BIOCRYST PHARMACEUTICALS INC
Form 424B5
November 17, 2009

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The information in this preliminary prospectus supplement is not complete and may be changed. This prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-155783

PROSPECTUS SUPPLEMENT (Subject to Completion) *Issued November 17, 2009*
(To Prospectus dated January 27, 2009)

5,000,000 Shares

BioCryst Pharmaceuticals, Inc.

COMMON STOCK

BioCryst Pharmaceuticals, Inc. is offering 5,000,000 shares of its common stock.

Our common stock is listed on The Nasdaq Global Market under the symbol BCRX. On November 16, 2009, the reported last sale price of our common stock on The Nasdaq Global Market was $12.32 per share.

Investing in our common stock involves risks. See Risk Factors beginning on page S-7 of this prospectus supplement.

PRICE $ A SHARE

	Price to Public	*Underwriting Discounts and Commissions*	*Proceeds to BioCryst*
Per Share	*$*	*$*	*$*
Total	*$*	*$*	*$*

We have granted the underwriters the right to purchase up to an additional 750,000 shares to cover over-allotments.

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

Morgan Stanley & Co. Incorporated expects to deliver the shares to purchasers on , 2009.

MORGAN STANLEY

JMP SECURITIES ***OPPENHEIMER & CO.***

, 2009

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document consists of two parts. The first part is the prospectus supplement, which describes the specific terms of this offering of our common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus. The second part is the accompanying prospectus, or the base prospectus, which describes more general information, some of which may not apply to this offering. You should read both this prospectus supplement and the accompanying prospectus, together with the additional information described under the caption Where You Can Find More Information below.

When acquiring any securities discussed in this prospectus supplement, you should rely only on the information provided in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference. Neither we nor any underwriters have authorized anyone to provide you with different information. We are not offering the common stock in any jurisdiction where the offer is prohibited. You should not assume that the information in this prospectus supplement, the accompanying prospectus, or any document incorporated by reference is accurate or complete at any date other than the respective dates of such documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

If the information set forth in this prospectus supplement differs in any way from the information set forth in the accompanying prospectus, you should rely on the information set forth in this prospectus supplement. If the information conflicts with any statement in a document which we have incorporated by reference, then you should consider only the statement in the more recent document.

Unless otherwise mentioned or unless the context requires otherwise, all references in this prospectus supplement and the accompanying prospectus to the Company, we, us and our refer to BioCryst Pharmaceuticals, Inc.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary does not contain all of the information that you should consider before investing in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the Risk Factors section of this prospectus supplement beginning on page S-7 and the financial statements and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision.

BioCryst Pharmaceuticals Inc.

We are a biotechnology company that designs, optimizes and develops novel drugs that block key enzymes involved in cancer, viral infections and autoimmune diseases. We integrate the disciplines of biology, crystallography, medicinal chemistry and computer modeling to discover and develop small molecule pharmaceuticals through the process known as structure-based drug design.

Our business strategy is to maximize sustainable value by moving our product candidate portfolio through clinical development, registration and ultimately to the market. We believe this is best achieved by retaining full product rights to our product candidates within specialty markets, while relying on collaborative arrangements with third parties for product candidates within larger markets or outside our areas of expertise.

Clinical Development Projects

We currently have three pivotal clinical trials and two Phase 2 clinical trials ongoing. In addition, we have a number of potential preclinical candidates to be evaluated for clinical study.

Peramivir

We are developing intravenous, or i.v., peramivir, a neuraminidase inhibitor, for the treatment of influenza.

Phase 3 Clinical Trials

We are advancing the clinical development of i.v. peramivir under a five-year, $179.9 million contract with the United States Department of Health and Human Services, or HHS, which we entered into in January 2007. The original contract award was for $102.6 million. In September 2009 we entered into a modification to the contract that awarded us an additional $77.2 million to complete Phase 3 development of i.v. peramivir. We expect this additional award to fully fund our internal and external costs associated with our ongoing Phase 3 clinical trials for i.v. peramivir.

In September 2009 we announced the initiation of two Phase 3 clinical trials of i.v. peramivir for the treatment of hospitalized patients with serious influenza. These studies are intended to support U.S. regulatory approval of peramivir as a treatment for influenza.

One study is a multicenter, randomized, double-blind, controlled study to evaluate the efficacy and safety of i.v. peramivir administered once-daily for five days in addition to standard of care, compared to standard of care alone, in adults and adolescents who are hospitalized due to serious influenza.

The other study is an open-label, randomized study of the anti-viral activity, safety and tolerability of 600 mg of i.v. peramivir administered once-daily, compared with split doses of 300 mg administered twice-daily for

five days in adult and adolescent hospitalized patients with confirmed or suspected influenza infection.

The combined enrollment target for these studies is approximately 700 patients. We expect to complete the studies in two Northern Hemisphere flu seasons. We also expect to conduct an external control cohort study to provide additional evidence of the efficacy of i.v. peramivir.

U.S. Government Order and Emergency Use Authorization

In September 2009 we received a request for proposal, or RFP, from HHS for the supply of i.v. peramivir for the treatment of critically ill influenza patients. In October 2009, the U.S. Food and Drug Administration, or FDA, in

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response to a request from the U.S. Centers for Disease Control and Prevention, issued an emergency use authorization, or EUA, permitting the use of i.v. peramivir in hospitalized adult and pediatric patients with confirmed or suspected 2009 H1N1 influenza infection who have not responded to oral or inhaled antivirals or in whom oral or inhaled antiviral therapy is not feasible, and in adult patients for whom therapy with an i.v. drug is judged clinically appropriate due to other circumstances.

On November 4, 2009 HHS ordered 10,000 courses of i.v. peramivir from us for an aggregate purchase price of $22.5 million. We shipped the entire order from existing inventory to HHS on November 4, 2009. In addition, separate from the RFP process, we donated and transferred to HHS an initial supply of 1,200 courses of i.v. peramivir to allow doctors and patients near-term access to the drug. As of the date of this prospectus supplement, i.v. peramivir is the only i.v. antiviral medication ordered by the HHS that has received an EUA from the FDA.

The minimum and maximum quantities of i.v. peramivir that may be ordered by HHS under the RFP are 1,000 and 40,000 treatment courses. We also are required to maintain the ability to manufacture additional courses for treatment or prophylaxis, dependent on the volume and size of orders received from HHS. Based on the RFP, we initiated manufacture of approximately 133,000 courses of i.v. peramivir at a cost of approximately $10 million, so that we would have additional inventory available in advance of potential orders. In addition, we have sufficient quantities of the active pharmaceutical ingredient, or API, of i.v. peramivir available to produce up to 350,000 additional courses. We believe that we have the capacity for large scale commercial production, including two API production facilities and one finished drug product manufacturer, all of which are in substantial compliance with the FDA s current Good Manufacturing Practices.

