

REGISTRATION NO. 333-87669

SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

AMENDMENT NO. 4  
TO

FORM S-3

REGISTRATION STATEMENT  
UNDER THE SECURITIES ACT OF 1933

BIOCRYST 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 AND CHIEF EXECUTIVE OFFICER  
BIOCRYST 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:

RICHARD R. PLUMRIDGE, ESQ.  
LUCI STALLER ALTMAN, ESQ.  
BRUCE E. CUNNINGHAM, ESQ.  
BROBECK, PHLEGER & HARRISON LLP  
370 INTERLOCKEN BLVD., SUITE 500  
BROOMFIELD, COLORADO 80021  
(303) 410-2000

JOHN W. WHITE, ESQ.  
CRAVATH, SWAINE & MOORE  
WORLDWIDE PLAZA  
825 EIGHTH AVENUE  
NEW YORK, NEW YORK 10019-7475  
(212) 474-1000

APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO THE PUBLIC: As soon as practicable on or after this Registration Statement is declared effective.

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, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. / /

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

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

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

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THE INFORMATION IN THIS PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. WE MAY NOT SELL THESE SECURITIES UNTIL THE REGISTRATION STATEMENT FILED WITH THE SECURITIES AND EXCHANGE COMMISSION IS EFFECTIVE. THIS PROSPECTUS IS NOT AN OFFER TO SELL THESE SECURITIES AND IT IS NOT SOLICITING AN OFFER TO BUY THESE SECURITIES IN ANY STATE WHERE THE OFFER OR SALE IS NOT PERMITTED.

SUBJECT TO COMPLETION, DATED NOVEMBER 1, 1999

P R O S P E C T U S

2,000,000 SHARES

[LOGO]

COMMON STOCK  
\$ PER SHARE  
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We are selling 2,000,000 shares of our common stock. We have granted the underwriters a 30-day option to purchase up to an additional 300,000 shares to cover over-allotments, if any.

Our common stock is quoted on the Nasdaq National Market under the symbol "BCRX." The last reported sale price of our common stock on the Nasdaq National Market on October 8, 1999 was \$ per share.

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INVESTING IN OUR COMMON STOCK INVOLVES CERTAIN RISKS. SEE "RISK FACTORS" BEGINNING ON PAGE 6.

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

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	PER SHARE	TOTAL
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Public Offering Price	\$	\$
Underwriting Discount	\$	\$
Proceeds to BioCryst (before expenses)	\$	\$

The underwriters expect to deliver the shares to purchasers on or about , 1999.

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SALOMON SMITH BARNEY

HAMBRECHT & QUIST

RAYMOND JAMES & ASSOCIATES, INC.

, 1999

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## PROSPECTUS SUMMARY

THIS SUMMARY HIGHLIGHTS INFORMATION CONTAINED ELSEWHERE IN THIS PROSPECTUS. YOU SHOULD READ THIS ENTIRE PROSPECTUS CAREFULLY, INCLUDING THE "RISK FACTORS" SECTION. IN ADDITION, WE INCORPORATE BY REFERENCE IMPORTANT BUSINESS AND FINANCIAL INFORMATION IN THIS PROSPECTUS.

### OUR COMPANY

BioCryst Pharmaceuticals, Inc. is a biotechnology company focused on the development of pharmaceuticals for the treatment of infectious, cardiovascular and other diseases and disorders. We designed our most advanced drug candidate, BCX-1812, to treat and prevent influenza. We licensed this drug candidate to The R.W. Johnson Pharmaceutical Research Institute and Ortho-McNeil Pharmaceutical, Inc., both Johnson & Johnson companies.

We have two other drug development programs underway. The first program is for development of a drug candidate for the treatment of T-cell cancers, a type of cancer that affects cells of the body's immune system. We are also developing a class of compounds that may help in the treatment of cardiovascular diseases and disorders.

Drug development typically occurs in several stages, which we refer to as early-stage development and late-stage development. Early-stage development includes drug discovery, preclinical studies prior to testing in humans and Phase I clinical trials in humans. Late-stage development includes Phase II and III clinical trials in humans and the regulatory approval process.

An important element of our business strategy is to control costs and overhead through contracting and entering into license agreements with other parties to share the risks and benefits of various stages of the drug development process. We focus on the discovery and early-stage development of our drug candidates and seek to establish partnerships with pharmaceutical companies for the late-stage development and commercialization of these compounds. This strategy should control our expenses, minimize risks and allow us to have a greater number of attractive drug candidates progress to late-stage development.

### OUR FLU DRUG CANDIDATE (BCX-1812)

Many people perceive influenza, commonly known as the flu, to be a transient, inconvenient viral infection that leaves its sufferers bed-ridden for a few days. In truth, however, it is a virulent, acute respiratory disease that is sometimes deadly. In North America, Western Europe and Japan, an estimated 70 million to 150 million individuals suffer from influenza annually. The flu is particularly dangerous to the elderly, young children and debilitated patients and accounts for approximately 20,000 deaths in the United States each year. The flu and associated complications are the sixth leading cause of death in the United States. A 1994 article in THE NEW ENGLAND JOURNAL OF MEDICINE estimated that the annual cost to the U.S. economy associated with influenza epidemics was in excess of \$12 billion.

In collaboration with scientists from The University of Alabama at Birmingham, we developed BCX-1812, our most advanced drug candidate. We designed BCX-1812 to inhibit an enzyme, called the neuraminidase enzyme, that helps the flu virus to replicate and spread throughout the body. By inhibiting the neuraminidase enzyme, we believe that BCX-1812 may be effective in the treatment and prevention of the flu.

Our preclinical studies demonstrated that BCX-1812 has the following benefits:

- excellent safety profile;
- inhibition of both influenza A and B;

- effective when taken orally;
- probable once-a-day dosage; and
- can be made into a liquid form, allowing for use by the elderly and young children.

In September 1998, we entered into an exclusive worldwide license agreement with The R.W. Johnson Pharmaceutical Research Institute and Ortho-McNeil, both Johnson & Johnson companies. These Johnson & Johnson companies have sole responsibility for the development, manufacture, marketing, sales and distribution of BCX-1812. We received an initial \$6.0 million payment from Ortho-McNeil and an additional \$6.0 million common stock equity investment from Johnson & Johnson Development Corporation. In June 1999, we received a \$2.0 million payment from Ortho-McNeil in connection with the initiation of Phase II clinical testing in the United States. In addition, we may receive cash payments upon specified developmental and regulatory milestones and royalties on any product sales.

Since the collaboration was established, BCX-1812 moved through Phase I clinical trials and a Phase II clinical study by August 1999. We recently announced preliminary results from a Phase II placebo-controlled, randomized study conducted by The R.W. Johnson Pharmaceutical Research Institute for the treatment of healthy volunteers infected with a strain of influenza A. The R.W. Johnson Pharmaceutical Research Institute advised us that the data from this Phase II study indicated a statistically significant reduction of flu virus in the body and that the drug was well-tolerated at all dosage levels. They also advised us that the planning of the Phase III clinical trials for the 1999/2000 influenza season is underway.

Our principal offices are located at 2190 Parkway Lake Drive, Birmingham, Alabama 35244, and our telephone number is (205) 444-4600.

THE OFFERING

Common stock offered.....	2,000,000 shares
Common stock to be outstanding after the offering.....	17,238,672 shares
Use of proceeds.....	For research and development activities, preclinical studies and clinical trials, working capital and general corporate purposes.

Unless we specifically state otherwise, the information in this prospectus does not take into account the issuance of up to 300,000 shares of common stock which the underwriters have the option to purchase solely to cover over-allotments. If the underwriters exercise their over-allotment option in full, 17,538,672 shares of common stock will be outstanding after the offering.

The number of shares of common stock to be outstanding immediately after the offering is based upon shares outstanding as of October 8, 1999 and does not take into account 2,255,736 shares of common stock issuable upon exercise of options outstanding at a weighted average exercise price of \$7.52 per share and 595,707 shares reserved under our existing stock option plan and employee stock purchase plan.

SUMMARY FINANCIAL DATA

	YEARS ENDED DECEMBER 31,					SIX MONTHS ENDED JUNE 30,	
	1994	1995	1996	1997	1998	1998	1999
(IN THOUSANDS, EXCEPT PER SHARE DATA)							
STATEMENT OF OPERATIONS DATA:							
Revenues:							
Collaborative and other research and development.....	\$ 269	\$ 223	\$ 1,558	\$ 1,000	\$ 6,371	\$ --	\$ 2,408
Interest and other.....	465	662	1,094	1,692	1,255	671	633
Total revenues.....	734	885	2,652	2,692	7,626	671	3,041
Expenses:							
Research and development.....	5,552	7,107	7,586	10,577	9,291	5,353	4,006
General and administrative.....	1,904	2,210	2,664	2,682	3,105	1,295	1,683
Interest.....	216	144	100	52	15	10	3
Total expenses.....	7,672	9,461	10,350	13,311	12,411	6,658	5,692
Net loss.....	\$ (6,938)	\$ (8,576)	\$ (7,698)	\$ (10,619)	\$ (4,785)	\$ (5,987)	\$ (2,651)
Net loss per share.....	\$ (1.02)	\$ (0.96)	\$ (0.69)	\$ (0.77)	\$ (0.34)	\$ (0.43)	\$ (0.18)
Weighted average shares outstanding....	6,787	8,905	11,171	13,780	14,120	13,926	14,981

The as-adjusted information that follows gives effect to this offering and assumes no exercise of the underwriters' over-allotment option.

	JUNE 30, 1999	
	ACTUAL	AS ADJUSTED
(IN THOUSANDS)		
BALANCE SHEET DATA:		
Cash, cash equivalents and securities held-to-maturity.....	\$ 24,317	\$ 69,827
Total assets.....	26,546	72,056
Accumulated deficit.....	(55,821)	(55,821)
Total stockholders' equity.....	25,199	70,709



## RISK FACTORS

AN INVESTMENT IN OUR COMMON STOCK INVOLVES SIGNIFICANT RISKS. YOU SHOULD CAREFULLY CONSIDER THE FOLLOWING RISKS BEFORE YOU DECIDE TO BUY OUR COMMON STOCK.

WE HAVE INCURRED SUBSTANTIAL LOSSES SINCE OUR INCEPTION IN 1986, EXPECT TO CONTINUE TO INCUR SUCH LOSSES, MAY NEVER BE PROFITABLE AND MAY NEED ADDITIONAL FINANCING

Since our inception in 1986, we have not been profitable. We expect to incur additional losses for the foreseeable future, and we expect our losses to increase as our research and development efforts progress. As of June 30, 1999, our accumulated deficit was approximately \$55.8 million. To become profitable, we must successfully develop drug candidates, enter into profitable agreements with other parties and our drug candidates must receive regulatory approval. These other parties must then successfully manufacture and market our drug candidates. It will be several years, if ever, before we receive royalties under our existing license agreements or any future license agreements. In addition, we never expect to generate revenue directly from product sales. If we do not generate revenue, or if our drug development expenses increase, we may need to raise additional funds through new or existing collaborations or through private or public equity or debt financings. If financing is not available on acceptable terms, or not available at all, we may not have enough capital to continue our current business strategy.

IF THE R.W. JOHNSON PHARMACEUTICAL RESEARCH INSTITUTE AND ORTHO-MCNEIL WERE TO TERMINATE, SUBSTANTIALLY MODIFY OR FAIL TO FULFILL THEIR OBLIGATIONS UNDER THEIR LICENSE AGREEMENT WITH US, WE WOULD LOSE SUBSTANTIALLY ALL OF OUR REVENUE

If The R.W. Johnson Pharmaceutical Research Institute and Ortho-McNeil change their exclusive worldwide license agreement with us, including by terminating it or failing to fulfill their obligations, we would lose substantially all of our revenue. Approximately 79.2% of our revenues for the six months ended June 30, 1999 and approximately 83.5% of our revenues for the year ended December 31, 1998 resulted from this license agreement. These revenues represent approximately 45.0% of our total revenues since our inception in 1986.

Under this agreement, The R.W. Johnson Pharmaceutical Research Institute and Ortho-McNeil have several rights that could delay or stop the development of our flu drug candidate, including sole discretion on all elements of research and development of BCX-1812, including timing and design of further clinical trials, sole control over the amount of resources devoted to the research and development of BCX-1812 and the right to terminate or cancel the agreement, which they may do at any time on four months notice.

IF OUR DEVELOPMENT COLLABORATIONS WITH OTHER PARTIES FAIL, THE DEVELOPMENT OF OUR DRUG CANDIDATES WILL BE DELAYED OR STOPPED

We rely completely upon other parties for many important stages of our drug development programs, including:

- discovery of proteins that cause or enable biological reactions necessary for the progression of the disease or disorder, called enzyme targets;
- execution of preclinical studies and late-stage development for our compounds and drug candidates; and
- manufacturing, sales, marketing and distribution of our drug candidates.

Even more critical to our success is our ability to enter into successful collaborations for the late-stage clinical development, regulatory approval, manufacture, marketing, sales and distribution of our

drug candidates. Our strategy is to rely upon other parties for all of these steps so that we can focus exclusively on the key areas of our expertise. This heavy reliance upon third parties for these critical functions presents several risks, including:

- these contracts may expire or the other parties to the contract may terminate them, as was the case with our Torii Pharmaceutical Co., Ltd. contract;
- our partners may choose to pursue alternative technologies, including those of our competitors;
- we may have disputes with a partner that could lead to litigation or arbitration;
- our partners may not devote sufficient capital or resources towards our drug candidates; and
- our partners may not comply with applicable government regulatory requirements.

If we cannot license enzyme targets from academic institutions or other biotechnology companies on acceptable terms, we will be unable to develop new drug candidates. If the contract research organizations that conduct our initial clinical trials breach their obligations to us, our inability to replace them would delay or possibly stop the development of our drug candidates. If we are unable to avoid all of these risks with our partners, we will not successfully complete late-stage development of our drug candidates.

#### IF THE CLINICAL TRIALS OF OUR DRUG CANDIDATES FAIL, WE WILL NOT BE ABLE TO MARKET OUR DRUG CANDIDATES

To receive the regulatory approvals necessary for the sale of our drug candidates, we or our licensees must demonstrate through clinical trials that each drug candidate is safe and effective. If we or our licensees are unable to obtain regulatory approval of our drug candidates, we will not be able to market our drug candidates, which would result in a decrease in, or complete absence of, revenue.

