federal, state and local laws, rules, orders, decrees, judgments, injunctions, licenses, permits or regulations relating to environmental matters (the "Environmental Laws"). To the Company's knowledge, none of the Company's property, assets or operations is the subject of any federal, state or local investigation evaluating whether any remedial action is needed to respond to a release of any substance regulated by or form the basis of liability under any Environmental Laws (a "Hazardous Material") into the environment or is in contravention of any federal, state, local or foreign law, order or regulation. The Company has not received any notice or claim, nor are there any pending or, to the Company's knowledge, threatened or reasonably anticipated lawsuits or other proceedings against it with respect to violations of an Environmental Law or in connection with the release of any Hazardous Material into the environment. The Company has no knowledge of any material contingent liability in connection with any release of Hazardous Material into the environment.

(r) The Company is insured by insurers of recognized financial responsibility against such losses and risks and in such amount as are customary in the business in which it is engaged. All policies of insurance insuring the Company or its business, assets, employees, officers and directors are in full force and effect, and the Company is in compliance with the terms of such policies in all material respects. There are no claims by the Company under any such policy or instrument as to which any insurance company is denying liability or defending under a reservation of rights clause.

(s) The Company maintains a system of internal accounting controls sufficient to provide reasonable assurances that (i) transactions are executed in accordance with management's general or specific authorization; (ii) transactions are recorded as necessary to permit preparation of financial

statements in conformity with generally accepted accounting principles and to maintain accountability for assets; (iii) access to assets is permitted only in accordance with management's general or specific authorization; and (iv) the recorded accountability for assets is compared with existing assets at reasonable intervals and appropriate action is taken with respect to any differences.

(t) Neither the Company nor, to the Company's knowledge, any employee or agent of the Company has made any payment of funds of the Company or received or retained any funds in violation of any law, rule or regulation, which payment, receipt or retention of funds is of a character required to be disclosed in the Prospectus.

(u) The Company has filed all federal, state, local and foreign tax returns and tax forms required to be filed, such returns and forms are complete and correct in all material respects, and all taxes shown by such returns or otherwise assessed that are due or payable have been paid, except such taxes as are being contested in good faith and as to which adequate reserves have been provided. All payroll withholdings required to be made by the Company with respect to employees have been made. The charges, accruals and reserves on the books of the Company in respect of any tax liability for any year not finally determined are adequate to meet any assessments or reassessments for additional taxes. There have been no tax deficiencies asserted and, to the best knowledge of the Company, no tax deficiency might be

reasonably asserted or threatened against the Company that could, individually or in the aggregate, have a Material Adverse Effect.

(v) No holder of any security of the Company has any right (other than a right that has been waived or any other right set forth in the Prospectus which is not exercisable for a period of at least 90 days after the date of the Prospectus) to require registration of shares of Common Stock or any other security of the Company because of the filing of the registration statement or the consummation of the transactions contemplated by this Agreement and, except as disclosed in the Prospectus, no person has the right to require registration under the Act of any shares of Common Stock or other securities of the Company. No person has the right, contractual or otherwise, to cause the Company to permit such person to underwrite the sale of any of the Shares. Except as described in or contemplated by the Prospectus, there are no outstanding options, warrants or other rights calling for the issuance of, and there are no commitments, plans or arrangements to issue, any shares of capital stock of the Company or any security convertible into or exchangeable or exercisable for capital stock of the Company.

(w) The Company owns or has obtained licenses (which such licenses are enforceable against the Company and, to the Company's best knowledge, the other parties thereto) for the patents, patent applications, inventions, technology, trademarks, trademark registrations, service marks, service mark registrations, trade names, copyrights, trade secrets and rights described in the Prospectus as being owned or used by or licensed to it or necessary for the conduct of its business as currently conducted (collectively, the "Intellectual Property"). Except as set forth in the Prospectus (i) there are no rights of

third parties to any such Intellectual Property; (ii) to the Company's best knowledge there is no infringement by third parties of any such Intellectual Property; (iii) there is no pending or, to the Company's best knowledge, threatened action, suit, proceeding or claim by others challenging the Company's rights in or to any such Intellectual Property, and the Company is unaware of any facts which would form a reasonable basis for any such claim; (iv) there is no pending or, to the Company's best knowledge, threatened action, suit, proceeding or claim by others challenging the validity or scope of any such Intellectual Property, and the Company is unaware of any facts which would form a reasonable basis for any such claim; (v) there is no pending or, to the Company's best knowledge, threatened action, suit, proceeding or claim by others that the Company infringes or otherwise violates any patent, trademark, copyright, trade secret or other proprietary rights of others, and the Company is unaware of any facts which would form a reasonable basis for any such claim; (vi) to the Company's best knowledge there is no patent or patent application which contains claims that dominate or may dominate any Intellectual Property described in the Prospectus as being owned by or licensed to the Company or that is necessary for the conduct of its business as currently conducted or that interferes with the issued or pending claims of any such Intellectual Property; and (vii) there is no prior art of which the Company is aware that may render any patent held by the Company invalid or any patent application held by the Company unpatentable which has not been disclosed to the U.S. Patent and Trademark Office.