Shionogi & Co., Ltd. Development of i.v. Peramivir

In February 2007 we entered into an exclusive license agreement with Shionogi & Co., Ltd., or Shionogi, to develop and commercialize peramivir in Japan and Taiwan and to perform a Phase 3 clinical trial in Hong Kong. The agreement provides for an upfront payment of $14 million and future clinical event milestone payments of up to $21 million. In July 2009 Shionogi announced positive results in two Phase 3 clinical trials of i.v. peramivir. One of these trials was conducted in patients with uncomplicated outpatient influenza and the other was for the treatment of influenza in patients with risk factors for complications. The studies were sponsored by Shionogi and conducted during the 2008-2009 influenza season. Shionogi and Green Cross Corporation, the license holder of peramivir in Korea pursuant to a June 2006 license agreement with us, co-conducted the portion of the studies in Korea. Doses of i.v. peramivir of 300 mg and 600 mg, administered in single and multiple doses were found to be generally safe and well-tolerated in these trials. Further analyses of the study data, including secondary efficacy endpoints and detailed safety, are underway. Further, Shionogi announced that it had filed its new drug application in October 2009 to seek regulatory approval for i.v. peramivir in Japan. This filing triggered a $7.0 million milestone payment to us under our license agreement with Shionogi.

Distribution Arrangements for Peramivir Outside the United States

We have entered into binding letters of intent with three parties to exclusively represent us and i.v. peramivir for influenza stockpiling opportunities, as well as for marketing and distribution of i.v. peramivir for seasonal influenza upon local regulatory approval, within specified territories outside the United States. The three parties are moksha8 Pharmaceuticals, Inc. for Brazil and Mexico, NT Pharma (Group) Co., Ltd. for China and Neopharm Group for Israel. Each of them has initiated discussions with key government officials in its respective territories to discuss peramivir s availability during the current global health emergency. We are in discussions with each of the parties regarding definitive agreements.

Forodesine HCl

Forodesine HCl is a transition-state analog inhibitor of the enzyme purine nucleoside phosphorylase, or PNP. In February 2006 we announced an exclusive licensing agreement with Mundipharma to develop and commercialize forodesine in markets across Europe, Asia and Australia for use in oncology. We have retained full development and commercialization rights to forodesine in the rest of the world, including North America.

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Continued Development of Oral Forodesine in Cutaneous T-Cell Lymphoma

Following the completion of a Phase 1/Phase 2 clinical trial of forodesine in patients with refractory cutaneous T-cell lymphoma, or CTCL, in October 2007 we initiated a pivotal trial with an oral formulation of forodesine for treatment of patients with CTCL. This trial is being conducted under an SPA agreement negotiated with the FDA and, if successful, will serve as a basis for a new drug application to the FDA using the oral formulation in patients with relapsed CTCL. In February 2007 we announced that the Committee for Orphan Medicinal Products of the European Medicines Agency had granted orphan drug designation to forodesine for the treatment of CTCL. In addition, the FDA has granted orphan drug designation to forodesine for the treatment of CTCL. The trial, which uses a non-randomized, open-label, single-arm design, continues to enroll subjects with CTCL stages IIB through IVA who have failed three systemic therapies. We are targeting completion of enrollment by the end of 2009 and expect to report preliminary data on this study in mid-2010.

Forodesine Trial Initiated for Chronic Lymphocytic Leukemia Patients

We have initiated a Phase 2 clinical trial that will evaluate forodesine in patients with chronic lymphocytic leukemia, or CLL. The trial is a single-arm exploratory study of single agent forodesine with response rate as the primary endpoint. The first patient was dosed during the first quarter of 2008 and the trial is ongoing. Based on an interim analysis of data from an exploratory Phase 2 single-arm, open-label program in patients with CLL who failed previous treatment and pharmacokinetic and pharmacodynamic study results from healthy patients, the dosing regimen in the ongoing Phase 2 CLL study was amended to evaluate 200 mg forodesine twice-daily. We expect to provide an update on this study by the end of 2009.

BCX-4208

BCX-4208 is a next-generation PNP inhibitor in clinical development. We have initiated a Phase 2 clinical trial of BCX-4208 for the treatment of gout, which is caused by elevated levels of uric acid in blood. We believe that BCX-4208 is a good candidate to control gout because data from a prior Phase 2 clinical trial of BCX-4208 for psoriasis indicated a dose related reduction in uric acid that was sustained for the duration of drug exposure. Our gout clinical trial is a Phase 2, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of BCX-4208 in subjects with gout. The trial contains two parts: Part 1 will study multiple doses of BCX-4208 against a placebo and Part 2 will study dose escalation. The trial s primary objective is to determine the effect of different doses of orally administered BCX-4208 on serum uric acid levels in patients with gout. The trial is expected to enroll up to 120 subjects and we expect to have initial data from Part 1 in mid-2010.

Preclinical Development Activities

Our discovery engine has been the primary source of our clinical pipeline and has also produced pre-clinical candidates. While we have focused extensively during the last two years on advancing our late stage clinical development projects, we believe that given our clinical progress to date and our current financial position, we are able to invest in developing our early clinical pipeline. In addition to our clinical programs, we also retain exclusive worldwide rights to potent inhibitors in various therapeutic areas and we are in the process of evaluating which are the most attractive. We have a disciplined approach to drug discovery and will continue to evaluate and test promising compounds to determine which should be taken into clinical testing.

Alliances

As part of our strategy, we expect to consider potential third-party alliances in large primary care markets and in areas where do not have the resources or expertise to advance the development of product candidates on our own. These

alliances could include preclinical development, clinical development, regulatory approval or marketing, sales and distribution of our product candidates.

In addition to our collaborative relationship with Shionogi and the letters of intent we have entered into for peramivir outside the United States, we have established collaborative relationships with Mundipharma International Holdings Limited for the development and commercialization of forodesine in Europe, Asia and Australia and with Green Cross Corporation for the development and commercialization of peramivir in Korea.

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Risk Factors

Our success is dependent on our ability to successfully develop our compounds, complete clinical trials and commercialize our products. Because none of our products have been approved by regulatory authorities, we may not be able to generate significant revenue or attain profitability. Furthermore, we are dependent on collaborative relationships and the expertise of third parties for drug development, commercialization and manufacturing. The process of establishing and implementing collaborative relationships is difficult, time-consuming and involves significant uncertainty. See Risk Factors beginning on page S-7 for a full discussion of these and other risks relating to our business and owning shares of our common stock.

We are a Delaware corporation originally founded in 1986. Our principal executive 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 supplement.

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THE OFFERING

Common stock offered	5,000,000 shares
Common stock to be outstanding after the offering	43,833,408 shares
Over-allotment option	750,000 shares
Use of proceeds	We intend to use the net proceeds of this offering for general corporate purposes, including funding our research and development efforts, clinical development of forodesine and BCX-4208 and pre-commercialization activities relating to i.v. peramivir and forodesine. See Use of Proceeds.
Nasdaq Global Market symbol	BCRX
Risk Factors	See Risk Factors beginning on page S-7 and the other information included in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus for a discussion of certain factors you should carefully consider before deciding to invest in shares of our common stock.