The clinical trial process is complex, uncertain and expensive. We incur substantial expense for, and devote significant time to, clinical trials, yet cannot be certain that the trials will ever result in the commercial sale of a product. Positive results from preclinical studies and early clinical trials do not ensure positive results in clinical trials designed to permit application for regulatory approval, called pivotal clinical trials. We may suffer significant setbacks in pivotal clinical trials, even after earlier clinical trials show promising results. Any of our drug candidates may produce undesirable side effects in humans that could cause us or regulatory authorities to interrupt, delay or halt clinical trials of a drug candidate. We, the FDA or foreign regulatory authorities may suspend or terminate clinical trials at any time if we or they believe the trial participants face unacceptable health risks. Clinical trials may fail to demonstrate that our drug candidates are safe or effective. Even if we or our licensees successfully complete clinical trials for our product candidates, our licensees might not file the required regulatory submissions in a timely manner and may not receive regulatory approval for the drug candidate.

We licensed our drug candidate, BCX-1812, to Ortho-McNeil and to The R.W. Johnson Pharmaceutical Research Institute, which is in the process of conducting clinical trials. However, the FDA may not accept The R.W. Johnson Pharmaceutical Research Institute's clinical protocols, the Phase III clinical trials may not begin in 1999, or at all, and any Phase III clinical trials may not be successful. Even if The R.W. Johnson Pharmaceutical Research Institute completes the Phase III trials, we do not know when, if ever, it will receive FDA or foreign regulatory agency approvals for, or when Ortho-McNeil will begin marketing of, BCX-1812. If The R.W. Johnson Pharmaceutical Research Institute is unable to begin clinical trials as planned, complete the clinical trials or demonstrate the safety and efficacy of our compounds, we will not receive any revenues from BCX-1812. Even if the results of The R.W. Johnson Pharmaceutical Research Institute's trials are positive, products are not likely to be commercially available for several years, if at all.

IF WE OR OUR LICENSEES DO NOT OBTAIN AND MAINTAIN GOVERNMENTAL APPROVALS FOR OUR PRODUCTS UNDER DEVELOPMENT, WE OR OUR PARTNERS WILL NOT BE ABLE TO SELL THESE POTENTIAL PRODUCTS

In the United States, we or our partners must obtain FDA approval for each drug that we intend to commercialize. The FDA approval process is typically lengthy and expensive, and approval is never certain. Products distributed abroad are also subject to foreign government regulation. The FDA or foreign regulatory agencies have not approved any of our drug candidates. Because of the risks and uncertainties in biopharmaceutical development, our drug candidates could take a significantly longer time to gain regulatory approval than we expect or may never gain approval. If the FDA delays regulatory approval of our drug candidates, our management's credibility, our company's value and our operating results may suffer. Even if the FDA or foreign regulatory agencies approve a drug candidate, the approval may limit the indicated uses for a drug candidate and/or may require post-marketing studies.

If we get approval to market our potential products, whether in the United States or internationally, we will continue to be subject to extensive regulatory requirements. These requirements are wide ranging and govern, among other things:

- adverse drug experience reporting regulations;
- product promotion;
- product manufacturing, including good manufacturing practice requirements; and
- product changes or modifications.

Our failure to comply with existing or future regulatory requirements, or our loss of, or changes to, previously obtained approvals, could have a material adverse effect on our business because we will not receive royalty revenues if we do not receive approval of our products for marketing.

In June 1995, we notified the FDA that we submitted incorrect efficacy data for our Phase II trials of BCX-34 applied to the skin for the treatment of cutaneous T-cell lymphoma and psoriasis. Cutaneous T-cell lymphoma is a skin cancer in which T-cells, which normally help fight disease in the body, duplicate rapidly and cause skin cancer. Psoriasis is a disease where the immune system attacks the body's own skin cells. The FDA inspected us and issued to us Lists of Inspectional Observations, on Form FDA 483, that cited our failure to follow good clinical practices. The FDA also issued a Form FDA 483 to a principal investigator at a clinical trial site, and the FDA notified us that they will not accept any work performed by this investigator without further validation. Because of these investigations by the FDA, our ongoing and future clinical studies or trials may receive increased scrutiny, which would delay the regulatory review process.

IF OUR DRUG CANDIDATES DO NOT ACHIEVE BROAD MARKET ACCEPTANCE, OUR BUSINESS MAY NEVER BECOME PROFITABLE

Our drug candidates, including our influenza neuraminidase inhibitors, may not gain the market acceptance required for us to be profitable even after they receive approval for sale by the FDA or foreign regulatory agencies. Influenza neuraminidase inhibitors are drugs designed to stop the spread of the flu virus in the body. The degree of market acceptance of any drug candidates that we or our partners develop will depend on a number of factors, including:

- cost-effectiveness of our drug candidates;
- their effectiveness relative to alternative treatment methods, such as the efficacy, cost and ease of use of our flu drug candidate over other products, including vaccines, existing drugs such as amantadine and rimantadine, Hoffmann-La Roche's and Glaxo Wellcome's influenza neuraminidase inhibitors and over-the-counter products;

- reimbursement policies of government and third-party payors; and
- marketing and distribution support for our drug candidates.

Physicians, patients, payors or the medical community in general may not accept or use our drug candidates even after the FDA or foreign regulatory agencies approve the drug candidates. If our drug candidates do not achieve significant market acceptance, we will not have enough revenues to become profitable.

IF COMPETITIVE PRODUCTS FROM OTHER COMPANIES ARE BETTER THAN OUR PRODUCT CANDIDATES, OUR FUTURE REVENUES MIGHT FAIL TO MEET OUR EXPECTATIONS AND THOSE OF FINANCIAL ANALYSTS

If our influenza neuraminidase inhibitor drug candidate, BCX-1812, receives FDA or foreign regulatory approval, it will have to compete with a number of products that are already on the market such as vaccines, the drugs amantadine and rimantadine and over-the-counter products, and with additional products that may beat BCX-1812 to the market. If approved, BCX-1812 will be, at best, the third neuraminidase inhibitor to the market, because the FDA and foreign regulatory agencies approved Glaxo-Wellcome plc's neuraminidase inhibitor product, and because the FDA also approved Hoffman-La Roche's neuraminidase inhibitor. Both Glaxo-Wellcome and Hoffmann-La Roche are large multinational pharmaceutical companies that have significant financial, technical and human resources and could therefore establish brand recognition and loyalty with consumers before BCX-1812 is on the market. In addition, a vaccine is currently in preclinical development that may immunize people against all strains of the flu virus, rendering flu drug products like ours obsolete. Products marketed by our competitors may prove to be more effective than our own, and our products, if any, may not offer an economically feasible or preferable alternative to existing therapies.

IF WE FAIL TO ADEQUATELY PROTECT OR ENFORCE OUR INTELLECTUAL PROPERTY RIGHTS OR SECURE RIGHTS TO PATENTS OF OTHERS, THE VALUE OF OUR INTELLECTUAL PROPERTY RIGHTS WOULD DIMINISH

Our success will depend in part on our ability and the abilities of our licensors to obtain patent protection for our products, methods, processes and other technologies to preserve our trade secrets, and to operate without infringing the proprietary rights of third parties. To date, the U.S. Patent and Trademark Office has issued to us nine U.S. patents for our various inventions. We have filed additional patent applications and provisional patent applications with the U.S. Patent and Trademark Office. We have filed a number of corresponding foreign patent applications and intend to file additional foreign and U.S. patent applications, as appropriate. We cannot predict:

- the degree and range of protection any patents will afford against competitors with similar products;
- if and when patents will issue;
- whether or not others will obtain patents claiming aspects similar to those covered by our patent applications; or
- whether we must initiate litigation or administrative proceedings which may be costly whether we win or lose.

If our products, methods, processes and other technologies infringe the proprietary rights of other parties, we could incur substantial costs and we may have to:

- obtain licenses or redesign our products or processes to avoid infringement;
- stop using the subject matter claimed in the patents held by others;

- pay damages; or
- defend litigation or administrative proceedings which may be costly whether we win or lose.

Our success is also dependent upon the skills, knowledge and experience, none of which is patentable, of our scientific and technical personnel. To help protect our rights, we require all employees, consultants, advisors and collaborators to enter into confidentiality agreements that prohibit the disclosure of confidential information to anyone outside of our company and require disclosure and assignment to us of their ideas, developments, discoveries and inventions. These agreements may not provide adequate protection for our 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, and if any of our proprietary information is disclosed, our business will suffer because our revenues depend upon our ability to license our technology and any such events would significantly impair the value of such a license.

OUR FAILURE TO RETAIN OUR EXISTING KEY PERSONNEL OR OUR FAILURE TO ATTRACT AND RETAIN ADDITIONAL KEY PERSONNEL WILL DELAY OR STOP THE DEVELOPMENT OF OUR DRUG CANDIDATES AND THE EXPANSION OF OUR BUSINESS

We are highly dependent upon our senior management and scientific team, the loss of whose services might impede the achievement of our development and commercial objectives. Although we maintain, and are 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 and Chief Executive Officer, we do not believe the proceeds would be adequate to compensate for his loss. We are actively seeking additional members for our senior management team. Competition for key personnel with the experience that we require is intense and we expect it to increase. Our inability to attract and retain the required number of skilled and experienced management, operational and scientific personnel, will harm our business because we rely upon these personnel for many critical functions of our business.

In addition, we rely on members of our scientific advisory board and consultants to assist us in formulating our research and development strategy. All of the members of the scientific advisory board and all of our consultants have other jobs and each such member or consultant may have commitments to other entities that may limit their availability to us.

IF USERS OF OUR DRUG CANDIDATES ARE NOT REIMBURSED FOR USE OF OUR DRUG CANDIDATES, FUTURE SALES OF OUR DRUG CANDIDATES WILL DECLINE

Most individuals who buy commercial drug products rely on reimbursement from their insurance provider or the government to cover the cost of the drug product. Many factors may determine whether insurance companies or other third-party payors will reimburse patients for purchasing our flu drug, BCX-1812, including:

- BCX-1812 only alleviates symptoms of, and does not cure, the flu;
- in most cases, the flu is not a life-threatening disease; and
- BCX-1812 may be more expensive than a vaccine or other drug products for treatment of the flu, including over-the-counter products.

IF WE FACE CLINICAL TRIAL LIABILITY CLAIMS RELATED TO THE USE OR MISUSE OF OUR COMPOUNDS EITHER IN CLINICAL TRIALS OR AFTER COMMERCIAL INTRODUCTION, THESE CLAIMS WILL DIVERT OUR MANAGEMENT'S TIME AND WE WILL INCUR LITIGATION COSTS

We face an inherent business risk of liability claims in the event that the use or misuse of our compounds results in personal injury or death. We may experience clinical trial liability claims in the future if our compounds are misused or cause harm before regulatory authorities approve them for marketing. We currently maintain clinical trial liability insurance coverage in the amount of \$1.0 million per occurrence and \$2.0 million in the aggregate, with an

additional \$5.0 million potentially available

under our umbrella policy. The insurance policy may not be sufficient to cover claims that may be made against us. Clinical trial liability insurance is expensive, difficult to obtain and may not be available in the future on acceptable terms, if at all. In addition, after commercial introduction of our products we may experience losses due to product liability claims. Although clinical trial claims are costly, product liability claims are even more complex, expensive and time-consuming and are more difficult to disprove. In clinical trial situations, we or our licensees must warn each participant of the adverse effects of the drug and each participant must sign waivers and acknowledgements. After regulatory authorities approve a drug for marketing, people who take the drug might not be aware of its potential adverse effects, and we would be liable for any harm caused by the drug. Any claims against us, regardless of their merit, could materially and adversely affect our financial condition, because litigation related to these claims would strain our financial resources in addition to consuming the time and attention of our management.

#### IF OUR COMPUTER SYSTEMS FAIL, WE MAY SUFFER MORE HARM THAN OTHER COMPANIES

Our drug development activities depend on the security, integrity and performance of the computer systems supporting them, and the failure of our computer systems would delay or stop our drug development efforts. We currently store all of our preclinical and clinical data at our facilities, do not store duplicate copies of all data off-site and could lose important data if our systems were impaired. Any significant degradation or failure of our computer systems could cause us to inaccurately calculate or lose our data. Loss of data could result in significant delays in our drug development process. We have not undertaken formal system protections, do not have a detailed emergency plan and any system failure could harm our business and operations.

#### IF, BECAUSE OF OUR USE OF HAZARDOUS MATERIALS, WE VIOLATE ANY ENVIRONMENTAL CONTROLS OR REGULATIONS THAT APPLY TO SUCH MATERIALS, WE MAY INCUR SUBSTANTIAL COSTS AND EXPENSES IN OUR REMEDIATION EFFORTS

Our research and development involves the controlled use of hazardous materials, chemicals and various radioactive compounds. We are subject to federal, state and local laws and regulations governing the use, storage, handling and disposal of these materials and some waste products. Accidental contamination or injury from these materials could occur. In the event of an accident, we could be liable for any damages that result and any liabilities could exceed our resources. Compliance with environmental laws and regulations could require us to incur substantial unexpected costs which would materially and adversely affect our results of operations.

#### BECAUSE STOCK OWNERSHIP IS CONCENTRATED, YOU AND OTHER INVESTORS WILL HAVE MINIMAL INFLUENCE ON STOCKHOLDER DECISIONS

Prior to this offering, our directors, executive officers and some principal stockholders and their affiliates, including Johnson & Johnson Development Corporation, beneficially own approximately 40.5% of our outstanding common stock. As a result, these holders, if acting together, are able to significantly influence matters requiring stockholder approval, including the election of directors. This concentration of ownership may delay, defer or prevent a change in our control.

#### WE HAVE ANTI-TAKEOVER PROVISIONS IN OUR CORPORATE CHARTER DOCUMENTS THAT MAY RESULT IN OUTCOMES WITH WHICH YOU DO NOT AGREE

Our board of directors has the authority to issue up to 5,000,000 shares of undesignated preferred stock and to determine the rights, preferences, privileges and restrictions of those shares without further vote or action by our stockholders. The rights of the holders of any preferred stock that may be issued in the future may adversely affect the rights of the holders of common stock. The issuance of preferred stock could make it more difficult for third parties to acquire a majority of our outstanding voting stock.

In addition, our certificate of incorporation provides for staggered terms for the members of the board of directors and super majority approval of the removal of any member of the board of directors and prevents our stockholders from acting by written consent. Our certificate also requires supermajority approval of any amendment of these provisions. These provisions and other provisions of our by-laws and of Delaware law applicable to us could delay or make more difficult a merger, tender offer or proxy contest involving us.

#### INVESTORS IN THIS OFFERING WILL SUFFER IMMEDIATE AND SUBSTANTIAL DILUTION

You will incur immediate and substantial dilution of \$20.35 in the net tangible book value per share of the shares you purchase in this offering. To the extent outstanding options to purchase common stock are exercised, there will be further dilution. The net tangible book value per share of existing stockholders will increase by \$2.48 because of this offering.