(x) The Company is not, and, upon the sale of the Shares to be issued and sold by it hereunder and application of the net proceeds from such sale as described in the Prospectus under the caption "Use of Proceeds," will not be an "investment company" within the meaning of the Investment Company Act of 1940, as amended.

(y) The Company is in compliance with all provisions of Florida Statutes Sec.517.075 and the regulations thereunder, relating to issuers doing business with Cuba.

(z) The Incorporated Documents heretofore filed were filed in a timely manner and, when they were filed (or, if any amendment with respect to any such document was filed, when such document was filed), conformed with the requirements of the Exchange Act and did not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading.

7. INDEMNIFICATION AND CONTRIBUTION. (a) The Company agrees to indemnify and hold harmless each Underwriter and each person, if any, who controls any Underwriter within the meaning of Section 15 of the Act or Section 20 of the Exchange Act from and against any and all losses, claims, damages, liabilities and expenses (including reasonable costs of investigation) arising out of or based upon any untrue statement or alleged untrue statement of a material fact contained in or in the Registration Statement or in any amendment thereto, or arising out of or based upon any omission or alleged omission to state therein a

material fact required to be stated therein or necessary to make the statements therein not misleading, or arising out of or based upon any untrue statement or alleged untrue statement of a material fact contained in any Prepricing Prospectus or in the Prospectus or in any amendment or supplement thereto, or arising out of or based upon any omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein, in light of the circumstances under which they were made, not misleading, except insofar as such losses, claims, damages, liabilities or expenses arise out of or are based upon any untrue statement or omission or alleged untrue statement or omission which has been made therein or omitted therefrom in reliance upon and in conformity with the information relating to such Underwriter furnished in writing to the Company by or on behalf of any Underwriter expressly for use in connection therewith; provided, however, that the indemnification contained in this paragraph (a) with respect to any Prepricing Prospectus shall not inure to the benefit of any Underwriter (or to the benefit of any person controlling such Underwriter) on account of any such loss, claim, damage, liability or expense arising from the sale of Shares by such Underwriter to any person if (i) a copy of the Prospectus shall not have been delivered or sent to such person within the time required by the Act and the untrue statement or alleged untrue statement or omission or alleged omission of a material fact contained in such Prepricing Prospectus was corrected in the Prospectus and (ii) the Company has delivered the Prospectus to the several Underwriters in requisite quantity on a timely basis to permit such delivery or sending. The foregoing indemnity agreement shall be in addition to any liability which the Company may otherwise have.

(b) If any action, suit or proceeding shall be brought against any Underwriter or any person controlling any Underwriter in respect of which indemnity may be sought against the Company, such Underwriter or such controlling person shall promptly notify the Company, and the Company shall assume the defense thereof, including the employment of counsel and payment of all fees and expenses. Such Underwriter or any such controlling person shall have the right to employ separate counsel in any such action, suit or proceeding and to participate in the defense thereof, but the fees and expenses of such counsel shall be at the expense of such Underwriter or such controlling person unless (i) the Company has agreed in writing to pay such fees and expenses, (ii) the Company has failed to assume the defense and employ counsel or (iii) the named parties to any such action, suit or proceeding (including any impleaded parties) include both such Underwriter or such controlling person and the Company and such Underwriter or such controlling person shall have been advised by its counsel that representation of such indemnified party and the Company by the same counsel would be inappropriate under applicable standards of professional conduct (whether or not such representation by the same counsel has been proposed) due to actual or potential differing interests between them (in which case the Company shall not have the right to assume the defense of such action, suit or proceeding on behalf of such Underwriter or such controlling person). It is understood, however, that the Company shall, in connection with any one such action, suit

or proceeding or separate but substantially similar or related actions, suits or proceedings in the same jurisdiction arising out of the same general allegations or circumstances, be liable for the reasonable fees and expenses of only one separate firm of attorneys (in addition to any local counsel, as deemed necessary or appropriate) at any time for all such Underwriters and controlling



persons not having actual or potential differing interests with you or among themselves, which firm shall be designated in writing by Smith Barney Inc., and that all such fees and expenses shall be reimbursed as they are incurred. The Company shall not be liable for any settlement of any such action, suit or proceeding effected without its written consent, but if settled with such written consent, or if there be a final judgment for the plaintiff in any such action, suit or proceeding, the Company agrees to indemnify and hold harmless any Underwriter and any such controlling person, to the extent provided in the preceding paragraph, from and against any loss, claim, damage, liability or expense by reason of such settlement or judgment.