The number of shares to be outstanding after this offering is based on 38,883,408 shares outstanding as of November 9, 2009 and excludes:

- 3,159,895 shares of common stock issuable upon the exercise of warrants at an exercise price of $10.25 per share; and
- 6,166,573 shares of common stock issuable upon the exercise of stock options outstanding under our stock option plans at a weighted average exercise price of $7.07 per share and 1,509,822 additional shares of common stock reserved for issuance under our stock option plan.

Except as otherwise noted, all information in this prospectus supplement assumes the underwriters do not exercise their over-allotment option.

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SUMMARY FINANCIAL DATA

The following summary financial information for the five years ended December 31, 2008 is derived from our audited financial statements. The following summary financial information as of September 30, 2009 and for the nine months ended September 30, 2009 and 2008 is derived from our unaudited financial statements. The unaudited financial statements have been prepared on the same basis as the audited financial statements and, in the opinion of management, include all adjustments, consisting only of normal recurring adjustments, considered necessary for a fair presentation of our financial condition and results of operations for such periods. The data should be read in conjunction with the financial statements, related notes, management s discussion and analysis of financial condition and results of operations, and other financial information incorporated by reference into this prospectus supplement. These historical results are not necessarily indicative of the results to be expected in the future. Interim results are not necessarily indicative of the results that may be expected for an entire year.

	Nine Months Ended September 30,		Year Ended December 31,				
	2009	2008	2008	2007	2006	2005	2004
	(in thousands, except per share data)						
Statement of Operations Data:							
Total revenues	$ 19,694	$ 22,321	$ 56,561	$ 71,238	$ 6,212	$ 152	$ 337
Research and development expenses	40,683	51,267	73,327	94,052	47,083	23,642	18,868
Net loss	(28,603)	(34,802)	(24,732)	(29,055)	(43,618)	(26,099)	(21,104)
Amounts per common share:							
Basic and diluted net loss per share	(0.75)	(0.91)	(0.65)	(0.89)	(1.50)	(1.01)	(1.00)
Weighted average shares outstanding	38,300	38,040	38,062	32,711	29,147	25,721	21,165

	As of September 30, 2009	
	Actual	As Adjusted
	(unaudited) (in thousands)	
Balance Sheet Data:		
Cash, cash equivalents and marketable securities	$ 38,492	$ 96,279
Total assets	60,588	118,375
Long-term deferred revenue	19,065	19,065
Accumulated deficit	(277,871)	(277,871)
Total stockholders equity	23,545	81,332

The preceding table summarizes our balance sheet data as of September 30, 2009:

on an actual basis; and

as adjusted to reflect our sale of the 5,000,000 shares of common stock offered by us at an assumed public offering price of $12.32 per share, which was the reported last sale price of our common stock on The Nasdaq Global Market on November 16, 2009, after deducting estimated underwriting discounts and commissions and offering expenses payable by us.

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RISK FACTORS

An investment in our common stock involves risks. You should consider carefully all of the information that is included or incorporated by reference in this prospectus supplement and the accompanying prospectus before investing in our common stock. In particular, you should evaluate the uncertainties and risks referred to or described below, which may adversely affect our business, financial condition or results of operations. Additional uncertainties and risks that are not presently known to us or that we currently deem immaterial may also adversely affect our business, financial condition or results of operations.

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. To become profitable, we must successfully manufacture and develop drug product candidates, receive regulatory approval, and successfully commercialize or enter into profitable agreements with other parties. It could be several years, if ever, before we receive royalties from any current or future license agreements or revenues directly from product sales.

Because of the numerous risks and uncertainties associated with developing our product candidates and their potential for commercialization, we are unable to predict the extent of any future losses. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. If we are unable to achieve and sustain profitability, the market value of our common stock will likely decline.

Our success depends upon our ability to advance our products through the various stages of development, especially through the clinical trial process.

To receive the regulatory approvals necessary for the sale of our product candidates, we or our partners must demonstrate through preclinical studies and clinical trials that each product candidate is safe and effective. 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 unlikely to show good results in the trials, unlikely to help advance a product to the point of a meaningful collaboration, or unlikely to have a reasonable commercial potential. We may suffer significant setbacks in pivotal clinical trials, even after earlier clinical trials show promising results. Clinical trials may not be adequately designed or executed, which could affect the potential outcome and analysis of study results. Any of our product 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 product candidate. These side effects could also result in the FDA or foreign regulatory authorities refusing to approve the product candidate for any targeted indications. We, our partners, 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 product candidates are safe or effective and have acceptable commercial viability.

Our ability to successfully complete clinical trials is dependent upon many factors, including but not limited to:

- our ability to find suitable clinical sites and investigators to enroll patients;
- the availability of and willingness of patients to participate in our clinical trials;

difficulty in maintaining contact with patients to provide complete data after treatment;

our product candidates may not prove to be either safe or effective;

clinical protocols or study procedures may not be adequately designed or followed by the investigators;

manufacturing or quality control problems could affect the supply of drug product for our trials; and

delays or changes in requirements by governmental agencies.

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Clinical trials are lengthy and expensive. We or our partners 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 partners successfully complete clinical trials for our product candidates, we or our partners might not file the required regulatory submissions in a timely manner and may not receive regulatory approval for the product candidate.

Our clinical trials may not adequately show that our drugs are safe or effective.

Progression of our drug products through the clinical development process is dependent upon our trials indicating our drugs have adequate safety profiles and show positive therapeutic effects in the patients being treated by achieving pre-determined endpoints according to the trial protocols. Failure to achieve either of these could result in delays in our trials or even require the performance of additional unplanned trials. This could result in delays in the development of our product candidates and could result in significant unexpected costs.

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.

As our clinical programs continue to grow and patient enrollment increases, our costs will increase. Our current and planned clinical trials plus the related development, manufacturing, regulatory approval process requirements, and additional personnel resources and testing required for supporting the development of our product candidates will consume significant capital resources. Our expenses, revenues and burn rate could vary significantly depending on many factors, including our ability to raise additional capital, the development progress of our collaborative agreements for our product candidates, the amount of funding we receive from HHS for peramivir, the amount of funding or assistance, if any, we receive from other governmental agencies or other new partnerships with third parties for the development of our product candidates, the amount or profitability of any orders for peramivir by any government agency or other party, the progress and results of our current and proposed clinical trials for our most advanced drug products, the progress made in the manufacturing of our lead products and the progression of our other programs.

We expect that we will be required to raise additional capital to complete the development and commercialization of our current product candidates and we may seek to raise capital at any time we deem market conditions to be favorable. Additional funding, whether through additional sales of securities or collaborative or other arrangements with corporate partners or from other sources, including governmental agencies, in general and from any HHS contract specifically, 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.

If HHS were to eliminate, reduce or delay funding from our contract, or dispute some of our incurred costs or other actions taken under the contract, this would have a significant negative impact on our revenues, cash flows and the development of peramivir.