#### OUR STOCK PRICE IS LIKELY TO BE HIGHLY VOLATILE AND THE VALUE OF YOUR INVESTMENT COULD DECLINE SIGNIFICANTLY

The market prices for securities of biotechnology companies in general have been highly volatile and may continue to be highly volatile in the future. Moreover, our stock has fluctuated frequently, and these fluctuations are often not related to our financial results. The 52-week range of the market price of our stock has ranged from \$5.50 to \$35.31 per share, which is a significantly greater change than that experienced by many other companies. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock:

- announcements of technological innovations or new products by us or our competitors;
- developments or disputes concerning patents or proprietary rights;
- our licensees achieving or failing to achieve development milestones;
- publicity regarding actual or potential medical results relating to products under development by us or our competitors;
- regulatory developments in both the United States and foreign countries;
- public concern as to the safety of pharmaceutical products;
- actual or anticipated fluctuations in our operating results;
- changes in financial estimates or recommendations by securities analysts;
- economic and other external factors or other disasters or crises; and
- period-to-period fluctuations in our financial results.

#### PROBLEMS WITH YEAR 2000 COMPLIANCE COULD DISRUPT OUR OPERATIONS

Beginning in the year 2000, the date fields coded in certain software products and computer systems will need to accept four digit entries in order to distinguish between years in the 1900s and years dated 2000 and higher (commonly known as the year 2000 problem). It is not clear what potential problems may arise as the biopharmaceutical industry, and other industries, try to resolve this year 2000 problem.

It is possible that our currently installed computer systems, software products or other business systems, or those of our suppliers or service providers, working either alone or in conjunction with other software or systems, will not accept input of, store, manipulate and output dates for the year 2000 or subsequent years without error or interruption. We attempted to review and resolve those aspects of the year 2000 problem that are within our direct control and adjust to or influence those



aspects that are not within our direct control. We have completed our assessment of our systems and expect that we will fully implement remediation and testing by the end of 1999. Our potential drug candidates do not have any year 2000 exposure. We have contacted our major vendors and suppliers with regard to their year 2000 compliance, and we will continue to monitor their compliance.

Some risks associated with the year 2000 problem are beyond our ability to control, including the extent to which our suppliers and service providers address the year 2000 problem. The failure by a third party to adequately address the year 2000 issue could have an adverse effect on their operations, which could have an adverse effect on us. We are assessing the possible effects on our operations of the possible failure of our key suppliers and providers, contractors and collaborators to identify and remedy potential year 2000 problems.

YOU SHOULD RELY ONLY ON THE INFORMATION CONTAINED IN THIS PROSPECTUS. WE HAVE NOT AUTHORIZED ANYONE TO PROVIDE YOU WITH DIFFERENT INFORMATION. WE ARE NOT MAKING AN OFFER OF THESE SECURITIES IN ANY STATE WHERE THE OFFER IS NOT PERMITTED. YOU SHOULD NOT ASSUME THAT THE INFORMATION PROVIDED BY THIS PROSPECTUS IS ACCURATE AS OF ANY DATE OTHER THAN THE DATE ON THE FRONT OF THIS PROSPECTUS.

#### INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements. The forward-looking statements are principally contained in the sections on "Prospectus Summary," "Business" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." These statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to:

- the progress of our product development programs, including The R.W. Johnson Pharmaceutical Research Institute and Ortho-McNeil's progress with respect to our influenza neuraminidase inhibitors;
- developments with respect to clinical development of drug candidates, clinical trials and the regulatory approval process;
- our estimates regarding our capital requirements and our needs for additional financing;
- developments relating to our selection and licensing of targets; and
- our ability to attract development partners with acceptable development, regulatory and commercialization expertise.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "potential" and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the heading "Risk Factors." Also, these forward-looking statements represent our estimates and assumptions only as of the date of this prospectus.

You should read this prospectus and the documents that we incorporate by reference in this prospectus completely and with the understanding that our actual future results may be materially different from what we expect. We may not update these forward-looking statements, even though our situation may change in the future. We qualify all of our forward-looking statements by these cautionary statements.

## USE OF PROCEEDS

We estimate that the net proceeds we will receive from the sale of 2,000,000 shares of common stock will be approximately \$45.5 million, or approximately \$52.4 million if the underwriters fully exercise their over-allotment option, after deducting the estimated underwriting discounts and offering expenses and assuming an offering price of \$24.50 per share. We expect to use the net proceeds of this offering as follows:

- to fund drug discovery and other research programs;
- to fund preclinical studies and clinical trials of our drug candidates;
- to provide working capital; and
- for general corporate purposes.

We have not determined the amount of net proceeds to be used for each of the specific purposes listed. Accordingly, we will have broad discretion to use the proceeds as we see fit.

Based upon the current status of our product development programs, we believe that the net proceeds from this offering, together with interest on those net proceeds, and our existing capital resources will satisfy our capital requirements through 2001.

Pending such uses, we intend to invest the net proceeds in interest-bearing, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the United States or its agencies.

## MARKET PRICE OF COMMON STOCK

Our common stock began trading publicly on the Nasdaq National Market under the symbol "BCRX." We completed the initial public offering of our common stock on March 4, 1994. The following table shows the range of high and low sale prices per share of our common stock as reported by the Nasdaq National Market for the periods indicated.

	COMMON STOCK PRICE	
	HIGH	LOW
Year ended December 31, 1997		
First Quarter.....	\$ 17.00	\$ 11.50
Second Quarter.....	14.75	10.06
Third Quarter.....	13.75	4.25
Fourth Quarter.....	8.38	6.25
Year ended December 31, 1998		
First Quarter.....	9.50	6.88
Second Quarter.....	9.13	6.00
Third Quarter.....	8.00	6.00
Fourth Quarter.....	8.44	4.38
Year ended December 31, 1999		
First Quarter.....	11.00	6.38
Second Quarter.....	9.50	6.38
Third Quarter.....	35.31	8.38
Fourth Quarter (through October 8, 1999).....	25.00	23.38

On October 8, 1999, the last sale price of our common stock reported by the Nasdaq National Market was \$24.50 per share. As of August 1, 1999, there were 483 holders of record of our common stock.

## DIVIDEND POLICY

We have not declared or paid cash dividends on our common stock in the past and do not intend to pay dividends on our common stock in the foreseeable future.

CAPITALIZATION

The following table shows our capitalization as of June 30, 1999 on an actual basis and as adjusted to reflect the sale of 2,000,000 shares of common stock in this offering, assuming an offering price of \$24.50 per share and after deducting the estimated underwriting discounts and offering expenses. This table should be read in conjunction with the financial statements and related notes incorporated in this prospectus by reference and "Management's Discussion and Analysis of Financial Condition and Results of Operations" appearing elsewhere in this prospectus.

	JUNE 30, 1999	
	ACTUAL	AS ADJUSTED
	-----	-----
	(IN THOUSANDS, EXCEPT SHARE DATA)	
Capital lease obligations, less current portion.....	\$ 15	\$ 15
	-----	-----
Stockholders' equity:		
Preferred stock, \$0.01 par value; 5,000,000 shares authorized; none issued and outstanding.....	--	--
Common stock, \$0.01 par value; 45,000,000 shares authorized; 14,987,634 issued and outstanding, and 16,987,634 shares issued and outstanding as adjusted for this offering.....	150	170
Additional paid-in capital.....	80,870	126,360
Accumulated deficit.....	(55,821)	(55,821)
	-----	-----
Total stockholders' equity.....	25,199	70,709
	-----	-----
Total capitalization.....	\$ 25,214	\$ 70,724
	=====	=====

The above data excludes 2,507,501 shares of common stock issuable upon exercise of options outstanding as of June 30, 1999 at a weighted average exercise price of \$7.37 per share.

DILUTION

Our net tangible book value as of June 30, 1999 was approximately \$25.0 million, or \$1.67 per share. Net tangible book value per share represents the amount of our total tangible assets less total liabilities divided by the total number of shares of common stock outstanding. After giving effect to the sale by us of 2,000,000 shares of common stock offered by this prospectus at an assumed offering price of \$24.50 per share and after deducting estimated underwriting discounts and offering expenses, our net tangible book value at June 30, 1999 would have been approximately \$70.5 million, or \$4.15 per share. This represents an immediate increase in net tangible book value of \$2.48 per share to existing stockholders and an immediate dilution of \$20.35 per share to new investors in this offering, as illustrated by the following table:

Assumed public offering price per share.....		\$ 24.50
Net tangible book value per share before the offering.....	\$ 1.67	
Increase per share attributable to new investors.....	2.48	
	-----	
Net tangible book value per share after the offering.....		4.15
		-----
Net tangible book value dilution per share to new investors.....		\$ 20.35
		=====

SELECTED FINANCIAL DATA

The following selected financial data should be read in conjunction with the financial statements and related notes, incorporated by reference in this prospectus, and "Management's Discussion and Analysis of Financial Condition and Results of Operations" appearing elsewhere in this prospectus. The selected historical financial data below as of and for each of the five years ended December 31, 1998 have been derived from our audited financial statements. Our selected historical financial data as of June 30, 1999 and for each of the six months ended June 30, 1998 and 1999 were derived from our unaudited condensed financial statements. We believe that the unaudited financial data fairly reflects our results of operations and financial condition for the respective periods.

	YEARS ENDED DECEMBER 31,					SIX MONTHS ENDED JUNE 30,	
	1994	1995	1996	1997	1998	1998	1999
(IN THOUSANDS, EXCEPT PER SHARE DATA)							
<b>STATEMENT OF OPERATIONS DATA:</b>							
<b>Revenues:</b>							
Collaborative and other research and development.....	\$ 269	\$ 223	\$ 1,558	\$ 1,000	\$ 6,371	\$ --	\$ 2,408
Interest and other.....	465	662	1,094	1,692	1,255	671	633
<b>Total revenues.....</b>	<b>734</b>	<b>885</b>	<b>2,652</b>	<b>2,692</b>	<b>7,626</b>	<b>671</b>	<b>3,041</b>
<b>Expenses:</b>							
Research and development.....	5,552	7,107	7,586	10,577	9,291	5,353	4,006
General and administrative.....	1,904	2,210	2,664	2,682	3,105	1,295	1,683
Interest.....	216	144	100	52	15	10	3
<b>Total expenses.....</b>	<b>7,672</b>	<b>9,461</b>	<b>10,350</b>	<b>13,311</b>	<b>12,411</b>	<b>6,658</b>	<b>5,692</b>
<b>Net loss.....</b>	<b>\$ (6,938)</b>	<b>\$ (8,576)</b>	<b>\$ (7,698)</b>	<b>\$ (10,619)</b>	<b>\$ (4,785)</b>	<b>\$ (5,987)</b>	<b>\$ (2,651)</b>
<b>Net loss per share.....</b>	<b>\$ (1.02)</b>	<b>\$ (0.96)</b>	<b>\$ (0.69)</b>	<b>\$ (0.77)</b>	<b>\$ (0.34)</b>	<b>\$ (0.43)</b>	<b>\$ (0.18)</b>
<b>Weighted average shares outstanding.....</b>	<b>6,787</b>	<b>8,905</b>	<b>11,171</b>	<b>13,780</b>	<b>14,120</b>	<b>13,926</b>	<b>14,981</b>

	DECEMBER 31,					JUNE 30,
	1994	1995	1996	1997	1998	1999
(IN THOUSANDS)						
<b>BALANCE SHEET DATA:</b>						
Cash, cash equivalents and securities held-to-maturity.....	\$ 10,873	\$ 11,414	\$ 35,785	\$ 24,643	\$ 27,012	\$ 24,317
Total assets.....	12,803	13,056	37,149	26,485	29,100	26,546
Accumulated deficit.....	(21,491)	(30,067)	(37,766)	(48,384)	(53,170)	(55,821)
Total stockholders' equity.....	11,176	11,326	35,403	25,285	27,682	25,199

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

YOU SHOULD READ THE FOLLOWING DISCUSSION AND ANALYSIS IN CONJUNCTION WITH OUR FINANCIAL STATEMENTS AND RELATED NOTES INCORPORATED IN THIS PROSPECTUS BY REFERENCE.

OVERVIEW

Since our inception in 1986, we have been engaged in research and development activities and organizational efforts, including:

- identification and licensing of enzyme targets;
- drug discovery;
- structure-based design of drug candidates;
- small-scale synthesis of compounds;
- conducting preclinical studies and clinical trials;
- recruiting our scientific and management personnel;
- establishing laboratory facilities; and
- raising capital.

Our revenues have generally been limited to license fees, milestone payments, interest income, collaboration research, development and option fees. Research and development revenue on cost-reimbursing agreements is recognized as expenses are incurred up to contractual limits. Research and development revenues, license fees, milestone payments and option fees are recognized as revenue when irrevocably due. Payments received that are related to future performance are deferred and taken into income as earned over a specified future performance period. We have not received any revenue from the sale of pharmaceutical products. It will be several years, if ever, before we will recognize significant revenues from royalties received pursuant to our license agreements, and we do not expect to ever generate revenues directly from product sales. Future revenues, if any, are likely to fluctuate substantially from quarter to quarter.

We have incurred operating losses since our inception. Our accumulated deficit at June 30, 1999 was \$55.8 million. We will require substantial expenditures relating to the development of our current and future drug candidates. During the three years ended December 31, 1998, we spent 44.7% of our research and development expenses on contract research and development, including:

- payments to consultants;
- funding of research at academic institutions;
- large scale synthesis of compounds;
- preclinical studies;
- engaging investigators to conduct clinical trials;
- hiring contract research organizations to monitor and gather data on clinical trials; and
- using statisticians to evaluate the results of clinical trials.

The above expenditures for contract research and development for our current and future drug candidates will vary from quarter to quarter depending on the status of our research and development projects. Changes in our existing and future research and development and collaborative relationships will also impact the status of our research and development projects. While we may, in some cases, be able to control the timing of development expenses, in part by accelerating or decelerating certain of these costs, many of these costs will be incurred irrespective of whether or not we are able to discover drug candidates or obtain collaborative partners for commercialization. As a result, we believe that quarter-to-quarter comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of future performance. If we fail to meet the clinical and financial expectations of securities analysts and investors, it could have a material adverse effect on the price of our common stock.

