

BIOCRYST PHARMACEUTICALS INC

Form 424B2

December 16, 2005

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**Filed pursuant to Rule 424(b)(2)
Registration No. 333-111226**

PROSPECTUS SUPPLEMENT

(To Prospectus Dated January 5, 2004)

1,088,038 Shares

Common Stock

We are offering 2,228,829 shares of our common stock to selected institutional investors, 1,088,038 of which will be offered pursuant to this prospectus supplement and the accompanying prospectus. The common stock will be purchased at the negotiated price of \$13.46 per share.

Our common stock is listed on the Nasdaq National Market under the symbol BCRX. On December 14, 2005, the last reported sale price of the common stock on the Nasdaq National Market was \$15.55 per share.

Investing in our common stock involves risks. See Risk Factors beginning on page S-4 of this prospectus supplement.

	Per Share	Maximum Offering
Offering price to selected institutional investors	\$ 13.46	\$ 30,000,038
Proceeds to BioCryst Pharmaceuticals, Inc. (before expenses) from the offering	\$ 13.46	\$ 30,000,038
Proceeds to BioCryst Pharmaceuticals, Inc. (before expenses) from sales pursuant to this prospectus supplement and the accompanying prospectus	\$ 13.46	\$ 14,644,991

We expect the total offering expenses to be approximately \$100,000 for all sales in the offering.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these notes, or passed upon the accuracy or adequacy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

December 14, 2005

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You should rely only on the information contained in this prospectus supplement, the accompanying prospectus or the documents incorporated or deemed incorporated by reference herein or therein. We have not authorized anyone to provide you with information different from or in addition to that contained in this prospectus supplement, the accompanying prospectus or the documents incorporated or deemed incorporated by reference herein or therein. We are not making an offer to sell or seeking an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

The information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated or deemed incorporated by reference herein or therein is complete and accurate as of the date of this prospectus supplement, but may have changed since that date.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a shelf registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC. This prospectus supplement describes the specific details regarding this offering, including the price, the amount of common stock being offered and the method of distributing the common stock being offered. The accompanying prospectus provides general information about us, some of which, such as the section entitled Plan of Distribution, may not apply to this offering. If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on this prospectus supplement. You should read both this prospectus supplement and the accompanying prospectus together with the additional information about us described in the accompanying prospectus in the section entitled Where You Can Find More Information.

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PROSPECTUS SUPPLEMENT SUMMARY

The items in the following summary are described in more detail in this prospectus supplement, the accompanying prospectus or in the documents incorporated or deemed incorporated by reference in this prospectus supplement or the accompanying prospectus. This summary provides an overview of selected information and does not contain all of the information that you should consider. Therefore, you should also read the more detailed information in this prospectus supplement, the accompanying prospectus and the documents incorporated or deemed incorporated by reference in this prospectus supplement or the accompanying prospectus. All references to we, us, our, and similar terms refer to BioCryst Pharmaceuticals, Inc.

The Offering

Common stock offered	2,228,829 shares, 1,088,038 of which will be offered pursuant to this prospectus supplement and the accompanying prospectus
Common stock to be outstanding after the offering	28,593,410 shares
Use of proceeds	We intend to use the net proceeds from the sale of the common stock offered by this prospectus supplement for general corporate purposes, which may include research and development activities, preclinical studies and clinical trials, capital expenditures, general working capital and acquisitions.
Nasdaq National Market symbol	BCRX

The total number of shares of common stock outstanding after this offering is based upon 26,364,581 shares outstanding as of September 30, 2005, and excludes:

3,462,552 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2005, at a weighted average exercise price of \$7.47 per share, under our stock option plans;

567,570 additional shares of common stock reserved for future issuance under our stock option and stock purchase plans as of September 30, 2005;

other changes in our outstanding shares of common stock since September 30, 2005; and

shares issuable upon exercise of rights issued under our stockholder rights plan.