Our projections of revenues and incoming cash flows are substantially dependent upon HHS reimbursement for the costs related to our peramivir program. If HHS were to eliminate, reduce or delay the funding for this program or disallow some of our incurred costs, we would have to obtain additional funding for development of this drug

candidate or significantly reduce or stop the development effort. Further, HHS may challenge actions that we have taken or may take under our contract, which could negatively impact our operating results and cash flows.

In contracting with HHS, we are subject to various U.S. government contract requirements, including general clauses for a cost-reimbursement research and development contract, which may limit our reimbursement or if we are found to be in violation could result in contract termination. U.S. government contracts typically contain

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extraordinary provisions which would not typically be found in commercial contracts. For instance, government contracts permit unilateral modification by the government, interpretation of relevant regulations (i.e., federal acquisition regulation clauses), and the ability to terminate without cause. As such, the company may be at a disadvantage as compared to other commercial contracts. In addition, U.S. government contracts are subject to audit and modification by the government at its sole discretion. If the government terminates its contract with us for its convenience or if we default by failing to perform in accordance with the contract schedule and terms, significant negative impact on our cash flows and operations could result.

Our contract with HHS has special contracting requirements, which create additional risks of reduction or loss of funding.

We have entered into a contract with HHS for the advanced development of our neuraminidase inhibitor, peramivir. In contracting with HHS, we are subject to various U.S. government contract requirements, including general clauses for a cost-reimbursement research and development contract. U.S. government contracts typically contain unfavorable termination provisions and are subject to audit and modification by the government at its sole discretion, which subjects us to additional risks. These risks include the ability of the U.S. government to unilaterally:

terminate or reduce the scope of our contract; and

audit and object to our contract-related costs and fees, including allocated indirect costs.

The U.S. government may terminate its contract with us either for its convenience or if we default by failing to perform in accordance with the contract schedule and terms. Termination for convenience provisions generally enable us to recover only our costs incurred or committed, and settlement expenses and profit on the work completed prior to termination. Termination for default provisions does not permit these recoveries.

As a U.S. government contractor, we are required to comply with applicable laws, regulations and standards relating to our accounting practices and are subject to periodic audits and reviews. As part of any such audit or review, the U.S. government may review the adequacy of, and our compliance with, our internal control systems and policies, including those relating to our purchasing, property, estimating, compensation and management information systems. Based on the results of its audits, the U.S. government may adjust our contract-related costs and fees, including allocated indirect costs. In addition, if an audit or review uncovers any improper or illegal activity, we may be subject to civil and criminal penalties and administrative sanctions, including termination of our contracts, forfeiture of profits, suspension of payments, fines and suspension or prohibition from doing business with the U.S. government. We could also suffer serious harm to our reputation if allegations of impropriety were made against us. In addition, under U.S. government purchasing regulations, some of our costs may not be reimbursable or allowed under our contracts. Further, as a U.S. government contractor, we are subject to an increased risk of investigations, criminal prosecution, civil fraud, whistleblower lawsuits and other legal actions and liabilities as compared to private sector commercial companies.

If we fail to successfully commercialize or establish collaborative relationships to commercialize certain of our drug product candidates or if any partner terminates or fails to perform its obligations under agreements with us, potential revenues from commercialization of our product candidates could be reduced, delayed or eliminated.

Our business strategy is to increase the asset value of our drug candidate portfolio. We believe this is best achieved by retaining full product rights or through collaborative arrangements with third parties as appropriate. As needed, potential third-party alliances could include preclinical development, clinical development, regulatory approval, marketing, sales and distribution of our drug product candidates.

Currently, we have established collaborative relationships with Mundipharma for the development and commercialization of forodesine and with each of Shionogi and Green Cross for the development and

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commercialization of peramivir. The process of establishing and implementing collaborative relationships is difficult, time-consuming and involves significant uncertainty, including:

- our partners may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, a change in business strategy, a change of control or other reasons;
- our contracts for collaborative arrangements may expire;
- 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;
- we do not have day to day control over the activities of our partners and have limited control over their decisions;
- our ability to generate future event payments and royalties from our partners depends upon their abilities to establish the safety and efficacy of our product candidates, obtain regulatory approvals and achieve market acceptance of products developed from our product candidates;
- we or our partners may fail to properly initiate, maintain or defend our intellectual property rights, where applicable, or a party may utilize our proprietary information in such a way as to invite litigation that could jeopardize or potentially invalidate our proprietary information or expose us to potential liability;
- our partners may not devote sufficient capital or resources towards our product candidates; and
- our partners may not comply with applicable government regulatory requirements.

If any partner fails to fulfill its responsibilities in a timely manner, or at all, our commercialization efforts related to that collaboration could be reduced, delayed or terminated, or it may be necessary for us to assume responsibility for activities that would otherwise have been the responsibility of our partner. If we are unable to establish and maintain collaborative relationships on acceptable terms, we may have to delay or discontinue further development of one or more of our product candidates, undertake commercialization activities at our own expense or find alternative sources of funding. Any delay in the development or commercialization of our compounds would severely affect our business, because if our compounds do not progress through the development process or reach the market in a timely manner, or at all, we may not receive additional future event payments and may never receive product or royalty payments.

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

We have not commercialized any products or technologies, and we may never be able to do so. We currently have no marketing capability and no direct or third-party sales or distribution capabilities and may be unable to establish these capabilities for products we plan to commercialize. In addition, 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 event or other collaborative payments.

Our ability to receive revenue from products we commercialize presents several risks, including:

- we or our collaborators may fail to successfully complete clinical trials sufficient to obtain FDA marketing approval;

many competitors are more experienced and have significantly more resources and their products could be more cost effective or have a better efficacy or tolerability profile than our product candidates;

we may fail to employ a comprehensive and effective intellectual property strategy which could result in decreased commercial value of our company and our products;

we may fail to employ a comprehensive and effective regulatory strategy which could result in a delay or failure in commercialization of our products;

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our ability to successfully commercialize our products are affected by the competitive landscape, which cannot be fully known at this time;

reimbursement is constantly changing which could greatly affect usage of our products; and

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 third parties, such as our development partners and contract research organizations, fail, the development of our drug product candidates will be delayed or stopped.

We rely heavily upon other parties for many important stages of our drug development programs, including but not limited to:

discovery of compounds that cause or enable biological reactions necessary for the progression of the disease or disorder, called enzyme targets;

licensing or design of enzyme inhibitors for development as drug product candidates;

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

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

execution of additional toxicology studies that may be required to obtain approval for our product candidates; and

manufacturing the starting materials and drug substance required to formulate our drug products and the drug products to be used in both our clinical trials and toxicology studies.

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, conduct our toxicology studies, manufacture our starting materials, drug substance and drug products or manage our regulatory function breached their obligations to us or perform their services inconsistent with industry standards and not in accordance with the required regulations, this would delay or prevent the development of our product candidates.