## RESULTS OF OPERATIONS

### SIX MONTHS ENDED JUNE 30, 1999 AND 1998

Collaborative and other research and development revenue increased to \$2.4 million in the first six months of 1999. This increase is attributable to the \$2.0 million milestone payment received from Ortho-McNeil in June 1999 and approximately \$0.4 million of research and development work performed for The R.W. Johnson Pharmaceutical Research Institute. There was no such revenue in the first six months of 1998. Interest and other income declined 5.7% to \$633,000 in the first six months of 1999 from \$671,000 in the first six months of 1998. The decline in interest and other income is primarily due to a decline in interest rates.

Research and development expenses decreased 25.2% to \$4.0 million in the first six months of 1999 from \$5.4 million in the first six months of 1998. The decrease is primarily attributable to a decrease in costs associated with conducting clinical trials and a reduction in contracted research costs at The University of Alabama at Birmingham. These costs tend to fluctuate from period to period depending upon the status of our research projects and collaborative efforts.

General and administrative expenses increased 30.0% to \$1.7 million in the first six months of 1999 from \$1.3 million in the first six months of 1998. The increase is primarily the result of a royalty payment to The University of Alabama at Birmingham in connection with the milestone payment received from Ortho-McNeil, and increased legal expenses.

Interest expense decreased to \$2,776 in the first six months of 1999 from \$9,914 in the first six months of 1998. The decrease was primarily due to a decline in capitalized lease obligations resulting in lesser interest expense. We obtained most of our leases in connection with the move to our facilities in April 1992.

### YEARS ENDED DECEMBER 31, 1998 AND 1997

Collaborative and other research and development revenue increased to \$6.4 million in 1998 from \$1.0 million in 1997, primarily due to the \$6.0 million in up-front fees received from Ortho-McNeil in 1998 for a license agreement for our influenza neuraminidase inhibitors compared to the \$1.0 million milestone payment received from Torii in 1997. Interest and other income decreased 25.9% to \$1.3 million in 1998 from \$1.7 million in 1997, primarily due to a decline in the weighted average investment for 1998.

Research and development expenses decreased 12.2% to \$9.3 million in 1998 from \$10.6 million in 1997. Such expenses vary from period to period based on the status of our projects. We completed two Phase III clinical trials in 1997. In 1998, we commenced two Phase I clinical trials for our complement inhibitor, continued our two Phase I/II clinical trials for an oral formulation of our purine nucleoside phosphorylase, or PNP, inhibitor and initiated preclinical studies for our influenza neuraminidase and complement inhibitors. Overall, the decline in costs associated with our PNP inhibitor project were partially offset by the increases in our complement inhibitor and influenza neuraminidase projects. As a result, there was a slight decrease in 1998 in the outside research and development efforts associated with our three primary research and development projects. We reduced some of our other discretionary costs, which were offset by one-time costs associated with signing an exclusive worldwide license agreement for our proprietary influenza neuraminidase inhibitors and certain related agreements in September 1998.

General and administrative expenses increased 15.8% to \$3.1 million in 1998 from \$2.7 million in 1997. The increase was primarily due to the fees and expenses incurred in connection with the license agreement and related agreements for our influenza neuraminidase inhibitors signed in September 1998.

Interest expense decreased 71.1% to \$14,986 in 1998 from \$51,880 in 1997. The decrease was primarily due to a decline in capitalized lease obligations resulting in lesser interest expense. We obtained most of our leases in connection with the move to our facilities in April 1992.

Collaborative and other research and development revenue decreased 35.8% to \$1.0 million in 1997 from \$1.6 million in 1996, primarily due to a \$1.0 million milestone payment received from Torii in 1997 compared to the \$1.5 million license fee received from Torii and a federal grant in 1996. Interest and other income increased 54.8% to \$1.7 million in 1997 from \$1.1 million in 1996, primarily due to interest earned on funds invested from our public offering in September 1996.

Research and development expenses increased 39.4% to \$10.6 million in 1997 from \$7.6 million in 1996. The increase was primarily attributable to costs associated with manufacturing compounds, clinical trials and preclinical studies and expenses associated with increased personnel. These costs tend to fluctuate from period to period depending upon the stage of development and the conduct of clinical trials.

General and administrative expenses increased 0.7% to \$2.7 million in 1997 from \$2.7 million in 1996. The increase was primarily attributable to increased personnel costs and the fact that 1996 expenses were reduced by the reversal of a liability recorded in 1995 for use taxes assessed that we successfully contested in 1996, and was partially offset by decreased fees and taxes on the Torii milestone in 1997 as compared to the fees and taxes on the Torii license in 1996 and decreased legal expenses in 1997.

Interest expense decreased 48.1% to \$51,880 in 1997 from \$100,031 in 1996. The decrease was primarily due to a decline in capitalized lease obligations and the current portion of long-term debt, resulting in lesser interest expense. We obtained most of our leases in connection with the move to our facilities in April 1992.

#### LIQUIDITY AND CAPITAL RESOURCES

Cash expenditures have exceeded revenues since our inception. Our operations have principally been funded through public offerings and private placements of equity and debt securities, equipment lease financing, facility leases, collaborative and other research and development agreements, licenses and options for licenses, research grants and interest income. In addition, we have attempted to contain costs and reduce cash flow requirements by renting scientific equipment and facilities, contracting with other parties to conduct certain research and development and using consultants. We expect to incur additional expenses, resulting in significant losses, as we continue and expand our research and development activities and undertake additional preclinical studies and clinical trials of compounds which have been or may be discovered. We also expect to incur substantial expenses related to the filing, prosecution, maintenance, defense and enforcement of patent and other intellectual property claims.

At December 31, 1998, our cash, cash equivalents and securities held-to-maturity were \$27.0 million, an increase of \$2.4 million from December 31, 1997, principally due to the \$6.0 million equity investment in us in connection with the influenza neuraminidase license which offset the cash used in operations. At June 30, 1999, our cash, cash equivalents and securities held-to-maturity were \$24.3 million, a decrease of approximately \$2.7 million from December 31, 1998, principally due to the cash used by operations for the six months ended June 30, 1999.

We have financed some of our equipment purchases with lease lines of credit. We currently have a \$500,000 line of credit with our bank to finance capital equipment. In January 1992, we entered into an operating lease for our current facilities which expires on June 30, 2003. We have an option to renew the lease for an additional three years at current market rates. The operating lease requires us to pay monthly rent ranging from \$21,405 and escalating annually to a minimum of \$24,814 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, 1998, we had long-term capital lease and operating lease obligations which provide for aggregate minimum payments of \$280,254 in 1999, \$288,128 in 2000 and \$285,816 in 2001.



In 1999, we increased the amount of office space we lease by approximately 1,700 square feet. This additional space should increase our annual lease obligations by less than \$15,000 annually.

Under the terms of our license agreement with The R.W. Johnson Pharmaceutical Research Institute and Ortho-McNeil for the development and commercialization of our influenza neuraminidase inhibitors, we received an initial \$6.0 million payment from Ortho-McNeil and an additional \$6.0 million common stock equity investment from Johnson & Johnson Development Corporation. In June 1999, we received a \$2.0 million milestone payment from Ortho-McNeil in connection with the initiation of Phase II clinical testing in the United States. In addition, we may receive cash payments upon specified developmental and regulatory milestones and royalties on product sales, if any. We cannot assure you that The R.W. Johnson Pharmaceutical Research Institute or Ortho-McNeil will continue to develop the product or, if they do so, that such development will result in receiving milestone payments, obtaining regulatory approval or achieving future sales of licensed products.

We previously entered into an exclusive license agreement with Torii under which Torii paid us \$1.5 million in initial license fees and made a \$1.5 million equity investment in us in 1996. The first milestone payment of \$1.0 million was received in 1997. This exclusive license agreement was terminated by Torii in July 1999.

We plan to finance our needs principally from the following:

- our existing capital resources and interest earned on that capital;
- payments under collaborative and licensing agreements with corporate partners; and
- through lease or loan financing and future public or private financings.

We believe that our available funds, including the net proceeds from this offering, will be sufficient to fund our operations at least through 2001. However, this is a forward-looking statement, and there may be changes that would consume available resources significantly before such time. Our long-term capital requirements and the adequacy of our available funds will depend upon many factors, including:

- the progress of our research, drug discovery and development programs;
- changes in existing collaborative relationships;
- our ability to establish additional collaborative relationships;
- the magnitude of our research and development programs;
- the scope and results of preclinical studies and clinical trials to identify drug candidates;
- competitive and technological advances;
- the time and costs involved in obtaining regulatory approvals;
- the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;
- our dependence on others, including The R.W. Johnson Pharmaceutical Research Institute and Ortho-McNeil, for development and commercialization of our product candidates, in particular, our neuraminidase inhibitors; and
- successful commercialization of our products consistent with our licensing strategy.

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 us. The issuance of preferred or common stock or convertible securities, on terms and prices significantly more favorable than those of the currently outstanding common stock, could have the effect of diluting or adversely affecting the holdings or rights of our existing stockholders. In addition, collaborative arrangements may require us to transfer certain material rights to such corporate partners. Insufficient funds may require us to delay, scale-back or eliminate certain of our research and development programs.

## RISKS ASSOCIATED WITH THE YEAR 2000

The year 2000 issue is the result of computer programs being written using two digits rather than four digits to represent the year. Thus, computer software may recognize a date using "00" as the year 1900 rather than the year 2000. This could result in system failures or miscalculations causing disruptions of operations, including a temporary inability to process certain data or engage in similar normal business activities.

**PLAN AND STATUS.** Our plan to resolve the year 2000 issue involves four phases: assessment, remediation, testing and implementation. We have completed an assessment of our systems. In 1997, we installed a computer network, upgraded our desktop computers and upgraded our information technology software to a common standard. Most of our information technology systems are identified by the manufacturer as year 2000 compliant because of this upgrade. Major vendors and suppliers have been contacted with regard to their year 2000 compliance and we will continue to monitor their compliance. Systems identified as not being year 2000 compliant will be brought into compliance by upgrading either the software or hardware. We have begun remediation and testing and expect our plan to be fully implemented by the end of 1999.

While we have queried our significant suppliers, vendors and other outside parties and will continue to monitor their year 2000 compliance status, we have no means of ensuring that suppliers, vendors and other outside parties will be year 2000 ready. The inability of suppliers, vendors and other outside parties, including the government, to complete their year 2000 compliance process in a timely fashion could materially impact us. We cannot determine the effect on us of non-compliance by suppliers, vendors and outside parties.

**COSTS.** Our costs incurred to date for year 2000 compliance have not been material and are not expected to be material when completed. We anticipate that we will be able to fund our costs from current funds available for operations. If, however, the costs are higher than anticipated, this could have a material adverse effect on our business, results of operations and financial condition.

**RISKS.** While we believe we have an effective program in place to resolve the year 2000 issue in a timely manner, as noted above, we have not completed all necessary phases of the year 2000 program for compliance. In the event that we, or other parties we depend upon, are not fully compliant by the year's end, we may not be able to complete the testing of our compounds and advance our projects into clinical trials as required to support the filings with the FDA which are necessary to our business. In addition, disruptions in the economy generally resulting from year 2000 issues could also materially adversely effect us. We are unable to estimate any potential liability or potential lost revenue at this time. We may not discover year 2000 compliance issues that will have a material adverse effect on our business, results of operations and financial condition.

**CONTINGENCY.** We have contingency plans for certain critical applications and are working on such plans for others. These contingency plans involve, among other actions, performing the work manually, increasing inventories and adjusting staffing strategies. These contingency plans may not be adequate.

## OVERVIEW

BioCryst Pharmaceuticals, Inc. is a biotechnology company focused on the development of pharmaceuticals for the treatment of infectious, cardiovascular and other diseases and disorders. Our most advanced drug candidate, BCX-1812, is designed to treat and prevent viral influenza. We licensed this drug candidate to The R.W. Johnson Pharmaceutical Research Institute, or PRI, and Ortho-McNeil Pharmaceutical, Inc., both Johnson & Johnson companies. They have informed us that the planning of Phase III trials for the 1999/2000 flu season is underway.

## OUR BUSINESS STRATEGY

Our business strategy is to use structure-based drug design technologies to develop innovative, small-molecule pharmaceuticals to treat a variety of diseases and disorders. We focus our drug development efforts on the development of potent, selective inhibitors of enzymes associated with several diseases. Enzymes are proteins that cause or enable biological reactions necessary for the progression of the disease or disorder. The specific enzymes on which we focus are called enzyme targets. Inhibition of these enzyme targets might be effective in the treatment of infectious, cardiovascular and other diseases and disorders. Inhibition means interfering with the functioning of an enzyme target, thereby stopping or slowing the progression of the disease or disorder. The principal elements of our strategy are:

- SELECT AND LICENSE PROMISING ENZYME TARGETS FOR THE DEVELOPMENT OF SMALL-MOLECULE PHARMACEUTICALS. We use our technical expertise and network of academic and industry contacts to evaluate and select promising enzyme targets to license for developing small-molecule pharmaceuticals. A small-molecule pharmaceutical is characterized by low molecular weight and can therefore be taken orally rather than administered intravenously. We choose enzyme targets that meet as many of the following criteria as possible:
  - serve important functions in disease pathways;
  - have well-defined active sites;
  - produce results in animal tests that would be indicative of results in humans; and
  - have the potential for short duration clinical trials.
- FOCUS ON HIGH VALUE-ADDED, STRUCTURE-BASED DRUG DESIGN TECHNOLOGIES. We focus our drug-discovery activities and expenditures on applications of structure-based drug design technologies to design and develop drug candidates. Structure-based drug design is a process by which we design a drug candidate through detailed analysis of the enzyme which the drug candidate must inhibit in order to stop the progression of the disease or disorder. We believe that structure-based drug design is a powerful tool for rapid and efficient development of small-molecule drug candidates that have the potential to be safe, effective and relatively inexpensive to manufacture. Our structure-based drug design technologies typically allow us to design and synthesize multiple drug candidates that inhibit the same enzyme target. We believe this strategy can lead to broad patent protection and enhance the competitive advantages of our compounds.
- DEVELOP INHIBITORS THAT ARE PROMISING CANDIDATES FOR COMMERCIALIZATION. We test multiple compounds to identify those that are most promising for clinical development. We base our selection of promising development candidates on product characteristics, including their availability at the site of activity in the human body, their activity in chemical tests and in laboratory animals or humans and their safety. We believe that this focused strategy allows us to eliminate unpromising candidates from consideration sooner without incurring substantial clinical costs. In addition, we select drug candidates on the basis of their potential for relatively efficient Phase I and Phase II clinical trials that require fewer patients to initially indicate safety and efficacy. We will

consider, however, more complex candidates with longer development cycles if we believe that they offer promising commercial opportunities.