Unless otherwise specifically stated, information throughout this prospectus supplement assumes no exercise of outstanding options to purchase shares of common stock.

Each share of our common stock sold in this offering includes a preferred share purchase right under our stockholder rights plan.

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1,114,414 of the shares of common stock we are selling in this offering will be issued to Kleiner Perkins Caulfield & Byers Holdings, LLC, or KPCB. As part of our stock purchase agreement for the offering, we are entering into a nomination and observer agreement with KPCB under which we will grant KPCB the right to appoint a member to our board of directors effective as of the closing of this offering. So long as KPCB and its affiliates continue to own not less than 560,000 shares of our common stock (appropriately adjusted for stock splits, reverse stock splits, stock dividends and the like), KPCB may appoint a director to serve on our board of directors. The director may resign from the board of directors at any time without notice, but we may not remove him or her from the board without cause as defined in the nomination and observer agreement. The nomination and observer agreement is included as an exhibit to our Current Report on Form 8-K that we will file with the Securities and Exchange Commission in connection with the consummation of this offering. See [Where You Can Find More Information](#) on page 16 of the accompanying prospectus.

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RISK FACTORS

Except for the historical information contained in this prospectus supplement or the accompanying prospectus or incorporated by reference, this prospectus supplement (and the information incorporated by reference in this prospectus supplement and the accompanying prospectus) contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed here or incorporated by reference. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section entitled **Risk Factors** beginning on page 4 of the accompanying prospectus as well as the section entitled **Certain Risk Factors That May Affect Future Results, Financial Condition and the Market Price of Securities** in our most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission. See **Where You Can Find More Information** on page 16 of the accompanying prospectus.

Investment in our securities involves a high degree of risk. You should consider carefully the Risk Factors, as well as other information in this prospectus supplement and the accompanying prospectus and the documents incorporated by reference herein or therein before purchasing any of our securities. Each of these risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

FORWARD-LOOKING STATEMENTS

This prospectus supplement contains or incorporates by reference forward-looking statements, which are subject to risks and uncertainties. These forward-looking statements can generally be identified by the use of words such as **may, will, intends, plans, believes, anticipates, expects, estimates, predicts, potential,** the negative of these expressions. Statements that describe our future plans, strategies, intentions, expectations, objectives, goals or prospects are also forward-looking statements. Discussions containing these forward-looking statements are principally contained in **Business and Management's Discussion and Analysis of Financial Condition and Results of Operations** incorporated by reference from our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q for the quarters ended since our most recent Annual Report, and our Current Reports on Form 8-K filed since November 7, 2005, as well as any amendments we make to those filings with the SEC.

These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties 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. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail in the section entitled **Risk Factors** beginning on page 4 of the accompanying prospectus. Also, these forward-looking statements represent our estimates and assumptions only as of the date of this prospectus supplement.

You should read this prospectus supplement, the accompanying prospectus and the documents that we incorporate by reference in this prospectus supplement and the accompanying 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,

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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 from the sale of the shares of common stock we are offering will be approximately \$29.9 million. Net proceeds is what we expect to receive after paying the expenses of the offering.

We intend to add the net proceeds of this offering to our general funds and use them for general corporate purposes, which may include, but are not limited to the purposes set forth in the accompanying prospectus. The amounts and timing of our actual expenditures for each purpose may vary significantly depending upon numerous factors, including the status of our product development efforts, regulatory approvals, competition, marketing and sales activities and the market acceptance of any products we introduce. Pending such uses, we intend to invest the net proceeds of this offering in investment grade, interest-bearing securities.