If we lose our relationship with any one or more of these parties, we could experience a significant delay in both identifying another comparable provider and then contracting for its services. We may be unable to retain an alternative provider on reasonable terms, if at all. Even if we locate an alternative provider, it is likely that this provider may need additional time to respond to our needs and may not provide the same type or level of service as the original provider. In addition, any provider that we retain will be subject to applicable FDA current Good Laboratory Practices, or cGLP, current Good Manufacturing Practices, or cGMP and current Good Clinical Practices, or cGCP, and comparable foreign standards. We do not have control over compliance with these regulations by these providers. Consequently, if these practices and standards are not adhered to by these providers, the development and commercialization of our product candidates could be delayed., and our business, financial condition and results of operations could be materially adversely affected.

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Our development of peramivir for influenza is subject to all disclosed drug development and potential commercialization risks and numerous additional risks. Any potential revenue benefits to us are highly speculative.

Further development and potential commercialization of peramivir is subject to all the risks and uncertainties disclosed in our other risk factors relating to drug development and commercialization. In addition, potential commercialization of peramivir is subject to further risks, including but not limited to the following:

- the injectable versions of peramivir are currently in clinical development and have been tested in a limited number of humans and may not be safe or effective;
- necessary government or other third-party funding and clinical testing for further development of peramivir may not be available timely, at all, or in sufficient amounts;
- the flu prevention or pandemic treatment concerns may not materialize at all, or in the near future;
- advances in flu vaccines could substantially replace potential demand for an antiviral such as peramivir;
- any substantial demand for pandemic or seasonal flu treatments may occur before peramivir can be adequately developed and tested in clinical trials;
- injectable forms of peramivir may not prove to be accepted by patients and physicians as a treatment for seasonal influenza compared to the other currently marketed antiviral drugs, which would limit revenue from non-governmental entities;
- numerous large and well-established pharmaceutical and biotech companies will be competing to meet the market demand for flu drugs and vaccines;
- the only major markets in which patents relating to peramivir have issued or been allowed are the United States, Canada, Japan, Australia and many contracting and extension states of the European Union, while no patent applications or issued patents for peramivir exist in other potentially significant markets;
- regulatory authorities may not make needed accommodations to accelerate the drug testing and approval process for peramivir; and
- in the next few years, it is expected that a limited number of governmental entities will be the primary potential customers for peramivir and if we are not successful at marketing peramivir to these entities for any reason, we will not receive substantial revenues from stockpiling orders from these entities.

If any or all of these and other risk factors occur, we will not attain significant revenues or gross margins from peramivir and our stock price will be adversely affected.

There are risks related to the potential emergency use or sale of peramivir.

To the extent that peramivir is used as a treatment for H1N1 flu (or other strains of flu), there can be no assurance that it will prove to be generally safe, well tolerated and effective. Emergency use of peramivir may create certain liabilities for the company. There is no assurance that we or our manufacturers will be able to fully meet the demand for peramivir in the event of additional orders. Further, we may not achieve a favorable price for additional orders of peramivir in the U.S. or in any other country. Our competitors may develop products that could compete with or replace peramivir. We may face competition in markets where we have no existing intellectual property protection or

are unable to successfully enforce our intellectual property rights.

There is no assurance that the non-U.S. partnerships that we have entered into for peramivir will result in any order for peramivir in those countries. There is no assurance that peramivir will be approved for emergency use or will achieve market approval in those countries. In the event that any emergency use is granted, there is no assurance that any order by any non-U.S. partnership will be substantial or will be profitable to the company. The sale of peramivir, emergency use or other use of peramivir in any country may create certain liabilities for the company.

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Because we have limited manufacturing experience, we depend on third-party manufacturers to manufacture our drug product candidates and the materials for our product candidates. If we cannot rely on third-party manufacturers, we will be required to incur significant costs and potential delays in finding new third-party manufacturers.

We have limited manufacturing experience and only a small scale manufacturing facility. We currently rely upon third-party manufacturers to manufacture the materials required for our drug product candidates and most of the preclinical and clinical quantities of our product candidates. We depend on these third-party manufacturers to perform their obligations in a timely manner and in accordance with applicable governmental regulations. Our third-party manufacturers may encounter difficulties with meeting our requirements, including but not limited to problems involving:

- inconsistent production yields;
- product liability claims;
- difficulties in scaling production to commercial and validation sizes;
- interruption of the delivery of materials required for the manufacturing process;
- scheduling of plant time with other vendors or unexpected equipment failure;
- potential catastrophes that could strike their facilities;
- potential impurities in our drug substance or drug products that could affect availability of product for our clinical trials or future commercialization;
- poor quality control and assurance or inadequate process controls; and
- lack of compliance with regulations and specifications set forth by the FDA or other foreign regulatory agencies.

These contract manufacturers may not be able to manufacture the materials required or our drug product candidates at a cost or in quantities necessary to make them commercially viable. We also have no control over whether third-party manufacturers breach their agreements with us or whether they may terminate or decline to renew agreements with us. To date, our third-party manufacturers have met our manufacturing requirements, but they may not continue to do so. Furthermore, changes in the manufacturing process or procedure, including a change in the location where the drug is manufactured or a change of a third-party manufacturer, may require prior review and approval in accordance with the FDA s cGMPs and comparable foreign requirements. This review may be costly and time-consuming and could delay or prevent the launch of a product. The FDA or similar foreign regulatory agencies at any time may also implement new standards, or change their interpretation and enforcement of existing standards for manufacture, packaging or testing of products. If we or our contract manufacturers are unable to comply, we or they may be subject to regulatory action, civil actions or penalties.

If we are unable to enter into agreements with additional manufacturers on commercially reasonable terms, or if there is poor manufacturing performance on the part of our third-party manufacturers, we may not be able to complete development of, or market, our product candidates.

Our raw materials, drug substances, and drug products are manufactured by a limited group of suppliers and some at a single facility. If any of these suppliers were unable to produce these items, this could significantly impact our supply of drugs for further preclinical testing and clinical trials.

If we or our partners 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 partners must obtain regulatory approval before marketing or selling our future drug products. If we or our partners 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 process of preparing for and obtaining FDA approval

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may be lengthy and expensive, and approval is never certain. Products distributed abroad are also subject to foreign government regulation and export laws of the U.S. Neither the FDA nor foreign regulatory agencies have approved any of our drug product candidates. Because of the risks and uncertainties in biopharmaceutical development, our product 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 product 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 product candidate, the approval may limit the indicated uses for a product 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, our clinical data and our manufacturing data at our facility. While we do store duplicate copies of most of our clinical data offsite and a significant portion of our data is included in regular backups of our systems, we could lose important 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 partners do not receive approval of our products for marketing.