An important element of our business strategy is to control fixed costs and overhead through contracting and entering into license agreements with other parties. With only 56 employees, we maintain a streamlined corporate infrastructure that focuses exclusively on our strongest areas of expertise. By contracting with other parties specializing in aspects of our business in which we are not as strong, we believe that we can control costs, enable our drug candidates to reach the market more quickly and reduce our business risk. Key elements of our contracting strategy include:

- ENTERING INTO RELATIONSHIPS WITH ACADEMIC INSTITUTIONS AND BIOTECHNOLOGY COMPANIES. Many academic institutions and biotechnology companies perform extensive research on the molecular and structural biology of potential drug development targets. By entering into relationships with these institutions, we believe we can significantly reduce the time, cost and risks involved in drug target development. Our collaborative relationships with such organizations may lead to the licensing of one or more drug targets. Upon licensing a drug target from these institutions, the scientists from these institutions typically become working partners as members of our structure-based drug design teams. We believe this makes us a more attractive development partner to these scientists. In addition, we collaborate with outside experts in a number of areas, including crystallography, molecular modeling, combinatorial chemistry, biology, pharmacology, oncology, immunology and infectious diseases. These collaborations enable us to complement our internal capabilities without adding costly overhead. We believe this strategy allows us to save valuable time and expense, complement our technology platform, and further diversify and strengthen our portfolio of drug candidates. An example of such a collaborative relationship is the arrangement that we have with The University of Alabama at Birmingham, or UAB, which has resulted in the initiation of most of our early drug development programs.
- LICENSING DRUG DEVELOPMENT CANDIDATES TO OTHER PARTIES. We plan to advance drug candidates through early-stage drug development, then license them to pharmaceutical or biotechnology partners for final development and global marketing. We believe partnerships are a good source of development payments, license fees, milestone payments and royalties. They also reduce the costs and risks of late-stage product development, regulatory approval, manufacturing and marketing. We believe that focusing on discovery and early-stage drug development while benefiting from pharmaceutical partners' proven development and commercialization expertise will reduce our internal expenses and allow us to have a larger number of drug candidates progress to late-stage drug development.

#### PRODUCTS UNDER DEVELOPMENT

The following table summarizes our development projects as of October 8, 1999:

PROGRAM AND INDICATION	DELIVERY FORM	DEVELOPMENT STAGE	WORLDWIDE RIGHTS
NEURAMINIDASE INHIBITOR (BCX-1812)			
Influenza	Oral	A Phase II--Completed	PRI/ Ortho-McNeil(1)
PNP INHIBITOR (BCX-34)			
Cutaneous T-Cell Lymphoma	Oral	Phase I/II--Underway	BioCryst
Other T-Cell Cancers	Intravenous	Phase I/II--Planned	BioCryst
COMPLEMENT INHIBITORS			
Cardiopulmonary Bypass Surgery	Intravenous	Preclinical--Ongoing	BioCryst

(1) We license our neuraminidase inhibitor, BCX-1812, to PRI and Ortho-McNeil, both Johnson & Johnson companies.

INFLUENZA BACKGROUND

OVERVIEW. Influenza, commonly known as the flu, is perceived by many people as a transient, inconvenient viral infection that leaves its sufferers bed-ridden for a few days. In truth, however, flu is a virulent, acute respiratory disease that is sometimes deadly. In North America, Western Europe and Japan, an estimated 70 million to 150 million individuals suffer from influenza annually. The flu is particularly dangerous to the elderly, young children and debilitated patients, accounting for approximately 20,000 deaths in the United States each year. The flu and associated complications are the sixth leading cause of death in the United States. A 1994 article in THE NEW ENGLAND JOURNAL OF MEDICINE estimated that the annual cost to the U.S. economy associated with influenza epidemics was in excess of \$12 billion.

Flu epidemics are regional outbreaks that cause an average of 40,000 flu-related deaths. Flu pandemics, however, are much more severe. Pandemics are worldwide outbreaks of a particular strain of the virus that occur relatively infrequently but can be disastrous. The Spanish flu pandemic of 1918-19 killed more than 20 million people worldwide. In the United States alone, the Asian flu of 1957-58 resulted in 70,000 deaths, and the Hong Kong flu of 1968-69 caused 34,000 deaths. The worldwide deaths caused by the Asian and Hong Kong pandemics topped 1.5 million, with an estimated impact to the world economy of \$32 billion. Due to increases in the world population and international air travel, mutation of the flu virus could spread rapidly, resulting in widespread morbidity and mortality.

SYMPTOMS AND TREATMENT OF INFLUENZA. Although influenza is considered a respiratory disease, flu sufferers usually become acutely ill with high fever, chills, headache, weakness, loss of appetite and aching joints. The flu sufferer may also have a sore throat, dry cough and burning eyes.

For most healthy children and adults, influenza is typically a moderately severe illness. However, for people with pre-existing medical conditions, influenza can be very severe and, in many cases, fatal. In these patients, bacterial infections may occur because the body's immune system is so weakened by influenza that its defenses against bacteria are low. Bacterial pneumonia is the most common complication of influenza.

The development of effective therapeutics has challenged medical researchers due to the seasonal variation in viral strains and the highly infectious nature of influenza. Patients, therefore, have limited treatment options. Amantadine and rimantadine are used for treatment of influenza A but are ineffective against influenza B. In addition, these drugs cause some adverse side effects, and the virus may develop resistance to these drugs.

Vaccines are available against the disease but have limitations: people require advance vaccination; vaccines are limited by their specificity to particular strains of the virus; and vaccines offer little protection if the vaccine is inaccurate. In addition, many people decline the required injections because of fear and/or discomfort. The ability of the virus to change its structure to avoid the body's natural defenses is a serious obstacle to developing an effective vaccine against influenza. Different strains can arise when surface antigens on the virus (the portion of the virus that causes an immune reaction in humans) undergo minor genetic mutations each year as the virus replicates. Because of this mutation ability, the immunity acquired in response to infection by a particular strain of the virus does not provide adequate protection against viruses that subsequently arise. The production of a new vaccine each year is not only complex and expensive, but also an inefficient method of global disease control.

INHIBITING INFLUENZA NEURAMINIDASE. Research during the past two decades has seen dramatic advances in understanding the molecular structure and function of the influenza virus. Considerable attention has been focused on the enzyme neuraminidase, which is located on the surface of the virus. Neuraminidase assists in the release and spread of the flu virus by breaking the chemical strands that

hold the new viruses to the cell surface, allowing the replicated virus to spread and infect other cells. This process progresses until the host's immune response can produce enough antibodies to bring the infection under control.

Research suggests that inhibiting the neuraminidase enzyme would keep new viruses attached to the cell surface, thereby preventing the spread of the virus and the further infection of other cells. The subsequent quantities of virus in the bloodstream would not be enough to cause disease but would be sufficient to induce the body to mount an immune response.

In addition to our neuraminidase inhibitor, both Hoffmann-La Roche, in collaboration with Gilead Sciences, and Glaxo Wellcome are developing neuraminidase inhibitors. Hoffmann-La Roche has developed an orally active neuraminidase inhibitor and filed a new drug application with the FDA for this twice-a-day treatment. Similarly, Glaxo Wellcome's neuraminidase inhibitor, which is administered by dry powder inhaler twice a day, received FDA approval and has recently been launched in the United States and other countries.

#### OUR INFLUENZA NEURAMINIDASE INHIBITOR

**BACKGROUND.** In 1987, scientists at The University of Alabama at Birmingham, or UAB, in collaboration with our scientists, began determining the molecular structure of the influenza neuraminidase enzyme from several different strains of influenza, using X-ray crystallography. Subsequently, our scientists and UAB scientists developed numerous new inhibitors of these enzymes using structure-based drug design. We licensed the influenza neuraminidase program from UAB in 1994 and proceeded to complete the studies of the enzyme's molecular structure needed to advance the development of neuraminidase inhibitors. The structure of the active site of influenza neuraminidase is similar among different viral strains. Because of this similarity, we believe that our neuraminidase inhibitors may be effective in the treatment and prevention of influenza, regardless of changes in the virus.

Four of the patented compounds from our development efforts emerged as viable product development candidates. We called them BCX-1812, 1827, 1898 and 1923. Preclinical studies demonstrated that our drug candidates have the following benefits:

- excellent safety profile;
- inhibition of both influenza A and B;
- effective when taken orally;
- probable once-a-day dosage; and
- can be made into a liquid form, allowing for use by the elderly and young children.

**CLINICAL DEVELOPMENT.** In September 1998, we entered into an exclusive worldwide license agreement with PRI and Ortho-McNeil to develop and market our proprietary influenza neuraminidase inhibitors to treat and prevent viral influenza. Since the collaboration was established, PRI selected BCX-1812 for clinical development and moved through Phase I clinical trials and a Phase II clinical study by August 1999. We recently announced preliminary results from a Phase II placebo-controlled, randomized study conducted by PRI for the treatment of healthy volunteers infected with a strain of influenza A. PRI advised us that the data from this Phase II study indicated a statistically significant reduction of flu virus in the body and that the drug was well-tolerated at all dosage levels. We have been informed by PRI that planning of Phase III clinical trials for the 1999/2000 influenza season is underway. The FDA may not accept the Phase III clinical protocols, PRI may not commence the Phase III clinical trials in 1999 or at all, or the Phase III clinical trials, if initiated, may not be successful.

## PNP INHIBITOR (BCX-34)

### T-CELL RELATED DISEASES

**OVERVIEW.** The human immune system employs specialized cells, including T-cells, to control infection by recognizing and attacking disease-causing viruses, bacteria and parasites. T-cells are an essential part of the body's immune system that serve a dual purpose--orchestrating and participating in the body's immune response. For the most part, this system works flawlessly to protect the body. However, there are diseases in which T-cells multiply uncontrollably (T-cell proliferative diseases) or attack normal cells (autoimmune diseases). Proliferating T-cells have been implicated in a number of T-cell cancers, including cutaneous T-cell lymphoma. Cutaneous T-cell lymphoma is a skin cancer in which T-cells, which normally help fight disease, duplicate rapidly and cause skin cancer.

**PNP INHIBITION.** Purine nucleoside phosphorylase, or PNP, is an enzyme that is believed to play an important role in T-cell proliferation, because PNP is necessary to maintain normal DNA synthesis in T-cells. We believe that inhibiting PNP is a new mechanism for suppressing T-cell replication without significantly affecting other cells, and we believe this may prove to have an impact on the treatment of several diseases.

### OUR PNP INHIBITOR

**BACKGROUND.** We designed our lead PNP inhibitor drug candidate, BCX-34, to suppress T-cell replication without significantly affecting other cells. BCX-34 has been in clinical trials since 1992. Our initial approach was to develop a cream formulation of BCX-34 applied to the skin, which, if effective, could have led to a rapid, cost-effective regulatory approval. We conducted two Phase III clinical trials in 1996 and 1997 to determine the effects of topical BCX-34 on psoriasis, an autoimmune disease that affects the skin, and cutaneous T-cell lymphoma. These trials, however, did not show statistically significant results between the treated and placebo groups. Therefore, we discontinued the topical program.

**CURRENT DEVELOPMENT STRATEGY.** We believe that, in order for BCX-34 to be effective, BCX-34 must be administered in a form and an amount that obtains adequate levels of the drug in the body. In the clinical trials we have completed with an oral formulation of BCX-34, the dose levels were inadequate to obtain clinically relevant results. These clinical trials, however, were effective in establishing the safety of BCX-34 at various dose levels and the maximum oral dose absorbable by the body.

Based on these studies, we have designed two new Phase I/II clinical trials to evaluate BCX-34 in the treatment of various T-cell cancers. Although the patient population for T-cell cancers is small, we believe that we can more quickly evaluate the efficacy of BCX-34 because these patients are suffering from a serious unmet medical need and have a generally unfavorable clinical outlook.

We are conducting one of these clinical trials to evaluate BCX-34 for the treatment of cutaneous T-cell lymphoma at the maximum oral dose. We expect to complete this trial in early 2000. We expect to start a second trial for treatment of various other T-cell cancers. We are designing this trial to evaluate higher blood levels of BCX-34, which can only be obtained with intravenous therapy.

These two clinical trials should provide us with the necessary information to begin other studies in T-cell related diseases. Hence, the outcome of these two studies of T-cell cancers will determine the future clinical evaluation of BCX-34. If we are unable to demonstrate the clinical efficacy of BCX-34 at these higher dose levels, we will likely discontinue developing BCX-34.

## COMPLEMENT INHIBITORS

### COMPLEMENT CASCADE

**OVERVIEW.** The human body is equipped with defense mechanisms that respond aggressively to infection or injury. This response is uniquely designed for each challenge whether caused by viruses,

bacteria, or other matter harmful to the body. Once the immune system recognizes a "foreign invader," complement is activated to destroy or remove it. The complement cascade is the term for a system of functionally linked enzymes that assists in the removal of bacteria or destruction of cells that the body does not recognize as its own.

If these enzymes do not operate properly, they can cause adverse biological effects including tissue damage. This occurs in an unregulated way in certain medical situations such as cardiopulmonary bypass surgery.

#### OUR COMPLEMENT INHIBITORS

**BACKGROUND.** Working closely with scientists of The University of Alabama at Birmingham, we characterized the three-dimensional structure of one of the components of the complement cascade. In 1997, using X-ray crystallographic and molecular modeling techniques, we designed and synthesized a class of small molecule compounds that are highly potent inhibitors of complement and certain other blood enzymes. These compounds may have applications in the treatment of several disorders by limiting the rapid and aggressive damage caused by the activation of complement proteins. In addition, preclinical studies to examine the safety and efficacy of several of these compounds are currently in progress.

**CLINICAL DEVELOPMENT.** We completed two Phase I studies of one of the drug candidates in our complement inhibitor program. These studies showed that the effective dose for blocking complement activation was too close to toxicologic limits to be used during cardiopulmonary bypass surgery. Hence, other compounds in this series are now being evaluated for clinical development.

#### TISSUE FACTOR/VIIA

A series of complicated reactions that are initiated by a group of enzymes in the body called the Tissue Factor/VIIa complex forms a blood clot. Animal tests show that blood clot formation can be minimized by inhibiting the Tissue Factor/VIIa complex. Tissue Factor/VIIa inhibitors may potentially be useful in various cardiovascular diseases and disorders. We are attempting to identify potential inhibitors of Tissue Factor/VIIa. We have an agreement with Sunol Molecular Corp. to expedite the discovery of new drug candidates designed to inhibit Tissue Factor/VIIa for our cardiovascular program. Under the terms of this agreement, Sunol conducts research and supplies us with tissue factor for our drug design program.