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Our net tangible book value on September 30, 2005 was approximately \$34.1 million, or approximately \$1.29 per share of common stock. Net tangible book value per share is determined by dividing our net tangible book value, which consists of tangible assets less total liabilities, by the number of shares of common stock outstanding on that date. Without taking into account any other changes in the net tangible book value after September 30, 2005, other than to give effect to our receipt of the estimated net proceeds from the sale of the maximum number of shares issuable in this offering (2,228,829 shares) at an offering price of \$13.46 per share, less our estimated offering expenses, our net tangible book value as of September 30, 2005 after giving effect to the items above, would have been approximately \$64.0 million, or \$2.24 per share. This represents an immediate increase in the net tangible book value of \$0.95 per share to existing stockholders and an immediate dilution of \$11.22 per share to new investors.

The following table illustrates this per share dilution:

Offering price per share		\$ 13.46
Net tangible book value per share as of September 30, 2005	\$ 1.29	
Increase in net tangible book value per share attributable to the offering	\$ 0.95	
Pro forma net tangible book value per share as of September 30, 2005, after giving effect to the offering		2.24
Dilution per share to new investors in the offering		\$ 11.22

The above table is based on 26,364,581 shares outstanding as of September 30, 2005 and excludes:

shares of common stock issuable upon the exercise of outstanding stock options as of September 30, 2005;

shares of common stock available for future grant under our stock option and stock purchase plans as of September 30, 2005;

other changes in our outstanding shares of common stock since September 30, 2005; and

shares issuable upon exercise of rights issued under our stockholder rights plan.

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PLAN OF DISTRIBUTION

We are offering the shares of common stock directly to selected institutional investors. The offering is not being made through an underwriter or placement agent. We have entered into a stock purchase agreement with KPCB, LPTV, LLC and TPG Biotechnology Partners, L.P. for the full amount of the offering. The stock purchase agreement is included as an exhibit to our Current Report on Form 8-K that we will file with the Securities and Exchange Commission in connection with the consummation of this offering. See [Where You Can Find More Information](#) on page 16 of the accompanying prospectus.

Our obligation to issue and sell shares to the purchasers is subject to the conditions set forth in the stock purchase agreement, which may be waived by us in our discretion. A purchaser's obligation to purchase shares is subject to conditions set forth in the stock purchase agreement as well, which also may be waived.

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We expect that the sale of 2,228,829 shares will be completed on or about December 16, 2005. We estimate the total expenses of this offering which will be payable by us will be approximately \$100,000.

The transfer agent for our common stock is American Stock Transfer & Trust, Inc.

Our common stock is traded on the Nasdaq National Market under the symbol BCRX.

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LEGAL MATTERS

Certain matters with respect to the legality and binding nature of the securities are being passed upon for us by Holme Roberts & Owen LLP, Denver, Colorado.

EXPERTS

The consolidated financial statements of BioCryst Pharmaceuticals, Inc. appearing in BioCryst Pharmaceuticals, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2004, have been audited by Ernst & Young LLP, independent auditors, as set forth in their report thereon included therein and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

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\$60,000,000

Common Stock

We may sell shares of common stock from time to time in one or more offerings and the total offering price, in the aggregate, will not exceed \$60,000,000. This means:

we will provide a prospectus supplement each time we issue common stock; and

the prospectus supplement will inform you about the specific terms of that offering and may also add, update or change information contained in this document.

You should carefully read this prospectus, the information incorporated by reference in this prospectus and any prospectus supplement before you decide to invest.

Our common stock, par value \$0.01 per share, trades on The Nasdaq National Market under the symbol BCRX. On December 15, 2003, the reported last sale price of our common stock on The Nasdaq National Market was \$6.66 per share.

Investing in our common stock involves risks. See Risk Factors beginning on page 4 of this prospectus.

The securities may be sold by us to or through underwriters or dealers, directly to purchasers or through agents designated from time to time. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution in this prospectus. If any underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable discounts or commissions and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement. This prospectus may not be used to sell any of the common stock unless accompanied by a prospectus supplement.

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

The date of this prospectus is January 5, 2004.