(c) Each Underwriter agrees, severally and not jointly, to indemnify and hold harmless the Company, its directors, its officers who sign the Registration Statement, and any person who controls the Company within the meaning of Section 15 of the Act or Section 20 of the Exchange Act, to the same extent as the foregoing indemnity from the Company to each Underwriter, but only with respect to information relating to such Underwriter furnished in writing to the Company by or on behalf of such Underwriter expressly for use in the Registration Statement, the Prospectus or any Prepricing Prospectus, or any amendment or supplement thereto. If any action, suit or proceeding shall be brought against the Company, any of its directors, any such officer or any such controlling person based on the Registration Statement, the Prospectus or any Prepricing Prospectus, or any amendment or supplement thereto, and in respect of which indemnity may be sought against any Underwriter pursuant to this paragraph (c), such Underwriter shall have the rights and duties given to the Company by paragraph (b) above (except that if the Company shall have assumed the defense thereof such Underwriter shall not be required to do so, but may employ separate counsel therein and participate in the defense thereof, but the fees and expenses of such counsel shall be at such Underwriter's expense), and the Company, its directors, any such officer, and any such controlling person shall have the rights and duties given to the Underwriters by paragraph (b) above. The foregoing indemnity agreement shall be in addition to any liability which the Underwriters may otherwise have.

(d) If the indemnification provided for in this Section 7 is unavailable to an indemnified party under paragraphs (a) or (c) hereof in respect of any losses, claims, damages, liabilities or expenses referred to therein, then an indemnifying party, in lieu of indemnifying such indemnified party, shall contribute to the amount paid or payable by such indemnified party as a result of such losses, claims, damages, liabilities or expenses (i) in such proportion as is appropriate to reflect the relative benefits received by the Company on the one hand and the Underwriters on the other hand from the offering of the Shares, or (ii) if the allocation provided by clause (i) above is not permitted by applicable law, in such proportion as is appropriate to reflect not only the relative benefits referred to in clause (i) above but also the relative fault of the Company on the one hand and the Underwriters on the other hand in connection with the statements or omissions that resulted in such losses, claims, damages, liabilities or expenses, as well as any other relevant equitable considerations. The relative benefits received by the Company on the one hand and the Underwriters on the other hand shall be deemed to be in the same proportion as the total net proceeds from the offering (before deducting expenses) received by the Company bear to the total underwriting discounts and commissions received by the Underwriters, in each case as set forth in the table on the cover page of the Prospectus; provided that, in the event that the Underwriters shall have purchased any Additional Shares hereunder, any determination of the relative benefits received by the Company and the Underwriters from the offering of the Shares shall include the net proceeds (before deducting expenses) received by the Company, and the underwriting discounts and commissions received by the Underwriters,

from the sale of such Additional Shares, in each case computed on the basis of the respective amounts set forth in the notes to the table on the cover page of the Prospectus. The relative fault of the Company on the one hand and the Underwriters on the other hand shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission or alleged omission to state a material fact relates to information supplied by the Company on the one hand or by the Underwriters on the other hand and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission.

(e) The Company and the Underwriters agree that it would not be just and equitable if contribution pursuant to this Section 7 were determined by a pro rata allocation (even if the Underwriters were treated as one entity for such purpose) or by any other method of allocation that does not take account of the equitable considerations referred to in paragraph (d) above. The amount paid or payable by an indemnified party as a result of the losses, claims, damages, liabilities and expenses referred to in paragraph (d) above shall be deemed to include, subject to the limitations set forth above, any legal or other expenses reasonably incurred by such indemnified party in connection with investigating any claim or defending any such action, suit or proceeding. Notwithstanding the provisions of this Section 7, no Underwriter shall be required to contribute any amount in excess of the amount by which the total price of the Shares underwritten by it and distributed to the public exceeds the amount of any damages which such Underwriter has otherwise been required to pay by reason of such untrue or alleged untrue statement or omission or alleged omission. No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. The Underwriters' obligations to contribute pursuant to this Section 7 are several in proportion to the respective numbers of Firm Shares set forth opposite their names in Schedule I hereto (or such numbers of Firm Shares increased as set forth in Section 10 hereof) and not joint.

(f) No indemnifying party shall, without the prior written consent of the indemnified party, effect any settlement of any pending or threatened action, suit or proceeding in respect of which any indemnified party is or could have been a party and indemnity could have been sought hereunder by such indemnified party, unless such settlement includes an unconditional release of such indemnified party from all liability on claims that are the subject matter of such action, suit or proceeding.

(g) Any losses, claims, damages, liabilities or expenses for which an indemnified party is entitled to indemnification or contribution under this Section 7 shall be paid by the indemnifying party to the indemnified party as such losses, claims, damages, liabilities or expenses are incurred. The indemnity and contribution agreements contained in this Section 7 and the representations and warranties of the Company set forth in this Agreement shall remain operative and in full force and effect, regardless of (i) any investigation made by or on behalf of any Underwriter or any person controlling any Underwriter, the Company, its directors or officers or any person controlling the Company, (ii) acceptance of any Shares and payment therefor hereunder, and (iii) any termination of this Agreement. A successor to any Underwriter or any person controlling any Underwriter, or to the Company, its directors or officers, or any person controlling the Company, shall be entitled to the benefits of the indemnity, contribution and reimbursement agreements contained in this Section 7.