#### PARAINFLUENZA

The parainfluenza virus, or PIV, affects approximately three million infants and young children per year in the United States. Complications arising from infection with PIV result in a significant portion of the cases of croup, bronchitis and pneumonia in children. In October 1999, we entered into an agreement with St. Jude Children's Research Hospital in Tennessee, University of Bath in England and University of St. Andrews in Scotland for research and development related to PIV. Under the agreement, St. Jude Children's Hospital, University of Bath and University of St. Andrews will provide us with compounds that will form the basis for our design and development of potential drug candidates for the treatment of PIV.



## STRUCTURE-BASED DRUG DESIGN

Structure-based drug design is a drug discovery approach by which we design synthetic compounds from detailed structural knowledge of the active sites of enzyme targets associated with particular diseases. Enzymes are proteins that act as catalysts for many vital biological reactions. Our goal generally is to design a compound that will fit in the active site of an enzyme (the active site of an enzyme is the area into which a chemical or biological molecule fits to initiate a biochemical reaction) and thereby interfere with the progression of disease.

Our structure-based drug design involves the application of both traditional biology and medicinal chemistry and an array of advanced technologies. We use X-ray crystallography, computer modeling of molecular structures and advanced chemistry techniques to focus on the three-dimensional molecular structure and active site characteristics of the enzymes that control cellular biology.

We believe that structure-based drug design technologies are superior to drug screening techniques. By identifying the target enzyme in advance and by discovering the chemical and molecular structure of the enzyme, we believe it is possible to design a better drug to interact with the enzyme. In addition, the structural data obtained by X-ray crystallographic analysis allows additional analysis and compound modification at each stage of the biological evaluation. This capability makes structure-based drug design a powerful tool for rapid and efficient development of drugs that are highly specific for particular enzyme target sites.

## RESEARCH AND DEVELOPMENT

We initiated our research and development program in 1986, with drug synthesis beginning in 1987. We have assembled a scientific research staff with expertise in a broad base of advanced research technologies including protein biochemistry, X-ray crystallography, chemistry and pharmacology. Our research facilities include protein biochemistry and organic synthesis laboratories, testing facilities, X-ray crystallography, computer and graphics equipment and facilities to make drug candidates on a small scale.

During the years ended December 31, 1996, 1997 and 1998, we spent an aggregate of \$27.5 million on research and development. Approximately \$15.2 million of that amount was spent on in-house research and development, and \$12.3 million was spent on contract research and development.

## COLLABORATIVE RELATIONSHIPS

### CORPORATE ALLIANCES

#### 3-DIMENSIONAL PHARMACEUTICALS, INC.

In October 1996, we signed a research collaboration agreement with 3-Dimensional Pharmaceuticals under which we will share resources and technology to develop inhibitors of complement enzymes. The agreement combines our capabilities in structure-based drug design with the selection power of 3-Dimensional Pharmaceuticals' Directed Diversity-Registered Trademark-technology, a proprietary method of directing combinatorial chemistry and high throughput screening toward specific molecular targets. In June 1999, we updated and renewed our original agreement to concentrate on selected complement enzymes as targets for the design of inhibitors. Under the terms of the agreement, the companies are responsible for their own research costs. If a drug candidate emerges as a result of the joint research, the companies will negotiate the product development and commercialization rights and responsibilities.

THE R.W. JOHNSON PHARMACEUTICAL RESEARCH INSTITUTE AND ORTHO-MCNEIL  
PHARMACEUTICAL, INC.

We have entered into an exclusive worldwide license agreement with PRI and Ortho-McNeil to develop and market our proprietary influenza neuraminidase inhibitors to treat and prevent viral influenza. We received an initial \$6.0 million payment from Ortho-McNeil and an additional \$6.0 million common stock equity investment from Johnson & Johnson Development Corporation. In June 1999, we received a \$2.0 million milestone payment from Ortho-McNeil in connection with the initiation of Phase II clinical testing in the United States. In addition, we may receive cash payments upon achievement of specified developmental and regulatory milestones and royalties on product sales, if any.

PRI will be responsible for research and development of the compounds, including expenses. Ortho-McNeil will market products approved by the FDA for marketing in the United States. Other Johnson & Johnson companies, including Janssen-Cilag, will market products approved for marketing outside the United States.

NOVARTIS AG

In 1990, we entered into an exclusive worldwide license agreement with Novartis AG, formerly Ciba-Geigy, for use of certain of our PNP inhibitors, not including BCX-34. We received an initial \$500,000 payment from Novartis, up to \$300,000 of which is refundable in circumstances specified in the agreement. The agreement also provides for Novartis to pay us royalties on sales, if any, of the PNP inhibitors. We may not receive any revenue based on this license agreement.

SUNOL MOLECULAR CORP.

In April 1999, we entered into an agreement with Sunol. This agreement requires Sunol to conduct research and supply us with protein targets for drug design to expedite the discovery of new drug candidates designed to inhibit Tissue Factor/VIIa for our cardiovascular program.

The initial focus of the agreement will be on identifying compounds that work to inhibit the coagulation cascade of Tissue Factor/VIIa. Tissue Factor/VIIa is a promising target for the development of anticoagulants for cardiopulmonary bypass surgery, angioplasty and other cardiovascular disorders. Sunol will produce Tissue Factor and provide us with quantities of the protein to assist in the identification of inhibitors specific to the activity of Tissue Factor/VIIa.

TORII PHARMACEUTICAL CO., LTD.

In 1996, we granted Torii an exclusive license, with the right to sublicense, 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. Torii terminated the exclusive license agreement, and the rights to develop, manufacture and commercialize BCX-34 and certain other PNP inhibitor compounds in Japan reverted to us. Torii paid us an aggregate of \$4.0 million for license fees, milestone payments and an equity investment.

ACADEMIC ALLIANCES

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

We have had a close relationship with The University of Alabama at Birmingham, or UAB, since our formation. Our Chairman and Chief Executive Officer, Dr. Bugg, was the previous Director of the UAB Center for Macromolecular Crystallography, and our President and Chief Operating Officer, Dr. Bennett, was the former President of UAB, the former Chairman of the Department of Medicine at UAB and a former Chairman of the Department of Microbiology at UAB. Several of our consultants are employed by UAB. UAB has one of the largest X-ray crystallography centers in the world with approximately 124 full-time staff members and approximately \$20.7 million in research grants and

contract funding in 1998. Three of our early programs, PNP, influenza and complement inhibitors, originated at UAB. When we were founded in 1986, we entered into an agreement with UAB which granted us exclusive rights to discoveries resulting from research relating to PNP. We also entered into an agreement with UAB that gives us the first option to obtain a non-exclusive license to patents and copyrights of UAB not developed in collaboration with us or an exclusive license, in some cases worldwide, to patents, copyrights or intellectual property arising from research of UAB collaborators or investigators under contract to us.

Subsequently, we entered into agreements with UAB for influenza neuraminidase and complement inhibitors. Under the terms of these agreements, UAB performed specific research for us in return for research payments and license fees. UAB has granted us certain rights to any discoveries in these areas resulting from research developed by UAB or jointly developed with us. We have agreed to pay certain royalties on sales of any resulting product and to share in future payments received from other third-party collaborators. UAB has received and will continue to receive a portion of any license fees, milestone payments and royalties we receive from PRI and Ortho-McNeil for the influenza collaboration. We have completed the research under the UAB influenza agreement. We are continuing to fund the research program under the complement inhibitors agreement, which entitles us to an assignment of, or a right to an exclusive license for, any inhibitors of specified complement enzymes developed by UAB scientists during the period of support or for a one-year period thereafter. These two agreements have initial 25-year terms, are automatically renewable for five-year terms throughout the life of the last patent and are terminable by us upon three-month's notice and by UAB under certain circumstances.

#### PATENTS AND PROPRIETARY INFORMATION

Our success will depend in part on our ability to obtain and enforce patent protection for our products, methods, processes and other proprietary technologies, preserve our trade secrets, and operate without infringing on the proprietary rights of other parties, both in the United States and in other countries. We own or have rights to certain proprietary information, proprietary technology, issued and allowed patents and patent applications which relate to compounds we are developing. We actively seek, when appropriate, protection for our products, proprietary technology and proprietary information by means of U.S. and foreign patents, trademarks and contractual arrangements. In addition, we rely upon trade secrets and contractual arrangements to protect certain of our proprietary information, proprietary technology and products.

To date, we have been issued seven U.S. patents which expire between 2009 and 2015 and relate to our PNP inhibitor compounds. We have also been issued a U.S. patent covering a manufacturing process for our PNP inhibitors, which expires in 2015, and have filed a patent application for new processes to prepare BCX-34 and other PNP inhibitors. The U.S. Patent and Trademark Office has also issued to us a U.S. patent relating to inhibitors of influenza neuraminidase, which expires in 2015. We have also tried to protect our technology through the following patent applications which are still pending: two provisional U.S. patent applications and a patent cooperation treaty application related to our neuraminidase inhibitors; two provisional U.S. patent applications related to compounds and methods for detecting influenza virus; a patent cooperation treaty application related to complement inhibitors; and a provisional application relating to inhibiting T-cell proliferation. Our pending applications may not result in issued patents, and our patents may not provide us with sufficient protection against competitive products or otherwise be commercially available.

Our success is also dependent upon the skills, knowledge and experience of our scientific and technical personnel, none of which is patentable. To help protect our rights, we require all employees, consultants, advisors and collaborators to enter into confidentiality agreements which prohibit the disclosure of confidential information to anyone outside of our company and requires disclosure and assignment to us of their ideas, developments, discoveries and inventions. These agreements may not

provide adequate protection for our 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.

#### MARKETING AND SALES

We lack experience in marketing, distributing and selling pharmaceutical products. Our strategy is to rely on collaborators, licensees or arrangements with others to provide for the marketing, distribution and sales of any products we may develop. We may not be able to establish and maintain acceptable commercial arrangements with collaborators, licensees or others to perform such activities.

If approved, BCX-1812 will likely be the third influenza neuraminidase inhibitor to the market behind the influenza neuraminidase inhibitors currently marketed by Glaxo Wellcome and in development by Hoffmann-LaRoche, in collaboration with Gilead Sciences. We believe this may provide marketing challenges. However, we believe that there may be some advantages to not being first to market. We expect that both Glaxo Wellcome and Hoffmann-La Roche will play a major role in establishing the influenza treatment market and creating a demand for neuraminidase inhibitors on which Ortho-McNeil will be able to capitalize if our neuraminidase inhibitor is approved for marketing. Because neuraminidase inhibitors represent a new class of drugs that could impact a large number of people, a major education effort will be required to promote acceptance by both the treating physicians and the target population.

#### COMPETITION

The pharmaceutical and biotechnology industries are intensely competitive. Many companies, including biotechnology, chemical and pharmaceutical companies, are actively engaged in activities similar to ours, including research and development of drugs for the treatment of infectious, T-cell related and cardiovascular 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 we do. In addition, some of them have considerable experience in preclinical testing, clinical trials and other regulatory approval procedures. There are also academic institutions, governmental agencies and other research organizations that are conducting research in areas in which we are working. They may also market commercial products, either on their own or through collaborative efforts.

We expect to encounter significant competition for any of the pharmaceutical products we plan 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 fields of PNP and complement inhibitors. In addition, we are aware that other companies or institutions are pursuing development of new drugs and technologies directly targeted at applications for which we are developing our drug compounds. For example, Glaxo Wellcome's influenza neuraminidase inhibitor has received approval from the FDA, and they recently received approval to market their inhibitor in the United States and other countries. This product is administered in the form of a dry-powder inhaler, which could be difficult to use and may cause patient discomfort. The FDA also approved the influenza neuraminidase inhibitor developed by Hoffmann-La Roche, in collaboration with Gilead Sciences. If approved, our influenza neuraminidase inhibitor, BCX-1812, will likely be the third neuraminidase inhibitor to the market. We believe this may provide marketing challenges. In addition, other therapies for the treatment or prevention of flu include vaccines and the drugs amantadine and rimantadine, as well as over-the-counter products. There is also a vaccine currently in preclinical development that may immunize people against all strains of the flu virus, rendering flu drug products like ours obsolete.

In order to compete successfully, we must develop proprietary positions in patented drugs for therapeutic markets that have not been satisfactorily addressed by conventional research strategies and, in the process, expand our expertise in structure-based drug design. Our products, even if successfully tested and developed, may not be adopted by physicians over other products and may not offer economically feasible alternatives to other therapies.

#### GOVERNMENT REGULATION

The FDA regulates the pharmaceutical and biotechnology industries in the United States, and our drug candidates are subject to extensive and rigorous domestic government regulations prior to commercialization. The FDA regulates, among other things, the development, testing, manufacture, safety, efficacy, record-keeping, labeling, storage, approval, advertising, promotion, sale and distribution of pharmaceutical products. In foreign countries, our products are also subject to extensive regulation by foreign governments. These government regulations will be a significant factor in the production and marketing of any pharmaceutical products that we develop. Failure to comply with applicable FDA and other regulatory requirements at any stage during the regulatory process may subject us to sanctions, including:

- delays;
- warning letters;
- fines;
- product recalls or seizures;
- injunctions;
- penalties;
- refusal of the FDA to review pending market approval applications or supplements to approval applications;
- total or partial suspension of production;
- civil penalties;
- withdrawals of previously approved marketing applications; and
- criminal prosecutions.

The regulatory review and approval process is lengthy, expensive and uncertain. Before obtaining regulatory approvals for the commercial sale of any products, we or our licensees must demonstrate that our product candidates are safe and effective for use in humans. The approval process takes many years, substantial expenses may be incurred and significant time may be devoted to clinical development.

Before testing potential candidates in humans, we carry out laboratory and animal studies to determine safety and biological activity. After completing preclinical trials, we must file an investigational new drug application, including a proposal to begin clinical trials, with the FDA. We have filed eight investigational new drug applications to date and plan to file, or rely on certain partners to file, additional investigational new drug applications in the future. Thirty days after filing an investigational new drug application, a Phase I human clinical trial can start unless the FDA places a hold on the study.

Our phase I trials are designed to determine safety in a small group of patients or healthy volunteers. We also assess tolerances and the metabolic and pharmacologic actions of our drug candidates at different doses. After we complete the initial trial, we conduct a Phase II trial to assess safety and

efficacy and establish the optimal dose in patients. If Phase II trial is successful, we or our licensees conduct a Phase III trial verify the results in a larger patient population. A Phase III trial is required for FDA approval to market a drug. A Phase III trial may require hundreds or even thousands of patients and is the most expensive to conduct. The goal in Phase III is to collect enough safety and efficacy data to obtain FDA approval for treatment of a particular disease.