In June 1995, we notified the FDA that we submitted incorrect data for our Phase 2 studies of BCX-34 applied to the skin for CTCL and psoriasis. In November 1995, the FDA issued 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 2 dose-ranging studies of topical BCX-34 for the treatment of CTCL 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. We are 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 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 product 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 and our partners are performing research on or developing products for the treatment of several disorders including T-cell mediated disorders (T-cell cancers and other autoimmune indications), gout, CTCL, CLL, influenza, and hepatitis C. 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. Such

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is the case with Eisai s Targretin for CTCL and the current neuraminidase inhibitors marketed by Glaxo Smith Kline and Roche for influenza. With respect to the neuraminidase inhibitors, these companies may develop i.v. formulations that could compete with peramivir. Further, several 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, influenza, hepatitis C, and in other therapeutic areas where we have discovery efforts ongoing. 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 partners to obtain, protect and enforce viable intellectual property rights including but not limited to trade name, trade mark and patent protection for our company and its products, methods, processes and other technologies we may license or develop, to preserve our trade secrets, and to operate without infringing the proprietary rights of third parties both domestically and abroad. The patent position of biotechnology and pharmaceutical companies is generally highly uncertain, involves complex legal and factual questions and has recently been the subject of much litigation. Neither the United States Patent and Trademark Office, or USPTO, the Patent Cooperation Treaty offices, nor the courts of the United States and other jurisdictions have consistent policies nor predictable rulings regarding the breadth of claims allowed or the degree of protection afforded under many biotechnology and pharmaceutical patents. Further, we do not have worldwide patent protection for our product candidates and our intellectual property rights may not be legally protected or enforceable in all countries throughout the world. The validity, scope, enforceability and commercial value of these rights, therefore, is highly uncertain.

Our success depends in part on avoiding the infringement of other parties patents and other intellectual property rights as well as avoiding the breach of any licenses relating to our technologies and products. In the U.S., patent applications filed in recent years are confidential for 18 months, while older applications are not published until the patent issues. As a result, avoiding patent infringement may be difficult and we may inadvertently infringe third-party patents or proprietary rights. These third parties could bring claims against us, our partners or our licensors that even if resolved in our favor, could cause us to incur substantial expenses and, if resolved against us, could additionally cause us to pay substantial damages. Further, if a patent infringement suit were brought against us, our partners or our licensors, we or they could be forced to stop or delay research, development, manufacturing or sales of any infringing product in the country or countries covered by the patent we infringe, unless we can obtain a license from the patent

holder. Such a license may not be available on acceptable terms, or at all, particularly if the third party is developing or marketing a product competitive with the infringing product. Even if we, our partners or our licensors were able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property.

If we or our partners are unable or fail to adequately initiate, protect, defend or enforce our intellectual property rights in any area of commercial interest or in any part of the world where we wish to seek regulatory approval for our products, methods, processes and other technologies, the value of the drug product candidates to produce revenue would diminish. Additionally, if our products, methods, processes, and other technologies or our

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commercial use of such products, processes, and other technologies, including but not limited to any trade name, trademark or commercial strategy infringe the proprietary rights of other parties, we could incur substantial costs. The USPTO and the patent offices of other jurisdictions have issued to us a number of 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 USPTO. We have filed a number of corresponding foreign patent applications and intend to file additional foreign and U.S. patent applications, as appropriate. We have also filed certain trademark and trade name applications worldwide. 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;
- if patents do issue we can not be sure that we will be able to adequately defend such patents and whether or not we will be able to adequately enforce such patents; or
- whether or not others will obtain patents claiming aspects similar to those covered by our patent applications.

If the USPTO or other foreign patent office upholds patents issued to others or if the USPTO 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 USPTO or other foreign patent 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 partners 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 or commercialize our product candidates and any such events would significantly impair the value of such product candidates.

There is a substantial risk of product liability claims in our business. If we are unable to obtain sufficient insurance, a product liability claim against us could adversely affect our business.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face even greater risks upon any commercialization by us of our product candidates. We have product liability insurance covering our clinical trials in the amount of approximately $11.0 million. Clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance or

increase our existing coverage at a reasonable cost to protect us against losses that could have a material adverse effect on our business. An individual may bring a product liability claim against us if one of our products or product candidates causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any product liability claim brought against us, with or without merit, could result in:

- liabilities that substantially exceed our product liability insurance, which we would then be required to pay from other sources, if available;

- an increase of our product liability insurance rates or the inability to maintain insurance coverage in the future on acceptable terms, or at all;

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withdrawal of clinical trial volunteers or patients;

damage to our reputation and the reputation of our products, resulting in lower sales;

regulatory investigations that could require costly recalls or product modifications;

litigation costs; and

the diversion of management s attention from managing our business.

If our facility incurs damage or power is lost for a significant length of time, our business will suffer.

We currently store numerous clinical and stability samples at our facility that could be damaged if our facility incurred physical damage or in the event of an extended power failure. We have backup power systems in addition to backup generators to maintain power to all critical functions, but any loss of these samples could result in significant delays in our drug development process.

In addition, we currently store most of our preclinical and clinical data at our facility. Duplicate copies of most 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 we fail to retain our existing key personnel or fail to attract and retain additional key personnel, the development of our drug product candidates and the expansion of our business will be delayed or stopped.

We are highly dependent upon our senior management and scientific team, the unexpected 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.

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 Investing in 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, 2009, the 52-week range of the market

price of our stock was from $0.85 to $13.47 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;

additional dilution through sales of our common stock or other derivative securities;

status of new or existing licensing or collaborative agreements and government contracts;

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announcements relating to the status of our programs;

we or our partners achieving or failing to achieve development milestones;

publicity regarding actual or potential medical results relating to products under development by us or our competitors;

publicity regarding certain public health concerns for which we are or may be developing treatments;

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;

changes in the structure of healthcare payment systems, including developments in price control legislation;

announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;

additions or departures of key personnel or members of our board of directors;

purchases or sales of substantial amounts of our stock by existing stockholders, including officers or directors;

economic and other external factors or other disasters or crises; and

period-to-period fluctuations in our financial results.

Because our stock ownership is concentrated, you and other investors will have limited influence on stockholder decisions. In addition, substantial sales of shares may impact the market price of our common stock.

As of September 30, 2009, our directors, executive officers and our stockholders who hold 5% or greater of our outstanding common stock, beneficially owned a significant portion of our outstanding common stock and common stock equivalents. As a result, these holders will likely be able to significantly influence our operations and matters requiring stockholder approval, including the election of directors. The interests of these stockholders may be different from the interests of other stockholders and they could take actions that might not be considered by other stockholders to be in their best interests. This concentration of ownership may delay, defer or prevent a change in our control.

In addition, if any of these significant stockholders sell substantial amounts of our common stock, the market price of our common stock may decline. These sales also might make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we consider appropriate. We are unable to predict when or if any of these stockholders may choose to sell their shares, nor can we predict the effect that sales may have on the then prevailing market price of our common stock.

We, our directors and executive officers and our significant stockholders affiliated with our directors have entered into 45-day lock-up agreements with the underwriters. However, these lockup agreements do not apply to an aggregate of

1,000,000 shares of our common stock held by entities affiliated with our significant stockholder Baker Brothers Investments and an aggregate of 600,000 shares of our common stock held by an entity affiliated with our director William W. Featheringill. As of September 30, 2009, affiliates of Baker Brothers Investments beneficially owned approximately 14.4% of our outstanding common stock prior to this offering and Mr. Featheringill beneficially owned approximately 9.2% of our outstanding common stock prior to this offering. See Underwriters.