8. CONDITIONS OF UNDERWRITERS' OBLIGATIONS. The several obligations of the Underwriters to purchase the Firm Shares hereunder are subject to the following conditions:

(a) If, at the time this Agreement is executed and delivered, it is necessary for the registration statement or a post-effective amendment thereto or an Abbreviated Registration Statement to

be declared effective before the offering of the Shares may commence, the registration statement or such post-effective amendment or Abbreviated Registration Statement shall have become effective not later than 5:30 P.M., New York City time, on the date hereof, or at such later date and time as shall be consented to in writing by you, and all filings, if any, required by Rules 424 and 430A under the Act shall have been timely made.

(b) Subsequent to the effective date of this Agreement, there shall not have occurred (i) any change, or any development involving a prospective change, in or affecting the condition (financial or other), business, prospects, properties, net worth, or results of operations of the Company not contemplated by the Prospectus, which in your opinion would materially, adversely affect the market for the Shares, or (ii) any event or development relating to or involving the Company, or any officer or director of the Company, which makes any statement made in the Prospectus untrue or which, in the opinion of the Company and its counsel or the Underwriters and their counsel, requires the making of any addition to or change in the Prospectus in order to state a material fact required by the Act or any other law to be stated therein or necessary in order to make the statements therein not misleading, if amending or supplementing the Prospectus to reflect such event or development would, in your opinion, materially, adversely affect the market for the Shares.

(c) You shall have received on the Closing Date an opinion of Brobeck Phleger & Harrison LLP, counsel for the Company, dated the Closing Date and addressed to you, that:

(i) The Company is a corporation duly incorporated and validly existing in good standing under the laws of the State of Delaware with full corporate power and authority to own, lease and operate its properties and to conduct its business as described in the Registration Statement and the Prospectus (and any amendment or supplement thereto), and is duly registered and qualified to conduct its business and is in good standing in each jurisdiction or place where the nature of its properties or the conduct of its business requires such registration or qualification, except where the failure so to register or qualify does not have a Material Adverse Effect;

(ii) The authorized capital stock of the Company is as set forth under the caption "Capitalization" in the Prospectus;

(iii) All the shares of capital stock of the Company outstanding prior to the issuance of the Shares have been duly authorized and validly issued, are fully paid and nonassessable and were issued and, based solely as to factual matters on the representations and warranties of the Company and the purchasers set forth in the applicable purchase agreement, sold in compliance with all applicable federal and state securities laws;

(iv) The Shares have been duly authorized and, when issued and delivered to the Underwriters against payment therefor in accordance with the terms hereof, will be validly issued, fully paid and nonassessable and free of (A) any preemptive rights arising under the Company's certificate of incorporation or the Delaware General Corporation Law or (B) to the knowledge of such counsel, similar rights that entitle or will entitle any person to acquire any shares of capital stock of the Company upon the issuance and sale of the Shares by the Company;

(v) The form of certificate for the Shares conforms in all material respects to the requirements of the Delaware General Corporation

Law;

15

(vi) The Registration Statement and all post-effective amendments, if any, have become effective under the Act and, to the knowledge of such counsel, no stop order suspending the effectiveness of the Registration Statement has been issued and no proceedings for that purpose are pending before or contemplated by the Commission; and any required filing of the Prospectus pursuant to Rule 424(b) has been made in accordance with Rule 424(b);

(vii) The Company has the corporate power and authority to enter into this Agreement and to issue, sell and deliver the Shares to the Underwriters as provided herein, and this Agreement has been duly authorized, executed and delivered by the Company;

(viii) To the knowledge of such counsel, the Company is not in default in the performance of any obligation, agreement or condition contained in any bond, debenture, note or other evidence of indebtedness included as an exhibit to the Registration Statement or any Incorporated Document, which default would have a Material Adverse Effect;

(ix) Neither the offer, sale or delivery of the Shares, the execution, delivery or performance of this Agreement, compliance by the Company with the provisions hereof nor consummation by the Company of the transactions contemplated hereby conflicts or will conflict with or constitutes or will constitute a breach of, or a default under, the certificate of incorporation or bylaws, or other organizational documents, of the Company or any agreement, indenture, lease or other instrument to which the Company is a party or by which the Company or any of its properties is bound that is an exhibit to the Registration Statement, or is known to such counsel after reasonable inquiry, or to the knowledge of such counsel will result in the creation or imposition of any lien, charge or encumbrance upon any property or assets of the Company, nor will any such action result in any violation of any existing law, regulation, ruling (assuming compliance with all applicable state securities and Blue Sky laws), judgment, injunction, order or decree known to such counsel and applicable to the Company or any of its properties;

(x) No consent, approval, authorization or other order of, or registration or filing with, any court, regulatory body, administrative agency or other governmental body, agency, or official is required on the part of the Company (except as have been obtained under the Act or such as may be required under state securities or Blue Sky laws governing the purchase and distribution of the Shares) for the valid issuance and sale of the Shares to the Underwriters as contemplated by this Agreement;

(xi) The Registration Statement and the Prospectus and any supplements or amendments thereto (except for the financial statements and

the notes thereto and the schedules and other financial and statistical data included therein, as to which such counsel need not express any opinion) comply as to form in all material respects with the requirements of the Act;