Initiation and completion of the clinical trial phases is dependent on several factors including things that are beyond our control. For example, the clinical trials are dependent on patient enrollment, but the rate at which patients enroll in the study depends on:

- the size of the patient population we intend to treat;
- the availability of patients;
- the willingness of patients to participate; and
- the patient meeting the eligibility criteria.

Delays in planned patient enrollment may result in increased expense.

After completion of the clinical trials of a product, we or our licensees must submit a new drug application to the FDA for marketing approval before commercialization of the product. The FDA may not grant approval on a timely basis, if at all. The FDA, as a result of the Food and Drug Administration Modernization Act of 1997, has six months to review and act upon license applications for priority therapeutics that are for a life-threatening or unmet medical need. Standard reviews can take between one and two years, and can even take longer if significant questions arise during the review process. The FDA may withdraw any required approvals, once obtained.

In addition to clinical development regulations, we and our contract manufacturers and collaborators must comply with the applicable FDA current good manufacturing practice regulations. Good manufacturing practice regulations include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation. Manufacturing facilities are subject to inspection by the FDA. Such facilities must be approved before we can use them in commercial manufacturing of our potential products. We or our contract manufacturers may not be able to comply with the applicable good manufacturing practice requirements and other FDA regulatory requirements. If we or our contract manufacturers fail to comply, our business, financial condition and results of operations will be materially adversely affected.

In June 1995, we notified the FDA that we submitted incorrect data for our Phase II studies of BCX-34 applied to the skin for cutaneous T-cell lymphoma and psoriasis. The FDA inspected us in November 1995 and issued us a List of Inspectional Observations, Form FDA 483, that cited our failure to follow good clinical practices. The FDA also inspected us in June 1996, the focus was on the two 1995 Phase II dose-ranging studies of topical BCX-34 for the treatment of cutaneous T-cell lymphoma and psoriasis. As a result of the investigation, the FDA issued us a Form FDA 483, which cited our failure to follow good clinical practices. As a consequence, our ongoing and future clinical studies may receive increased scrutiny, which may delay the regulatory review process.

Also in June 1996, the FDA investigated one of the clinical trial sites that participated in our 1995 Phase II dose-ranging studies of BCX-34 applied to the skin for the treatment of cutaneous T-cell lymphoma and psoriasis. As a result, the FDA issued a Form FDA 483 to the principal investigator at a clinical site which cited a number of deficiencies, including:

- improper delegations of authority by the principal investigator;
- failures to follow the protocols;
- deviations from established procedures of the institutional review board; and

- discrepancies or deficiencies in documentation and reporting.

Following the failure of BCX-34 applied to the skin in 1997, we discontinued the development of BCX-34 applied to the skin. In November 1997, the FDA notified us that they would not accept work performed by the deficient investigator without further validation. The majority of the work performed by this investigator was for BCX-34 applied to the skin, which was discontinued in 1997. However, work performed by this investigator for oral BCX-34 will not be accepted by the FDA to support efficacy in any new drug application.

SCIENTIFIC ADVISORY BOARD AND CONSULTANTS

Our scientific advisory board is comprised of five scientific advisors who are leaders in certain of our core disciplines or who otherwise have specific expertise in our therapeutic focus areas. We also have consulting agreements with a number of other scientists with expertise in our core disciplines or who are specialists in diseases or treatments on which we focus. The scientific advisory board meets as a group at scheduled meetings and the consultants meet more frequently, on an individual basis, with our scientific personnel and management to discuss our ongoing research and drug discovery and development projects.

The scientific advisory board consists of the following individuals:

NAME	POSITION
Albert F. LoBuglio, M.D. (Chairman).....	Professor of Medicine and the Director of The University of Alabama at Birmingham Comprehensive Cancer Center.
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.
Herbert A. Hauptman, Ph.D. ....	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, retired, Director of DNA Resources at Celera Genomics Corporation, recipient of the Nobel Prize in Medicine (1978).

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 and the consultants are all employed by or have consulting agreements with entities other than us, some of which may compete with us in the future. The scientific advisors and the consultants are expected to devote only a small portion of their time to our business, although no specific time commitment has been established. They are not expected to participate actively in our affairs or in the development of our technology. Several 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 us. The loss of the services of the scientific advisors and the consultants could adversely affect us to the extent that we are pursuing

research or development in areas relevant to the scientific advisors' and consultants' expertise. To the extent members of our scientific advisory board or the consultants have consulting arrangements with or become employed by any of our competitors, we 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 subsidiary of Warner-Lambert, that uses a core technology similar to ours.

Any inventions or processes independently discovered by the scientific advisors or the consultants may not become our property 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 our competitors pursuant to sponsored research agreements. We require the scientific advisors and the consultants to enter into confidentiality agreements which prohibit the disclosure of confidential information to anyone outside of our company and require disclosure and assignment to us of their ideas, developments, discoveries or inventions. However, our competitors may gain access to trade secrets and other proprietary information developed by us and disclosed to the scientific advisors and the consultants.

#### HUMAN RESOURCES

As of October 8, 1999, we had 56 employees, of whom 43 were engaged in research and development and 13 were in general and administrative functions. Our scientific staff, 19 of whom hold Ph.D. or M.D. degrees, has diversified experience in biochemistry, pharmacology, X-ray crystallography, synthetic organic chemistry, computational chemistry, medicinal chemistry and pharmacology. We consider our relations with our employees to be satisfactory.

#### PROPERTIES

Our administrative offices and principal research facility are located in 42,950 square feet of leased office space in Riverchase Industrial/Research Park in Birmingham, Alabama. The lease runs through June 30, 2003 with an option to lease for an additional three years at current market rates. We believe that our facilities are adequate for our current operations.

#### LEGAL PROCEEDINGS

We are not currently a party in any material legal proceedings.



MANAGEMENT

EXECUTIVE OFFICERS AND DIRECTORS

The following table shows information about our executive officers and directors as of October 8, 1999:

NAME	AGE	POSITION
Charles E. Bugg, Ph.D.....	58	Chairman, Chief Executive Officer and Director
J. Claude Bennett, M.D.....	65	President, Chief Operating Officer, Medical Director and Director
John A. Montgomery, Ph.D. ....	75	Senior Vice President, Secretary, Chief Scientific Officer and Director
Ronald E. Gray.....	58	Chief Financial Officer, Assistant Secretary and Treasurer
John R. Uhrin.....	46	Vice President, Corporate Development
William W. Featheringill.....	56	Director
Edwin A. Gee, Ph.D.....	79	Director
Zola P. Horovitz, Ph.D.....	64	Director
Joseph H. Sherrill, Jr.....	58	Director
William M. Spencer, III.....	78	Director
Randolph C. Steer, M.D., Ph.D.....	49	Director

Messrs. Featheringill and Spencer and Dr. Gee are members of our Compensation and Audit Committees.

CHARLES E. BUGG, PH.D. was named Chairman of the Board, Chief Executive Officer and Director in November 1993 and President in January 1995. Dr. Bugg relinquished the position of President in December 1996 when Dr. Bennett joined BioCryst in that position. Prior to joining BioCryst, Dr. Bugg had served as the Director of the Center for Macromolecular Crystallography, Associate Director of the Comprehensive Cancer Center and Professor of Biochemistry at The University of Alabama at Birmingham since 1975. He was a Founder of BioCryst and served as BioCryst's first Chief Executive Officer from 1987 to 1988 while on a sabbatical from The University of Alabama at Birmingham. Dr. Bugg also served as Chairman of our scientific advisory board from January 1986 to November 1993. He continues to hold the position of Professor Emeritus in Biochemistry and Molecular Genetics at The University of Alabama at Birmingham, a position he has held since January 1994.

J. CLAUDE BENNETT, M.D. was named President and Chief Operating Officer in December 1996 and elected a Director in January 1997. He was appointed our Medical Director in August 1999. Prior to joining BioCryst, Dr. Bennett was President of The University of Alabama at Birmingham from October 1993 to December 1996, Professor and Chairman of the Department of Medicine of The University of Alabama at Birmingham from January 1982 to October 1993, and Professor and Chairman of the Department of Microbiology from January 1970 to December 1982. Dr. Bennett served on BioCryst's scientific advisory board from 1989 to 1996. He continues to hold the position of Distinguished University Professor Emeritus at The University of Alabama at Birmingham, a position he has held since January 1997.

JOHN A. MONTGOMERY, PH.D. has been a Director since November 1989 and has been Secretary and Chief Scientific Officer since joining BioCryst in February 1990. He was Executive Vice President from February 1990 until May 1997, at which time he was named Senior Vice President. Dr. Montgomery was a Founder of BioCryst. Prior to joining BioCryst, Dr. Montgomery served as Senior Vice President of Southern Research Institute of Birmingham from January 1981 to February 1990. He continues to hold the position of Distinguished Scientist at Southern Research Institute, a position he has held since February 1990.

RONALD E. GRAY joined BioCryst in January 1993 as Chief Financial Officer. Mr. Gray received the additional title of Assistant Secretary in December 1993 and Treasurer in January, 1995. 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 previously Vice President of Finance, Secretary and Treasurer of CyCare Systems, Inc., a health care information processing company.

JOHN R. UHRIN joined BioCryst in March 1998 as Vice President, Corporate Development with 21 years of sales and marketing experience in the pharmaceutical, biotechnology, medical and managed care industries. He joined BioCryst following 11 years at Genentech, Inc. From 1987 to 1998, he held various management positions at Genentech, most recently as Director of Special Markets/Managed Care. Prior to working for Genentech, he held various sales and management positions with Eli Lilly from 1977 to 1987.

WILLIAM W. FEATHERINGILL was elected a Director in May 1995. Since June 1995, Mr. Featheringill has been Chairman and Chief Executive Officer of Electronic Healthcare Systems, a software company, and President, Chief Executive Officer and director, since 1973, of Private Capital Corporation, a venture capital management company. From 1988 to 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. MACESS Corporation merged with Sungard Data Systems in late 1995. From 1985 to December 1994, Mr. Featheringill was the developer, Chairman and President of Complete Health Services, Inc., a health maintenance organization. Complete Health Services, Inc. was acquired by United HealthCare Corporation in June 1994. Mr. Featheringill is a director of Citation Corporation.

EDWIN A. GEE, PH.D. was elected a Director in August 1993. Dr. Gee, who retired in 1985 as Chairman of the Board and Chief Executive Officer of International Paper Company, has been active as an executive in biotechnology, pharmaceutical and specialty chemical companies since 1970. He is Chairman Emeritus and a director of OSI Pharmaceuticals, Inc., one of the leading biotechnology companies for the diagnosis and treatment of cancer.

ZOLA P. HOROVITZ, PH.D. was elected a Director in August 1994. Dr. Horovitz was Vice President of Business Development and Planning at Bristol-Myers Squibb from 1991 until his retirement in April 1994 and previously was Vice President of Licensing at the same company from 1990 to 1991. Prior to 1990, he spent over 30 years with The Squibb Institute for Medical Research, most recently as Vice President Research, Planning, & Scientific Liaison. He has been an independent consultant in pharmaceutical sciences and business development since his retirement from Bristol-Myers Squibb in April 1994. He serves on the Board of Directors of Avigen, Inc., Clinitor Inc., Diacrin, Inc., Magainin Pharmaceuticals, Inc., Procept Corporation, Roberts Pharmaceutical Corporation and Synaptic Pharmaceutical Corp. Dr. Horovitz is also Chairman of Magainin Pharmaceuticals, Inc.

JOSEPH H. SHERRILL, JR. was elected a Director in May 1995. Mr. Sherrill served as President of R.J. Reynolds Asia Pacific, based in Hong Kong, where he oversaw R.J. Reynolds' operations across Asia, including licensing, joint ventures and a full line of operating companies from August 1989 to his retirement in October 1994. Prior management positions with R.J. Reynolds include Senior Vice President of Marketing for R.J. Reynolds International, President and Chief Executive Officer of R.J. Reynolds Tabacos de Brazil, and President and General Manager of R.J. Reynolds Puerto Rico.

WILLIAM M. SPENCER, III was a Founder and has been a Director of BioCryst since its inception. 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 has served 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. Dr. Steer serves on the Board of Directors of Techne Corporation.

PRINCIPAL STOCKHOLDERS

The following table shows information regarding beneficial ownership of our common stock as of September 20, 1999 by:

- each of our directors and executive officers;
- all directors and executive officers as a group; and
- each person known by us to be the beneficial owner of more than five percent of our common stock.

NAME OF BENEFICIAL OWNER	NUMBER OF SHARES BENEFICIALLY OWNED(1)	PERCENT OF COMMON STOCK BENEFICIALLY OWNED	
		BEFORE OFFERING	AFTER OFFERING
William W. Featheringill..... 100 Brookwood Place #410 Birmingham, Alabama 35209	2,699,872(2)	17.7%	15.6%
Johnson & Johnson Development Corporation..... One Johnson & Johnson Plaza New Brunswick, New Jersey 08933	918,836(3)	6.0	5.3
Max Cooper..... 121 Summit Parkway Birmingham, Alabama 35209	780,100(4)	5.1	4.5
Charles E. Bugg, Ph.D.....	609,127(5)	3.9	3.4
William M. Spencer, III.....	539,858(6)	3.5	3.1
Joseph H. Sherrill, Jr.....	421,500(7)	2.8	2.4
John A. Montgomery, Ph.D. ....	160,620(8)	1.0	0.9
J. Claude Bennett, M.D. ....	107,460(9)	*	*
Ronald E. Gray.....	88,672(10)	*	*
Randolph C. Steer, M.D., Ph.D. ....	74,999(11)	*	*
Zola P. Horovitz, Ph.D.....	43,749(11)	*	*
Edwin A. Gee, Ph.D. ....	39,999(11)	*	*
John R. Uhrin.....	26,246(12)	*	*
All executive officers and directors as a group (11 persons).....	4,812,102(13)	29.4	26.2

\* Less than one percent.

- (1) Gives effect to the shares of common stock issuable within 60 days after September 20, 1999 upon the exercise of all options and other rights beneficially held by the indicated stockholder on that date.
- (2) Includes 364,900 shares of common stock held by the Featheringill Family Trust of which he is a beneficial owner and 32,500 shares of common stock issuable upon exercise of stock options.
- (3) Johnson & Johnson Development Corporation is a wholly owned subsidiary of Johnson & Johnson and shares investment and voting power with Johnson & Johnson.
- (4) Based on filings made by Mr. Cooper with the SEC.