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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 4,905,000 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 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, referred to as the 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 beneficially owned approximately 9.2% as of September 30, 2009, but owned more than 15% at the time the Rights were put in place) of our common stock on terms not approved by the board of directors. In August 2007, this plan was amended for a transaction involving funds managed by or affiliated with Baker Brother Investments such that they could purchase up to 25% without triggering the Rights. At September 30, 2009, such group beneficially owned approximately 14.4% of our stock.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

As of the date of this prospectus supplement, we cannot specify with certainty the particular uses for the net proceeds we will receive from this offering. Management will have broad discretion in the application of the net proceeds, including any of the purposes described in Use of Proceeds. The failure by our management to apply these funds effectively could have a material adverse effect on our business.

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.

Exercise of outstanding options and warrants will dilute stockholders and could decrease the market price of our common stock.

As of September 30, 2009, we had issued and outstanding approximately 38.7 million shares of common stock, outstanding options to purchase approximately 6.3 million additional shares of common stock and warrants (exercisable at $10.25 per share) to purchase an additional 3.2 million shares of our common stock. The existence of the outstanding options and warrants may adversely affect the market price of our common stock and the terms under which we could obtain additional equity capital.

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FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the information we incorporate by reference, contain forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, referred to as the Exchange Act, which are subject to the safe harbor created in Section 21E. All statements other than statements of historical facts contained in this prospectus supplement, the accompanying prospectus and the information we incorporate by reference are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as may, could, will, should, expect, plan, anticipate, bel estimate, intend, predict, seek, potential or continue or the negative of these words or similar expressions. Sta that describe our future plans, strategies, intentions, expectations, objectives, goals or prospects are also forward-looking statements. These forward-looking statements include, but are not limited to, statements about:

- the initiation, timing, progress and results of our preclinical testing, clinical trials, and other research and development efforts;
- the potential funding from our contract with HHS for the development of peramivir;
- the potential for a stockpiling order or profit from any order for peramivir;
- the potential use of peramivir as a treatment for H1N1 flu (or other strains of flu);
- the further preclinical or clinical development and commercialization of our product candidates, including peramivir, forodesine and other PNP inhibitor and hepatitis C development programs;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- our ability to establish and maintain collaborations;
- plans, programs, progress and potential success of our collaborations, including Mundipharma for forodesine and Shionogi and Green Cross for peramivir;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our ability to operate our business without infringing the intellectual property rights of others;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the timing or likelihood of regulatory filings and approvals;
- our financial performance; and
- competitive companies, technologies and our industry.

These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these

forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Risk Factors and elsewhere in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference. Any forward-looking statement reflects our current views with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future growth. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

Discussions containing these forward-looking statements are also contained in 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, our Current Reports on Form 8-K, as well as any amendments we make to those filings with the SEC.

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USE OF PROCEEDS

We estimate that the net proceeds to us from our sale of the 5,000,000 shares of common stock offered by us at an assumed public offering price of $12.32 per share, which was the reported last sale price of our common stock on The Nasdaq Global Market on November 16, 2009, will be approximately $57.8 million, after deducting estimated underwriting discounts and commissions and offering expenses payable by us. If the underwriters exercise their over-allotment option in full, we estimate that the net proceeds to us will be approximately $66.5 million. We intend to use the net proceeds of this offering for general corporate purposes, including funding our research and development efforts, clinical development of forodesine and BCX-4208 and pre-commercialization activities relating to i.v. peramivir and forodesine.

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CAPITALIZATION

The following table sets forth our cash, cash equivalents and marketable securities and our capitalization as of September 30, 2009:

- on an actual basis; and
- on an as adjusted basis to give effect to the sale of the 5,000,000 shares of common stock offered by us at an assumed public offering price of $12.32 per share, which was the reported last sale price of our common stock on The Nasdaq Global Market on November 16, 2009, after deducting estimated underwriting discounts and commissions and offering expenses payable by us.

The information presented in this table should be read in conjunction with, and is qualified in its entirety by reference to, the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, including our financial statements and related notes incorporated by reference herein.

	As of September 30, 2009	
	Actual	As Adjusted
	(unaudited) (in thousands)	
Cash, cash equivalents and marketable securities	$ 38,492	$ 96,279
Current and long-term debt		
Stockholders equity:		
Preferred stock: shares authorized 5,000,000; Series B Junior Participating Preferred Stock, $.001 par value; shares authorized 95,000; no shares issued and outstanding		
Common stock, $.01 par value: shares authorized 95,000,000; 38,734,715 shares issued and outstanding, actual; 43,734,715 shares issued and outstanding, as adjusted	387	437
Additional paid-in capital	300,989	358,726
Accumulated other comprehensive income	40	40
Accumulated deficit	(277,871)	(277,871)
Total stockholders equity	23,545	81,332
Total capitalization	$ 23,545	$ 81,332

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DILUTION

As of September 30, 2009, our net tangible book value was approximately $42.0 million, or approximately $1.08 per share of common stock. Net tangible book value per share represents the amount of our total assets, excluding deferred collaboration expenses, less total liabilities, excluding deferred collaboration revenues, divided by the 38,734,715 shares of our common stock outstanding as of September 30, 2009. After giving effect to our sale of the 5,000,000 shares of common stock offered by us at an assumed public offering price of $12.32 per share, which was the reported last sale price of our common stock on The Nasdaq Global Market on November 16, 2009, and after deducting estimated underwriting discounts and commissions and offering expenses payable by us, the net tangible book value as of September 30, 2009 would have been approximately $99.8 million, or approximately $2.28 per share. This represents an immediate increase in net tangible book value of $1.20 per share to existing stockholders and an immediate dilution in net tangible book value of $10.02 per share to new investors purchasing shares of common stock at the assumed public offering price.

The following table illustrates this dilution on a per share basis:

Assumed public offering price per share		$ 12.32
Net tangible book value per share as of September 30, 2009	$ 1.08	
Increase in net tangible book value per share attributable to new investors	1.20	
Net tangible book value per share as of September 30, 2009 after giving effect to this offering		2.28
Dilution in net tangible book value per share to new investors		$ 10.04

In the discussion and table above, we assume no exercise of outstanding options. As of September 30, 2009, there were outstanding options to purchase a total of 6,315,630 shares of common stock at a weighted average exercise price of $6.98 per share and warrants to purchase 3,159,895 shares of common at an exercise price of $10.25 per share. To the extent that any of these stock options or warrants are exercised, there may be further dilution to new public investors.

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PRICE RANGE OF COMMON STOCK AND DIVIDEND POLICY

Our common stock is listed on The Nasdaq Global Market under the symbol BCRX. The following table sets forth, for the periods indicated, the range of high and low sales prices for our common stock, as reported by The Nasdaq Global Market.