(xii) To the knowledge of such counsel, (A) there are no legal or governmental proceedings pending or threatened against the Company, or to which the Company or any of its properties is subject, which are required to be described in the Registration Statement or Prospectus (or any amendment or supplement thereto) that are not described as required and (B) there are no agreements, contracts, indentures, leases or other instruments that are required to be described in the Registration Statement or the Prospectus (or any amendment or supplement thereto) or to be filed as an exhibit to the Registration Statement that are not described or filed as required, as the case may be;

16

(xiii) The Company has all necessary Permits (except where the failure to so have any such Permits, individually or in the aggregate, would not have a Material Adverse Effect to own its properties and to conduct its business as now being conducted as described in the Prospectus;

(xiv) The statements in: (A) the Registration Statement and the Prospectus under the captions "Risk Factors-Control by Existing Management and Stockholders; Effect of Certain Anti-Takeover Considerations", "Risk Factors-Shares Eligible for Future Sale", and (B) the Annual Report of the Company on Form 10-K/A for the fiscal year ended December 31, 1995 under the captions "Business-Properties" and "Executive Compensation-Employment Agreement", insofar as they are descriptions of specific contracts, agreements or other legal documents to which the Company is a party, or refer to statements of law or legal conclusions applicable to the Company, are accurate in all material respects and present fairly the information purported to be shown;

(xv) Except as described in the Prospectus, such counsel does not know of any holder of any securities of the Company or any other person who has the right, contractual or otherwise, to cause the Company to sell or otherwise issue to them, or to permit them to underwrite the sale of, any of the Shares or the right to have any Common Stock or other securities of the Company included in the Registration Statement or the right, as a result of the filing of the Registration Statement, to require the Company to register under the Act any shares of Common Stock or other securities of the Company, and any registration rights in connection with the offering contemplated hereby have been waived;

(xvi) The Company is not an "investment company" or a person "controlled" by an "investment company" within the meaning of the Investment Company Act of 1940, as amended; and

(xvii) All documents incorporated by reference in the Prospectus (excluding any financial statements and footnotes thereto and other financial or statistical data included or incorporated by reference

therein, as to which such counsel need express no opinion), at the time they were filed with the Commission, complied as to form in all material respects with the requirements of the Exchange Act.

In addition, such counsel shall state that although such counsel does not assume any responsibility for the accuracy, completeness or fairness of the statements in the Registration Statement, such counsel has participated in the preparation of the Registration Statement and the Prospectus, including review and discussion of the contents thereof with representatives of the Underwriters and their counsel, officers and representatives of the Company, and representatives of the independent certified public accountants of the Company, and nothing has come to the attention of such counsel that has caused it to believe that the Registration Statement, at the time the Registration Statement became effective, contained an untrue statement of a material fact or omitted to state a material fact required to be stated therein or necessary to make the statements therein not misleading, or that the Prospectus, as of its date and as of the Closing Date or the Option Closing Date, as the case may be, contained or contains an untrue statement of a material fact or omitted or omits to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading, or that any amendment or supplement to the Prospectus, as of its date, and as of the Closing Date or the Option Closing Date, as the case may be, contained or contains an untrue statement of a material fact or omitted or omits to state a material fact necessary in order to make the statements therein, in light of the

circumstances under which they were made, not misleading (it being understood that such counsel need express no opinion with respect to the financial statements and the notes thereto and the schedules and other financial and statistical data included in the Registration Statement or the Prospectus).

In rendering their opinion as aforesaid, counsel may rely as to matters of fact upon certificates of officers of the Company and public officials and upon an opinion or opinions, each dated the Closing Date, of other counsel retained by them or the Company as to laws of any jurisdiction other than the United States or the State of New York or the corporation law of the State of Delaware, provided that (1) each such local counsel is acceptable to the Underwriters, (2) such reliance is expressly authorized by each opinion so relied upon and a copy of each such opinion is delivered to the Underwriters and is, in form and substance, satisfactory to them and counsel for the Underwriters and (3) counsel shall state in their opinion that they believe that they and the Underwriters are justified in relying thereon.

(d) You shall have received on the Closing Date an opinion of Pollock, Vande Sande & Priddy, R.L.L.P., patent counsel for the Company, dated the Closing Date and addressed to you, that:

(i) to the knowledge of such counsel after reasonable inquiry, the Company owns or has obtained licenses for all applications relating to the Intellectual Property described in the Prospectus as being owned or used by or licensed to the Company;

(ii) to the best knowledge of such counsel after reasonable inquiry (A) except as described in the Prospectus, there are no rights of third parties to any Intellectual Property described in the Prospectus as being owned by or licensed to the Company or that is necessary for the conduct of its business; (B) there is no infringement by third parties of any such Intellectual Property; (C) there is no pending or threatened action, suit, proceeding or claim by others challenging the rights of the Company in or to such Intellectual Property, and such counsel is unaware of any facts which would form a reasonable basis for any such claim; (D) there is no pending or threatened action, suit, proceeding or claim by others challenging the validity or scope of such Intellectual Property, and such counsel is unaware of any facts which would form a reasonable basis for any such claim; (E) there is no pending or threatened action, suit, proceeding or claim by others that the Company infringes or otherwise violates any patent, trademark, copyright, trade secret or other proprietary right of others, and such counsel is unaware of any facts which would form a reasonable basis for any such claim; (F) there is no patent or patent application which contains claims that dominate or may dominate any Intellectual Property described in the Prospectus as being owned or used by or licensed to the Company or that is necessary for the conduct of its business or that interferes with the issued or pending claims of any such Intellectual Property; and (G) there is no prior art that may render any patent held by the Company invalid or any patent application held by the Company unpatentable which has not been disclosed to the U.S. Patent and Trademark Office; and