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You should rely only on the information contained or incorporated by reference into this prospectus or any applicable prospectus supplement. We have not authorized anyone to provide you with different information. We are not making an offer of the common stock to be sold under this prospectus in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front of the document, or that the information contained in any document incorporated by reference is accurate as of any date other than the date

of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a shelf registration process. Under this shelf registration process, we may sell common stock in one or more offerings up to a total dollar amount of \$60,000,000. Each time we sell any common stock under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. We may also add, update or change in a prospectus supplement any of the information contained in this prospectus or in documents we have incorporated by reference into this prospectus. This prospectus, together with the applicable prospectus supplements and the documents incorporated by reference into this prospectus, includes all material information relating to this offering. You should carefully read both this prospectus and the applicable prospectus supplement together with the additional information described under "Where You Can Find More Information" before buying our common stock in this offering.

ABOUT BIOCRYST PHARMACEUTICALS, INC.

BioCryst Pharmaceuticals, Inc. is a biotechnology company focused on designing, optimizing and developing novel small molecule pharmaceuticals that block key enzymes essential for cancer, cardiovascular and autoimmune diseases and viral infections. Our most advanced drug candidate, BCX-1777, is an investigational purine nucleoside phosphorylase (PNP) inhibitor for the treatment of T-cell mediated disorders.

BioCryst is a Delaware corporation originally founded in 1986. Our principal offices are located at 2190 Parkway Lake Drive, Birmingham, Alabama 35244, and our telephone number is (205) 444-4600. Our web site is located at <http://www.biocryst.com>. The information on our web site is not incorporated by reference into this prospectus.

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 building potent, selective inhibitors of enzymes associated with targeted 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. BioCryst aims to design compounds that will inhibit an enzyme target by fitting the active site of a particular enzyme. 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 the development of small-molecule pharmaceuticals. We choose enzyme targets that meet as many of the following criteria as possible:

serve important functions in disease pathways;

have known animal or cell-based models that would be indicative of results in humans;

address large potential markets and significant unmet medical needs, including pursuing niche markets where the results have potential application to broader markets and needs;

have multiple potential clinical applications; and

offer rapid development and commercialization opportunities.

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 target, which the drug candidate must

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inhibit in order to stop the progression of the disease or disorder. We believe that structure-based drug design is a powerful tool for 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 or License 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 desirable product characteristics, such as initial indications of safety and efficacy. 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. We maintain a streamlined corporate infrastructure that focuses exclusively on our strongest areas of expertise. By contracting with other specialty organizations, 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 development. Our collaborative relationships with such organizations may lead to the licensing of one or more drug targets or compounds. Upon licensing a drug target or promising compound from one of these institutions, the scientists from the institution 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, cardiology, 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, 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 several of our early drug development programs.

Developing Drug Development Candidates or Licensing Them to Other Parties. We generally plan to advance drug candidates through initial and/or early-stage drug development. For larger disease indications requiring complex clinical trials, our strategy is to license drug candidates 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, and increase the effectiveness, of late-stage product development, regulatory approval, manufacturing and marketing. We believe that focusing on discovery and early-stage drug development while benefiting from our 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. However, after establishing a lead product candidate, we are willing to license that candidate during any stage of the development process we determine to be beneficial to the company and to the ultimate development and commercialization of that drug candidate. For some smaller niche disease indications markets, we may choose to complete development, manufacture, and where appropriate, market and distribute any approved drugs ourselves, such as BCX-1777 for T-cell leukemias.