- (5) Includes 539,084 shares of common stock issuable upon exercise of stock options.
- (6) Includes 43,749 shares of common stock issuable upon exercise of stock options and 10,000 shares of common stock held by Mr. Spencer's spouse. Mr. Spencer disclaims beneficial ownership of the 10,000 shares of common stock held by his spouse.
- (7) Includes 32,500 shares of common stock issuable upon exercise of stock options, 10,000 shares of common stock which Mr. Sherrill holds jointly with his spouse, 1,000 shares of common stock held by Mr. Sherrill's son and 10,000 shares of common stock held by Mr. Sherrill's spouse. Mr. Sherrill disclaims beneficial ownership of the 11,000 shares of common stock held by his spouse and son.
- (8) Includes 127,498 shares of common stock issuable upon exercise of stock options and 12,600 shares of common stock held by Dr. Montgomery's spouse. Dr. Montgomery disclaims beneficial ownership of the 12,600 shares of common stock held by his spouse.
- (9) Includes 102,725 shares of common stock issuable upon exercise of stock options.
- (10) Includes 1,500 shares of common stock held by the retirement accounts of Mr. Gray and his spouse and 78,394 shares of common stock issuable upon exercise of stock options.
- (11) Represents shares of common stock issuable upon exercise of stock options.
- (12) Includes 21,666 shares of common stock issuable upon exercise of stock options.
- (13) See Note (2) and Notes (5) through (12).

## RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Dr. Charles E. Bugg, an executive officer and Director of BioCryst, is a Professor Emeritus of The University of Alabama at Birmingham and is paid an annual stipend of \$9,040 by The University of Alabama at Birmingham. Dr. Bennett, an executive officer and Director of BioCryst, is a consultant to and a Distinguished University Professor of The University of Alabama at Birmingham and is paid an annual stipend of \$12,500 by The University of Alabama at Birmingham Education Foundation. We paid approximately \$877,000 in 1998 and approximately \$281,000 in the eight months ended August 31, 1999 to The University of Alabama at Birmingham for royalty payments, conducting clinical trials, research and data analysis.

Dr. John A. Montgomery, an executive officer and Director of BioCryst, is a former executive officer of Southern Research Institute. He is currently a Distinguished Scientist at Southern Research Institute and was paid approximately \$6,482 by Southern Research Institute in 1998 for various consulting services unrelated to the services performed by Southern Research Institute for us. We paid approximately \$209,000 in 1998 and approximately \$28,000 in the eight months ended August 31, 1999 to Southern Research Institute for research, library use and supplies.

Johnson & Johnson Development Corporation owns 918,836 shares of our common stock, which represents 6% of our common stock before the offering and 5.3% after the offering. Johnson & Johnson Development Corporation, the R.W. Johnson Pharmaceutical Research Institute and Ortho-McNeil are all Johnson & Johnson companies. In September 1998, we entered into an exclusive worldwide license agreement with The R.W. Johnson Pharmaceutical Research Institute and Ortho-McNeil to develop and market our proprietary influenza neuraminidase inhibitors. We received an initial \$6.0 million payment from Ortho-McNeil and an additional \$6.0 million common stock equity investment from Johnson & Johnson Development Corporation. In June 1999, we received a \$2.0 million milestone payment from Ortho-McNeil in connection with the initiation of Phase II clinical testing in the United States. In addition, we may receive cash payments upon achievement of specified developmental and regulatory milestones and royalties on product sales, if any. The R.W. Johnson Pharmaceutical Research Institute and Ortho-McNeil are responsible for all development, regulatory and commercialization expenses. The agreement is subject to termination by The R.W. Johnson Pharmaceutical Research Institute and Ortho-McNeil at any time and by us in certain circumstances.

UNDERWRITING

Subject to the terms and conditions stated in the underwriting agreement, each underwriter named below has severally agreed to purchase, and we have agreed to sell to such underwriter, the number of shares set forth opposite the name of such underwriter.

NAME	NUMBER OF SHARES
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Salomon Smith Barney Inc. ....	
Hambrecht & Quist LLC.....	
Raymond James & Associates, Inc.....	
Total.....	2,000,000 =====

The underwriting agreement provides that the obligations of the several underwriters to purchase the shares included in this offering are subject to approval of legal matters by counsel and other conditions, including receipt of certificates from us, receipt of letters from our accountants, the status of the trading of our common stock on Nasdaq or securities on the New York Stock Exchange or Nasdaq and the absence of a banking moratorium, hostilities or a crisis. The underwriters are obligated to purchase all the shares (other than those covered by the over-allotment option described below) if they purchase any of the shares.

The underwriters propose to offer some of the shares directly to the public at the public offering price set forth on the cover page of this prospectus and some of the shares to certain dealers at the public offering price less a concession not in excess of \$ \_\_\_\_\_ per share. The underwriters may allow, and such dealers may reallow, a concession not in excess of \$ \_\_\_\_\_ per share on sales to other dealers. If all of the shares are not sold at the initial offering price, the representatives may change the public offering price and the other selling terms.

We have granted the underwriters a 30-day option to purchase up to an additional 300,000 shares to cover over-allotments, if any. The underwriters may exercise such option solely for the purpose of covering over-allotments, if any, in connection with this offering. To the extent such option is exercised, each underwriter will be obligated, subject to the conditions stated above, to purchase a number of additional shares approximately proportionate to such underwriter's initial purchase commitment.

Our officers and directors and Johnson & Johnson Development Corporation have agreed that, for a period of 90 days from the date of this prospectus, they will not, without the prior written consent of Salomon Smith Barney Inc., dispose of or hedge any shares of our common stock or any securities convertible into or exchangeable for common stock. Salomon Smith Barney Inc. in its sole discretion may release any of the securities subject to these lock-up agreements at any time without notice.

The common stock is quoted on the Nasdaq National Market under the symbol "BCRX."

The following table shows the underwriting discounts and commissions to be paid to the underwriters by us in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares of common stock.

	PAID TO US	
	NO EXERCISE	FULL EXERCISE
Per share.....	\$	\$
Total.....	\$	\$

In connection with the offering, Salomon Smith Barney Inc., on behalf of the underwriters, may purchase and sell shares of common stock in the open market. These transactions may include

over-allotment, syndicate covering transactions and stabilizing transactions. Over-allotment involves syndicate sales of common stock in excess of the number of shares to be purchased by the underwriters in the offering, which creates a syndicate short position. Syndicate covering transactions involve purchases of the common stock in the open market after the distribution has been completed in order to cover syndicate short positions. Stabilizing transactions consist of certain bids or purchases of common stock made for the purpose of preventing or retarding a decline in the market of price of the common stock while the offering is in progress.

The underwriters also may impose a penalty bid. Penalty bids permit the underwriters to reclaim a selling concession from a syndicate member when Salomon Smith Barney Inc., in covering syndicate short positions or making stabilizing purchases, repurchases shares originally sold by that syndicate member.

Any of these activities may cause the price of the common stock to be higher than the price that otherwise would exist in the open market in the absence of such transactions. These transactions may be effected on the Nasdaq National Market or in the over-the-counter market, or otherwise and, if commenced, may be discontinued at any time.

In addition, in connection with this offering, the underwriters (and selling group members) may engage in passive market making transactions in the common stock on the Nasdaq National Market, prior to the pricing and completion of the offering. Passive market making consists of displaying bids on the Nasdaq National Market no higher than the bid prices of independent market makers and making purchases at prices no higher than those independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are limited to a specified percentage of the passive market maker's average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of the common stock to be higher than the price that otherwise would exist in the open market in the absence of such transactions. If passive market making is commenced, it may be discontinued at any time.

We estimate that the total expenses, excluding underwriting discounts and commissions, of this offering will be \$550,000.

We have agreed to indemnify the underwriters against liabilities to which they may become subject, including liabilities that may arise under the Securities Act of 1933, the Securities Exchange Act of 1934 or other federal or state statutory law or regulation, at common law or otherwise or to contribute to payments the underwriters may be required to make in respect of any of those liabilities.

#### LEGAL MATTERS

The validity of the common stock offered in this prospectus will be passed upon for BioCryst by Brobeck, Phleger & Harrison LLP, Broomfield, Colorado. As of October 8, 1999, a member of Brobeck, Phleger & Harrison LLP beneficially owned a total of 5,000 shares of our common stock. Other legal matters in connection with this offering will be passed upon for the underwriters by Cravath, Swaine & Moore, New York, New York.

#### EXPERTS

Ernst & Young LLP, independent auditors, have audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 1998, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in this registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

The statements in this prospectus under the sections "Risk Factors--If we fail to adequately protect or enforce our intellectual property rights or secure rights to patents of others, the value of such rights would diminish" and "Business--Patents and Proprietary Information" and other references in this prospectus to U.S. patent matters have been reviewed and approved by Pollock, Vande Sande & Amernick, R.L.L.P., our patent counsel, as experts on such matters and are included in this prospectus in reliance upon that review and approval.



#### WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission, or the SEC. You may read and copy any document we file at the public reference facilities of the SEC located at 450 Fifth Street, N.W., Washington D.C. 20549. You may obtain information on the operation of the SEC's public reference facilities by calling the SEC at 1-800-SEC-0330. You can also access copies of such material electronically on the SEC's home page on the World Wide Web at <http://www.sec.gov>.

This prospectus is part of a registration statement (Registration No. 333-87669) we filed with the SEC. The SEC permits us to "incorporate by reference" the information that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and information that we file with the SEC after the date of this prospectus will automatically update and supercede this information. We incorporate by reference the following documents filed by us with the SEC (File No. 0-27066). We also incorporate by reference any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, after the date of this prospectus until the termination of this offering:

1. Our Annual Report on Form 10-K for the fiscal year ended December 31, 1998.
2. Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 1999, and June 30, 1999.
3. Our Proxy Statement dated April 2, 1999 filed in connection with our 1999 Annual Meeting of Stockholders.
4. The description of our common stock which is contained in our registration statement on Form 8-A filed under the Exchange Act on January 8, 1994, including any amendment or reports filed for the purpose of updating such description.

If you request a copy of any or all of the documents incorporated by reference, we will send to you the copies requested at no charge. However, we will not send exhibits to such documents, unless such exhibits are specifically incorporated by reference in such documents. You should direct requests for such copies to: Mr. Ronald E. Gray, Chief Financial Officer, BioCryst Pharmaceuticals, Inc., 2190 Parkway Lake Drive, Birmingham, Alabama 35244, (205) 444-4600.

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2,000,000 SHARES

[LOGO]

COMMON STOCK

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P R O S P E C T U S

, 1999

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SALOMON SMITH BARNEY  
HAMBRECHT & QUIST  
RAYMOND JAMES & ASSOCIATES, INC.

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PART II  
INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

The following table sets forth all costs and expenses, other than the underwriting discounts and commissions, payable by the company in connection with the sale of common stock being registered hereby. All of the amounts shown are estimates except the SEC registration fee, the NASD filing fee and the Nasdaq National Market additional listing fee.

	AMOUNT TO BE PAID -----
SEC registration fee.....	\$ 15,985
NASD filing fee.....	6,250
Nasdaq additional listing of shares fee.....	17,500
Accounting fees and expenses.....	40,000
Legal fees and expenses.....	260,000
Printing and engraving expenses.....	150,000
Transfer Agent and registrar fees.....	5,000
Miscellaneous.....	55,265
	-----
Total.....	\$ 550,000 =====

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 Registrant 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 the Registrant's 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.
- 5.1 Opinion of Brobeck, Phleger & Harrison LLP.+
- 23.1 Consent of Brobeck, Phleger & Harrison LLP (included in the opinion filed as Exhibit 5.1).+
- 23.2 Consent of Ernst & Young LLP, independent accountants.+
- 23.3 Consent of Pollock, Vande Sande & Amernick, R.L.L.P., special patent counsel to the Registrant.++
- 24.1 Power of Attorney (included with signature page).+
- 27.1 Financial Data Schedule.+

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+ Previously filed

++To be filed by amendment.

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 provisions described in Item 15 above, 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 payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of our 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:

- (1) To file, during any period in which offers or sales are being made of the securities offered hereby, a post-effective amendment to this Registration Statement;
- (i) To include any prospectus required by Section 10(a)(3) of the Act;
- (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and

price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement;

- (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that the undertakings set forth in paragraphs (i) and (ii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 (the "Exchange Act") that are incorporated by reference in this registration statement.

(2) That, for the purpose of determining any liability under the Act, each such post-effective amendment 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.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

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

The undersigned Registrant hereby undertakes that:

(1) For purposes of determining any liability under the Act, 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 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 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.

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 Registration Statement to be signed on our behalf by the undersigned, thereunto duly authorized, in the City of Birmingham, State of Alabama, on November 1, 1999.

BIOCRYST PHARMACEUTICALS, INC.

By: /s/ CHARLES E. BUGG  
 -----  
 Charles E. Bugg, Ph.D. Chairman and Chief  
 Executive Officer

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities indicated on November 1, 1999.

SIGNATURE	TITLE
----- /s/ CHARLES E. BUGG ----- Charles E. Bugg, Ph.D.	Chairman, Chief Executive Officer and Director (principal executive officer)
----- * ----- J. Claude Bennett, M.D.	President, Chief Operating Officer and Director
----- * ----- John A. Montgomery, Ph.D.	Senior Vice President, Secretary, Chief Scientific Officer and Director
----- * ----- Ronald E. Gray	Chief Financial Officer (principal financial and accounting officer)
----- * ----- William W. Featheringill	Director
----- * ----- Edwin A. Gee, Ph.D.	Director
----- * ----- Zola P. Horovitz, Ph.D.	Director
----- * ----- Joseph H. Sherrill, Jr.	Director
----- * ----- William M. Spencer, III	Director
----- * ----- Randolph C. Steer, M.D., Ph.D.	Director

\*By: /s/ CHARLES E. BUGG  
 -----  
 Charles E. Bugg, Ph.D.  
 ATTORNEY-IN-FACT\*\*

\*\* Pursuant to the power of attorney filed as part of the signature page to the Registration Statement on Form S-3, No. 333-87669, filed September 23, 1999.

EXHIBIT INDEX

- 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 the Registrant's 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.
- 5.1 Opinion of Brobeck, Phleger & Harrison LLP.+
- 23.1 Consent of Brobeck, Phleger & Harrison LLP (included in the opinion filed as Exhibit 5.1).+
- 23.2 Consent of Ernst & Young LLP, independent accountants.+
- 23.3 Consent of Pollock, Vande Sande & Amernick, R.L.L.P., special patent counsel to the Registrant.++
- 24.1 Power of Attorney (included with signature page).+
- 27.1 Financial Data Schedule.+

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+ Previously filed

++To be filed by amendment.