(iii) the statements in: (A) the Prospectus under the captions "Risk Factors--Uncertainty of Protection of Patents and Proprietary Rights", "Business--Patents and Proprietary Information" and other references therein to patent and licensing matters, and (B) the Annual Report of the Company on Form 10-K for the fiscal year ended December 31, 1995 under the caption "Business-Patents and Proprietary Information," and other references therein to patent and licensing matters, insofar as such statements constitute a summary of legal matters, documents or proceedings referred to therein, are accurate and fairly present the information purported to be shown.

(e) You shall have received on the Closing Date an opinion of Fenwick & West, regulatory counsel for the Company, dated the Closing Date and addressed to you, to the effect that the statements in: (A) the Prospectus under the captions "Risk Factors--Uncertainty Associated with Preclinical and Clinical Testing," "Risk Factors--Government Regulation; No Assurance of Product Approval," and "Business--Government Regulation" and (B) the Annual Report of the Company on Form 10-K/A for the fiscal year ended December 31, 1995 under the caption "Business-Government Regulation", insofar as such statements constitute descriptions or summaries of the Federal Food, Drug, and Cosmetic Act ("FDC Act") or the regulations of the Food and Drug Administration ("FDA") or of relevant FDA requirements or procedures or the Form 483's, are accurate and complete in all material respects and fairly present the information set forth therein shown in light of the circumstances under which they were made.

(f) You shall have received on the Closing Date an opinion of Bradley, Arant, Rose & White, counsel for the Company, dated the Closing Date and addressed to you, to the effect that the statements in: (A) the Registration Statement and the Prospectus under the caption "Business-Legal Proceedings" and (B) the Annual Report of the Company on Form 10K/A for the fiscal year ended December 31, 1995 under the captions "Legal Proceedings" insofar as they describe legal proceedings, or refer to statements of laws or legal conclusions applicable to the Company, are accurate in all material respects and present fairly the information therein.

(g) You shall have received on the Closing Date an opinion of Dewey Ballantine, counsel for the Underwriters, dated the Closing Date and addressed to you, with respect to the matters referred to in clauses (iv) (other than subclause (B) thereof), (vi), (vii), (xi) and the penultimate paragraph of Section 8(c) hereof and such other related matters as you may request.

(h) You shall have received letters addressed to you and dated the date hereof and the Closing Date from Ernst & Young LLP, independent certified public accountants, substantially in the forms heretofore approved by you.

(i) (i) No stop order suspending the effectiveness of the Registration Statement shall have been issued and no proceedings for that purpose shall have been instituted or, to the knowledge of the Company, contemplated by the Commission at or prior to the Closing Date and any request of the Commission for additional information (to be included in the registration statement or the Prospectus or any Prepricing Prospectus or otherwise) shall have been complied with; (ii) there shall not have been any change in the capital stock of the Company nor any material increase in the short-term debt (other than in the ordinary course of business) or long-term debt of the Company from that set forth or contemplated in the Registration Statement or the Prospectus (or any amendment or supplement thereto); (iii) there shall not have been, since the respective dates as of which information is given in the Registration Statement and the Prospectus (or any amendment or supplement thereto), except as may otherwise be stated in or contemplated by the Registration Statement and Prospectus (or any amendment or supplement thereto), any material adverse change in the condition (financial or otherwise), business, prospects, properties, net worth or results of operations of the Company; (iv) the Company shall not have any liabilities or obligations, direct or contingent (whether or not in the ordinary course of business), that are material to the Company other than those reflected in or contemplated by the Registration Statement or the Prospectus (or any amendment or supplement thereto); and (v) all the representations and warranties of the Company contained in this Agreement shall be true and correct in all material respects on and as of the date hereof and on and as of the Closing Date as if made on and as of the Closing Date, and you shall have received a certificate, dated the Closing Date and signed by the chief executive officer and the chief financial officer



(j) The Company shall not have failed at or prior to the Closing Date to have performed or complied with any of its agreements herein contained and required to be performed or complied with by it hereunder at or prior to the Closing Date.

(k) The Company shall have furnished or caused to be furnished to you such further certificates and documents as you shall have reasonably requested.

All such opinions, certificates, letters and other documents will be in compliance with the provisions hereof only if they are satisfactory in form and substance to you and counsel for the Underwriters.

Any certificate or document signed by any officer of the Company and delivered to you, or to counsel for the Underwriters, shall be deemed a representation or warranty by the Company to each Underwriter as to the statements made therein.