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The following table summarizes BioCryst's development projects as of November 30, 2003:

Program and Candidate Disease Category/Indication	Delivery Form	Development Stage	Worldwide Rights
PNP Inhibitor (BCX-1777) Oncology, T-cell related diseases	Intravenous	Phase I	BioCryst
	Oral	Phase I	BioCryst
Tissue Factor/ Factor VIIa Inhibitors Cardiovascular/ Acute coronary events, anticoagulation, oncology	Intravenous (BCX-3607)	Preclinical	BioCryst
	Oral	Lead Optimization	BioCryst
Hepatitis C Polymerase Inhibitors Viral/ Hepatitis C	Oral	Lead Optimization	BioCryst
PNP Inhibitor (BCX-4208) Autoimmune, inflammation/ T-cell related diseases, Psoriasis	Oral	Preclinical	BioCryst

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RISK FACTORS

An investment in our stock involves a high degree of risk. You should consider carefully the following risks, along with all of the other information included in or incorporated by reference into this prospectus and any prospectus supplement, before deciding to buy our common stock. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial may also impair our business operations. If we are unable to prevent events that have a negative effect from occurring, then our business may suffer. Negative events are likely to decrease our revenue, increase our costs, make our financial results poorer and/or decrease our financial strength, and may cause our stock price to decline. In that case, you may lose all or a part of your investment in our common stock.

Risks Relating to Our Business

We have incurred substantial losses since our inception in 1986, expect to continue to incur such losses and may never be profitable

Since our inception in 1986, we have not been profitable. We expect to incur additional losses for the foreseeable future, and our losses could increase as our research and development efforts progress. As of September 30, 2003, our accumulated deficit was approximately \$101.4 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. We or these other parties must then successfully manufacture and market our drug candidates. It could be several years, if ever, before we receive royalties from any future license agreements or revenues directly from product sales.

If we fail to obtain additional financing, we may be unable to complete the development and commercialization of our product candidates or continue our research and development programs.

To date, we have financed our operations primarily from sale of our equity securities and, to a lesser extent, revenues from collaborations and interest. In 2003, our operations have been consuming approximately \$1,000,000 per month, but we expect that our monthly cash used by operations will continue to increase for the next several years. During 2004, we plan to both expand our existing clinical programs and initiate clinical programs for several new disease indications. These additional trials and the related manufacturing, personnel resources and testing required to support these studies will consume significant capital resources and significantly increase our expenses and our net loss.

If we proceed fully with the development of these programs, we will need to raise additional capital during 2004 to advance these programs through the development stage to the point of being a candidate for either commercialization or outlicensing. 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 for development and commercialization of our product candidates; and
- successful commercialization of our products consistent with our licensing strategy.

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We will be required to raise additional capital to complete the development and commercialization of our current product candidates. 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, with 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.

We have not commercialized any products or technologies and our future revenue generation is uncertain

We have not yet commercialized any products or technologies, and we may never be able to do so. Our revenue from collaborative agreements is dependent upon the status of our preclinical and clinical programs. If we fail to advance these programs to the point of being able to enter into successful collaborations, we will not receive any future milestone or other collaborative payments.

Any future revenue directly from product sales would depend on our ability to successfully complete clinical studies, obtain regulatory approvals, manufacture, market and commercialize any approved drugs.

If our development collaborations with other parties fail, the development of our drug candidates will be delayed or stopped

We rely heavily 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;

license or design enzyme inhibitors for development as drug candidates;

execution of some preclinical studies and late-stage development for our compounds and drug candidates;

management of our clinical trials, including medical monitoring and data management;

management of our regulatory function; and

manufacturing, sales, marketing and distribution of our drug candidates.

Our failure to engage in successful collaborations at any one of these stages would greatly impact our business. If we do not license enzyme targets or inhibitors from academic institutions or from other biotechnology companies on acceptable terms, our product development efforts would suffer. Similarly, if the contract research organizations that conduct our initial or late-stage clinical trials or manage our regulatory function breached their obligations to us, this would delay or prevent the development 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, manufacturing, marketing, sales and distribution of our drug candidates. Our general 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. For some smaller niche markets, we may perform these steps ourselves and outsource those functions where we do not have the internal 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;

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;

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our partners may not devote sufficient capital or resources towards our drug candidates; and

our partners may not comply with applicable government regulatory requirements.

Any problems encountered with our current or future partners could delay or prevent the development of our compounds, which would severely affect our business, because if our compounds do not reach the market in a timely manner, or at all, we may never receive any milestone, product or royalty payments.

If the clinical trials of our drug candidates fail, our drug candidates will not be marketed, which would result in a complete absence of product related revenue

To receive the regulatory approvals necessary for the sale of our drug candidates, we or our licensees must demonstrate through preclinical studies and clinical trials that each drug candidate is safe and effective. If we or our licensees are unable to demonstrate that our drug candidates are safe and effective, our drug candidates will not receive regulatory approval and will not be marketed, which would result in a complete absence of product related revenue. The clinical trial process is complex and uncertain. Because of the cost and duration of clinical trials, we may decide to discontinue development of product candidates that are either unlikely to show good results in the trials or unlikely to help advance a product to the point of a meaningful collaboration. 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. These side effects could cause us or regulatory authorities to interrupt, delay or halt clinical trials of a drug candidate. These side effects could also result in the FDA or foreign regulatory authorities refusing to approve the drug candidate for any targeted indications. We, our licensees, 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.

Clinical trials are lengthy and expensive. We or our licensees incur substantial expense for, and devote significant time to, preclinical testing and clinical trials, yet cannot be certain that the tests and trials will ever result in the commercial sale of a product. For example, clinical trials require adequate supplies of drug and sufficient patient enrollment. Delays in patient enrollment can result in increased costs and longer development times. Even if we or our licensees successfully complete clinical trials for our product candidates, we or our licensees might not file the required regulatory submissions in a timely manner and may not receive regulatory approval for the drug candidate.

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, which would significantly harm our business because we will receive no revenue

We or our licensees must obtain regulatory approval before marketing or selling our future drug products. If we or our licensees are unable to receive regulatory approval and do not market or sell our future drug products, we will never receive any revenue from such product sales. 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. If we or our licensees fail to obtain regulatory approval we will be unable to market and sell our future drug products. We have several drug products in various stages of preclinical and clinical development; however, we are unable to determine when, if ever, any of these products will be commercially available. 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

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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.

The FDA regulates, among other things, the record keeping and storage of data pertaining to potential pharmaceutical products. We currently store most of our preclinical research data at our facility. While we do store duplicate copies of most of our clinical data offsite, we could lose important preclinical data if our facility incurs damage. 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 product or royalty revenues if we or our licensees do not receive approval of our products for marketing.

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, which 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. BioCryst is no longer developing BCX-34; however, as a consequence of these two investigations, our ongoing and future clinical studies may receive increased scrutiny, which may delay the regulatory review process.

We may be unable to establish sales, marketing and distribution capabilities necessary to successfully commercialize products we may successfully develop

We currently have no marketing capability and no direct or third-party sales or distribution capabilities. If we successfully develop a drug candidate and decide to commercialize it ourselves rather than relying on third parties, we may be unable to establish marketing, sales and distribution capabilities necessary to commercialize and gain market acceptance for that product.

If our drug candidates do not achieve broad market acceptance, our business may never become profitable

Our drug candidates may not gain the market acceptance required for us to be profitable even if they successfully complete initial and final clinical trials and receive approval for sale by the FDA or foreign regulatory agencies. 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 safety and effectiveness relative to alternative treatments;

reimbursement policies of government and third-party payers; and

marketing and distribution support for our drug candidates.

Physicians, patients, payers 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.

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We face intense competition, and if we are unable to compete effectively, the demand for our products, if any, may be reduced

The biotechnology and pharmaceutical industries are highly competitive and subject to rapid and substantial technological change. We face, and will continue to face, competition in the licensing of desirable disease targets, licensing of desirable drug candidates, and development and marketing of our product candidates from academic institutions, government agencies, research institutions and biotechnology and pharmaceutical companies. Competition may also arise from, among other things:

other drug development technologies;

methods of preventing or reducing the incidence of disease, including vaccines; and

new small molecule or other classes of therapeutic agents.