The several obligations of the Underwriters to purchase Additional Shares hereunder are subject to the satisfaction on and as of any Option Closing Date of the conditions set forth in this Section 8, except that, if any Option Closing Date is other than the Closing Date, the certificates, opinions and letters referred to in paragraphs (c) through (i) and paragraph (k) shall be dated the Option Closing Date in question and the opinions called for by paragraphs (c), (d), (e), (f) and (g) shall be revised to reflect the sale of Additional Shares.

9. EXPENSES. The Company agrees to pay the following costs and expenses and all other costs and expenses incident to the performance by it of its obligations hereunder: (i) the preparation, printing or reproduction, and filing with the Commission of the registration statement (including financial statements and exhibits thereto), each Prepricing Prospectus, the Prospectus, and each amendment or supplement to any of them; (ii) the printing (or reproduction) and delivery (including postage, air freight charges and charges for counting and packaging) of such copies of the registration statement, each Prepricing Prospectus, the Prospectus, the Incorporated Documents and all amendments or supplements to any of them as may be reasonably requested for use in connection with the offering and sale of the Shares; (iii) the preparation, printing, authentication, issuance and delivery of certificates for the Shares, including any stamp taxes in connection with the offering of the Shares; (iv) the printing (or reproduction) and delivery of this Agreement, the preliminary and supplemental Blue Sky Memoranda and all other agreements or documents printed (or reproduced) and delivered in connection with the offering of the Shares; (v) the additional listing of the Shares on The Nasdaq National Market; (vi) the registration or qualification of the Shares for offer and sale under the securities or Blue Sky laws of the several states as provided in Section 5(g) hereof (including the reasonable fees, expenses and disbursements of counsel for the Underwriters relating to the preparation, printing or reproduction, and delivery of the preliminary and supplemental Blue Sky Memoranda and such registration and qualification); (vii) the filing fees and the reasonable fees and expenses of counsel for the Underwriters in connection with any filings required to be made with the National Association of Securities Dealers, Inc. in connection with the offering; (viii) the transportation and other expenses incurred by or on behalf of representatives of the Company in connection with presentations to prospective purchasers of the Shares; (ix) the fees and expenses of the Company's accountants and the fees and expenses of counsel (including local and special counsel) for the Company; and (x) the performance by the Company of its other obligations under this Agreement.

10. EFFECTIVE DATE OF AGREEMENT. This Agreement shall become effective: (i) upon the execution and delivery hereof by the parties hereto; or (ii) if, at the time this Agreement is executed and delivered, it is necessary for the registration statement or a post-effective amendment thereto or an Abbreviated Registration Statement to be declared or, in the case of any Abbreviated Registration Statement, to become effective before the offering of the Shares may commence, when notification of the effectiveness of the registration statement or such post-effective amendment has been released by the Commission or such Abbreviated Registration Statement has become effective pursuant to Rule 462(b) under the Act. Until such time as this Agreement shall have become effective, it may be terminated by the Company, by notifying you, or by you, by notifying the Company.

If any Underwriter shall fail or refuse to purchase Firm Shares which it is obligated to purchase on the Closing Date and arrangements satisfactory to the non-defaulting Underwriters and the Company for the purchase of such Firm Shares by the non-defaulting Underwriters or by another party or parties satisfactory to the non-defaulting Underwriters and the Company are not made within 36 hours after such default, this Agreement shall terminate without liability on the part of the non-defaulting Underwriters or the Company. In any such case which does not result in termination of this Agreement, either the non-defaulting Underwriters or the Company shall have the right to postpone the Closing Date, but in no event for longer than seven (7) days, in order that the required changes, if any, in the Registration Statement and the Prospectus or any other documents or arrangements may be effected. Any action taken under this paragraph shall not relieve the defaulting Underwriter from liability in respect of such default under this Agreement. The term "Underwriter" as used in this Agreement includes, for all purposes of this Agreement, any party not identified in this Agreement who purchases Firm Shares which a defaulting Underwriter is obligated, but fails or refuses, to purchase.

Any notice under this Section 10 may be given by telegram, telecopy or telephone but shall be subsequently confirmed by letter.

11. TERMINATION OF AGREEMENT. This Agreement shall be subject to termination in your absolute discretion, without liability on the part of any Underwriter to the Company, by notice to the Company, if prior to the Closing Date or any Option Closing Date (if different from the Closing Date and then only as to the Additional Shares), as the case may be, (i) trading in securities generally on the New York Stock Exchange, the American Stock Exchange or The Nasdaq National Market shall have been suspended or materially limited, (ii) a general moratorium on commercial banking activities in New York shall have been declared by either federal or state authorities, or (iii) there shall have occurred any outbreak or escalation of hostilities or other international or domestic calamity, crisis or change in political, financial or economic conditions, the effect of which on the financial markets of the United States is such as to make it, in your judgment, impracticable or inadvisable to commence or continue the offering of the Shares at the offering price to the public set forth on the cover page of the Prospectus or to enforce contracts for the resale of the Shares by the Underwriters. Notice of such termination may be given by telegram, telecopy or telephone and shall be subsequently confirmed by letter.