Developments by others may render our product candidates or technologies obsolete or noncompetitive.

We are performing research on or developing products for the treatment of several disorders including T-cell mediated disorders (T-cell cancers, psoriasis, and rheumatoid arthritis), cardiovascular, oncology, and hepatitis C, and there are a number of competitors to products in our research pipeline. If one or more of our competitors' products or programs are successful, the market for our products may be reduced or eliminated.

Compared to us, many of our competitors and potential competitors have substantially greater:

capital resources;

research and development resources, including personnel and technology;

regulatory experience;

preclinical study and clinical testing experience;

manufacturing and marketing experience; and

production facilities.

Any of these competitive factors could reduce demand for our products.

If we fail to adequately protect or enforce our intellectual property rights or secure rights to patents of others, the value of those 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. If we or our partners are unable to adequately protect or enforce our intellectual property rights for our products, methods, processes and other technologies, the value of the drug candidates that we license to derive revenue would diminish. Additionally, if our products, methods, processes and other technologies infringe the proprietary rights of other parties, we could incur substantial costs. The U.S. Patent and Trademark Office has issued to us a number of U.S. patents for our various inventions and we have in-licensed several patents from various institutions. 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 assure you as to:

the degree and range of protection any patents will afford against competitors with similar products;

if and when patents will issue; or

whether or not others will obtain patents claiming aspects similar to those covered by our patent applications.

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If the U.S. Patent and Trademark Office upholds patents issued to others or if the U.S. Patent and Trademark Office grants patent applications filed by others, we may have to:

obtain licenses or redesign our products or processes to avoid infringement;

stop using the subject matter claimed in those patents; or

pay damages.

We may initiate, or others may bring against us, litigation or administrative proceedings related to intellectual property rights, including proceedings before the U.S. Patent and Trademark Office. Any judgment adverse to us in any litigation or other proceeding arising in connection with a patent or patent application could materially and adversely affect our business, financial condition and results of operations. In addition, the costs of any such proceeding may be substantial whether or not we are successful.

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.

If we fail to retain our existing key personnel or fail to attract and retain additional key personnel, the development of our drug candidates and the expansion of our business will be delayed or stopped

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. Competition for key personnel with the experience that we require is intense and is expected to continue 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 are otherwise employed and each such member or consultant may have commitments to other entities that may limit their availability to us.

If users of our drug products are not reimbursed for use, future sales of our drug products will decline

The lack of reimbursement for the use of our product candidates by hospitals, clinics, patients or doctors will harm our business. Medicare, Medicaid, health maintenance organizations and other third-party payers may not authorize or otherwise budget for the reimbursement of our products. Governmental and third-party payers are increasingly challenging the prices charged for medical products and services. We cannot be sure that third-party payers would view our product candidates as cost-effective, that reimbursement will be available to consumers or that reimbursement will be sufficient to allow our product candidates to be marketed on a competitive basis. Changes in reimbursement policies, or attempts to contain costs in the health care industry could limit or restrict reimbursement for our product candidates and would materially and adversely affect our business, because future product sales would decline and we would receive less product or royalty revenue.

If we face clinical trial liability claims related to the use or misuse of our compounds in clinical trials, our management's time will be diverted 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 have not experienced any clinical trial liability claims to date, but we may experience these claims in the future. After commercial introduction of our products we

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may experience losses due to product liability claims. We currently maintain clinical trial liability insurance coverage in the amount of \$5.0 million per occurrence and \$5.0 million in the aggregate, with an additional \$2.0 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 may not be available in the future on acceptable terms, if at all. 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, our business will suffer

Our drug development activities depend on the security, integrity and performance of the computer systems supporting them, and the failure of our computer systems could delay our drug development efforts. We currently store most of our preclinical and clinical data at our facility. Duplicate copies of all critical data are stored off-site in a bank vault. 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 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.