12. INFORMATION FURNISHED BY THE UNDERWRITERS. The statements set forth in the last paragraph on the cover page, the stabilization and passive market making legends on the inside front cover page and the statements in the first, third and seventh paragraphs under the caption "Underwriting" in any Prepricing Prospectus and in the Prospectus constitute the only information furnished by or on behalf of the Underwriters as such information is referred to in Sections 6(b) and 7 hereof.

13. MISCELLANEOUS. Except as otherwise provided in Sections 5, 10 and 11 hereof, notice given pursuant to any provision of this Agreement shall be in writing and shall be delivered (i) if to the Company, at the office of the Company at 2190 Parkway Lake Drive, Birmingham, Alabama 35244, Attention: Charles F. Bugg, Ph.D., President and Chief Executive Officer, with a copy to Brobeck, Phleger & Harrison LLP, 1301 Avenue of the Americas, New York, New York 10019, Attention: Richard R. Plumridge, Esq., or (ii) if to you, care of Smith Barney Inc., 388 Greenwich Street, New York, New York 10013, Attention: Manager, Investment Banking Division, with a copy to Dewey Ballantine, 1301 Avenue of the Americas, New York, New York 10019, Attention: Frederick W. Kanner, Esq.

This Agreement has been and is made solely for the benefit of the several Underwriters, the Company, its directors, its officers who sign the Registration Statement and the controlling persons referred to in Section 7 hereof and, to the extent provided herein, their respective successors and assigns and no other person shall acquire or have any right under or by virtue of this Agreement. Neither the term "successor" nor the term "successors and assigns" as used in this Agreement shall include a purchaser from any Underwriter of any of the Shares in his status as such purchaser.

14. APPLICABLE LAW; COUNTERPARTS. This Agreement shall be governed by and construed in accordance with the laws of the State of New York applicable to contracts made and to be performed within the State of New York.

This Agreement may be signed in various counterparts which together constitute one and the same instrument. If signed in counterparts, this Agreement shall not become effective unless at least one counterpart hereof shall have been executed and delivered on behalf of each party hereto.

Please confirm that the foregoing correctly sets forth the agreement between the Company and the several Underwriters.

Very truly yours,

BIOCRIST PHARMACEUTICALS, INC.

By: \_\_\_\_\_

Charles E. Bugg  
President and Chief Executive Officer

Confirmed as of the date first above-mentioned on behalf of themselves and the other several Underwriters named in Schedule I hereto.

SMITH BARNEY INC.  
NEEDHAM & COMPANY, INC.

By: SMITH BARNEY INC.

By: \_\_\_\_\_

Managing Director

SCHEDULE I

BIOCRIST PHARMACEUTICALS, INC.

Underwriter -----	Number of Firm Shares -----
Smith Barney Inc. . . . .	
Needham & Co., Inc. . . . .	
	-----
Total . . . . .	2,000,000
. . . . .	=====



[BROBECK, PHLEGER & HARRISON LLP LOGO]

September 24, 1996

Biocryst Pharmaceuticals, Inc.  
2190 Parkway Lake Drive  
Birmingham, Alabama 35244

Ladies and Gentlemen:

We have assisted in the preparation and filing by Biocryst Pharmaceuticals, Inc. (the "Company") of a Registration Statement on Form S-3, as amended through August 21, 1966 (the "Registration Statement"), with the Securities and Exchange Commission, relating to the sale of up to 2,300,000 shares (the "Shares") of Common Stock, \$0.01 par value (the "Common Stock"), of the Company. A form of underwriting agreement (the "Underwriting Agreement") is filed as an exhibit to the Registration Statement.

We have examined such records and documents and have made such examination of laws as we considered necessary to form a basis for the opinion set forth herein. In our examination, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as originals, and the conformity with the originals of all documents submitted to us as copies thereof.

Based upon and subject to the foregoing, we are of the opinion that the Shares have been duly authorized and, when sold and paid for in accordance with the terms of the Underwriting Agreement, well be validly issued, fully paid and nonassessable.

We hereby consent to the use of our name in the Registration Statement under the caption "Legal Matters" in the related Prospectus and consent to the filing of this opinion as an exhibit thereto.

Very truly yours,

/s/ BROBECK, PHLEGER & HARRISON LLP  
BROBECK, PHLEGER & HARRISON LLP

CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the reference to our firm under the captions "Experts" and "Selected Financial Data" and to the use of our report dated January 24, 1996, in Amendment No. 2 to the Registration Statement (Form S-3 No. 333-07183) and related Prospectus of BioCryst Pharmaceuticals, Inc. for the registration of 2,300,000 shares of its common stock.

/s/ERNST & YOUNG LLP

Birmingham, Alabama  
September 20, 1996



CONSENT OF EXPERTS

We hereby consent to the reference to our firm under the caption "Experts" in the Prospectus which is part of the Registration Statement.

/s/ Burton A. Amernick  
POLLOCK, VANDE SANDE & PRIDDY,  
R.L.L.P.

Washington, D.C.  
September 24, 1996