Risks Relating to Our Common Stock

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 price has fluctuated frequently, and these fluctuations are often not related to our financial results. For the twelve months ended September 30, 2003, the 52-week range of the market price of our stock has been from \$0.82 to \$7.37 per share. 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;
- status of new or existing licensing or collaborative agreements;
- we or 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.

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Because stock ownership is concentrated, you and other investors will have minimal influence on stockholder decisions

As of November 30, 2003, our directors, executive officers and some principal stockholders and their affiliates, including Johnson & Johnson Development Corporation, beneficially owned approximately 40.4% (directors and officers owned 28.2%) of our outstanding common stock and common stock equivalents. 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 3,178,500 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 supermajority 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.

In June 2002, our board of directors adopted a stockholder rights plan and, pursuant thereto, issued preferred stock purchase rights (Rights) to the holders of our common stock. The Rights have certain anti-takeover effects. If triggered, the Rights would cause substantial dilution to a person or group of persons who acquires more than 15% (19.9% for William W. Featheringill, a Director who already owns more than 15%) of our common stock on terms not approved by the board of directors.

We have never paid dividends on our common stock and do not anticipate doing so in the foreseeable future

We have never paid cash dividends on our stock. We currently intend to retain all future earnings, if any, for use in the operation of our business. Accordingly, we do not anticipate paying cash dividends on our common stock in the foreseeable future.

Risks Relating to This Offering

The projections contained in this prospectus or any applicable prospectus supplement, and the registration statement of which this prospectus or any applicable prospectus supplement may be a part, are based on assumptions that may not materialize

The projections of our business included in this prospectus or any applicable prospectus supplement are based on assumptions which we believe are reasonable as of the date of the prospectus or prospectus supplement. No assurance can be given, however, regarding the attainability of the projections or the reliability of the assumptions on which they are based. Certain of the assumptions used may not materialize and unanticipated events may occur. Therefore, our actual results of operations may vary from the projections contained within this prospectus or any applicable prospectus supplement, and such variations may be material.

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Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively

We have not designated the amount of net proceeds we will use for any particular purpose. Accordingly, our management will have broad discretion as to the application of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of this offering. Our stockholders may not agree with the manner in which our management proposes to allocate and spend the net proceeds. Moreover, our management may use the net proceeds for corporate purposes that may not increase our market value or make us profitable.

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INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains or incorporates by reference, and the applicable prospectus supplement may contain, forward-looking statements, which are subject to risks and uncertainties. These forward-looking statements can generally be identified by the use of words such as may, will, intends, plans, believes, anticipates, expects, estimates, predicts, potential, the negative of these words or similar expressions. Statements that describe our future plans, strategies, intentions, expectations, objectives, goals or prospects are also forward-looking statements. Discussions containing these forward-looking statements are principally contained in Business and Management's Discussion and Analysis of Financial Condition and Results of Operations incorporated by reference from our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q for the quarters ended since our most recent Annual Report, and our Current Report on Form 8-K filed on December 16, 2003 as well as any amendments we make to those filings with the SEC.

These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties 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. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail in 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.

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USE OF PROCEEDS

Except as otherwise described in the applicable prospectus supplement, the net proceeds from the sale of the common stock offered hereunder will be added to our general funds and used for general corporate purposes, which may include, but are not limited to:

research and development activities;

preclinical studies and clinical trials, including increased manufacturing of compounds;

capital expenditures; and

general working capital.

We may also use a portion of the net proceeds to acquire or invest in businesses, assets, products and technologies that are complementary to our own, although we are not currently contemplating or negotiating any such acquisitions.

The amounts and timing of our actual expenditures for each purpose may vary significantly depending upon numerous factors, including the status of our product development efforts, regulatory approvals, competition, marketing and sales activities and the market acceptance of any products we introduce. Pending such uses, we intend to