	High	Low
Year Ended December 31, 2007		
1st Quarter	$ 12.50	$ 7.80
2nd Quarter	10.05	6.57
3rd Quarter	13.18	7.20
4th Quarter	8.33	5.68
Year Ended December 31, 2008		
1st Quarter	$ 6.53	$ 2.81
2nd Quarter	4.98	2.58
3rd Quarter	3.60	2.40
4th Quarter	3.18	.85
Year Ending December 31, 2009		
1st Quarter	$ 2.37	$ 1.15
2nd Quarter	4.99	1.65
3rd Quarter	13.47	3.65
4th Quarter (through November 16, 2009)	12.70	7.68

The reported last sale price of our common stock on The Nasdaq Global Market on November 16, 2009 was $12.32 per share. As of November 9, 2009 there were approximately 238 holders of record of our common stock.

We have never paid cash dividends and do not anticipate paying cash dividends in the foreseeable future.

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DESCRIPTION OF CAPITAL STOCK

The following summary description of our capital stock summarizes general terms and provisions that apply to the capital stock. Because this is only a summary, it does not contain all of the information that may be important to you. This summary is subject to and qualified in its entirety by reference to our restated certificate of incorporation, as amended, by-laws, as amended, and the rights agreement, as amended, each of which are on file with the SEC. See Where You Can Find More Information.

Authorized and Outstanding Capital Stock

Our authorized capital stock consists of 95,000,000 shares of common stock, par value $0.01 per share, and 5,000,000 shares of preferred stock, par value $0.01 per share, of which 95,000 shares are designated Series B Junior Participating Preferred Stock with a par value of $0.001 per share. On November 9, 2009, there were 38,883,408 shares of common stock outstanding and no shares of preferred stock outstanding.

Common Stock

Holders of our common stock are entitled to one vote per share on all matters submitted to a vote of stockholders and may not cumulate votes for the election of directors. Common stockholders have the right to receive dividends as and when declared by the Board of Directors from funds legally available therefor, subject to any preferential dividend rights of any preferred stock then outstanding. Upon our dissolution or liquidation, common stockholders are entitled to receive all assets legally available for distribution to stockholders, subject to any preferential rights of any preferred stock then outstanding. Holders of common stock have no preemptive rights and have no rights to convert their common stock into any other securities.

Preferred Stock

Preferred stock may be issued from time to time in one or more series, each such series to have such terms as determined by our Board of Directors. Our Board of Directors has the authority to determine and fix such voting powers, full or limited, or no voting powers, and such designations, preferences and relative participating, optional or other special rights, and qualifications, limitations or restrictions thereof, including without limitation dividend rights, conversion rights, redemption privileges and liquidation preferences, without further vote or action by our stockholders. We will distribute a prospectus supplement with regard to each particular series of preferred stock that will describe the terms and provisions of that series of preferred stock. The rights of the holders of any preferred stock that may be issued 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.

Preferred Stock Purchase Rights

In June 2002, our board of directors adopted a stockholder rights plan and, pursuant thereto, issued preferred stock purchase rights, referred to as the Rights, to the holders of our common stock. Each share of common stock issued after adoption of the rights plan also includes one preferred share purchase right. 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 beneficially owned approximately 9.2% as of September 30, 2009 but owned more than 15% at the time the Rights were put in place) of our common stock on terms not approved by the board of directors. In August 2007, this plan was amended for a transaction involving funds managed by or affiliated with Baker Brother Investments such that they could purchase up to 25% without triggering

the Rights. On September 30, 2009, such group beneficially owned approximately 14.4% of our stock. The rights are not exercisable until the distribution date, as defined in the Rights Agreement, dated June 17, 2002, by and between the Company and American Stock Transfer & Trust Company, as Rights Agent, as amended. The Rights will expire at the close of business on June 24, 2012, unless that final expiration date is extended or unless the rights are earlier redeemed or exchanged by the Company.

Each Right entitles the registered holder to purchase from the Company one one-thousandth of a share of Series B Junior Participating Preferred Stock, referred to as Series B, par value $0.001 per share, at a purchase price of $26.00, subject to adjustment. Shares of Series B purchasable upon exercise of the Rights will not be redeemable.

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Each share of Series B will be entitled to a dividend of 1,000 times the dividend declared per share of common stock. In the event of liquidation, each share of Series B will be entitled to a payment of 1,000 times the payment made per share of common stock. Each share of Series B will have 1,000 votes, voting together with the common stock. Finally, in the event of any merger, consolidation, or other transaction in which shares of common stock are exchanged, each share of Series B will be entitled to receive 1,000 times the amount received per share of common stock.

Anti-Takeover Provisions

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.

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UNDERWRITERS

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus supplement, the underwriters named below, for whom Morgan Stanley & Co. Incorporated is acting as representative, have severally agreed to purchase, and we have agreed to sell to them, severally, the number of shares of common stock indicated below:

Name	Number of Shares
Morgan Stanley & Co. Incorporated	
JMP Securities LLC	
Oppenheimer & Co. Inc.	
Total:	5,000,000

The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus supplement and the accompanying prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters over-allotment option described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the public offering price listed on the cover page of this prospectus supplement, and part to certain dealers at a price that represents a concession not in excess of $ a share under the public offering price. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representative.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to 750,000 additional shares of common stock at the public offering price listed on the cover page of this prospectus supplement, less underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the shares of common stock offered by this prospectus supplement and the accompanying prospectus. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional shares of common stock as the number listed next to the underwriter s name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

The following table shows the underwriting discounts and commissions that we are to pay the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters over-allotment option to purchase up to an additional 750,000 shares of common stock.

	Paid by BioCryst	
	No Exercise	**Full Exercise**
Per share	$	$
Total	$	$

The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately $425,000.

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We, our directors and executive officers and our significant stockholders affiliated with our directors have agreed that, without the prior written consent of Morgan Stanley & Co. Incorporated on behalf of the underwriters, we and they will not, during the period ending 45 days after the date of this prospectus supplement:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock;

- in our case only, file any registration statement with the Securities and Exchange Commission relating to the offering of any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock; or

- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock.

whether any such transaction described in the first and third bullet points above is to be settled by delivery of common stock or such other securities, in cash or otherwise.

The restrictions described in the immediately preceding paragraph to do not apply:

- in our case, to (1) the sale of the common stock offered hereby, (2) the issuance by us of any shares of common stock upon the exercise of an option or warrant or the conversion of a security outstanding on the date of this prospectus supplement, or (3) the grant by us of shares of common stock or options to purchase shares of common stock pursuant to existing employee benefit plans or director compensation plans;

- in the case of our directors, executive officers and significant stockholders, to (1) transactions relating to shares of common stock or other securities acquired in open market transactions after the completion of this offering, provided that no filing under Section 16(a) of the Exchange Act will be required or voluntarily made in connection with subsequent sales of such shares of common stock or other securities acquired in such open market transactions; (2) transfers of shares of common stock or any security convertible into common stock (a) as a bona fide gift, (b) to affiliates of the transferor or (c) by will or the laws of descent and distribution; (3) distributions of shares of common stock or any other security to limited partners or stockholders of the transferor; provided that in the case of any transfer or distribution pursuant to clause (2) or (3), (i) each donee, transferee or distributee agrees in writing to be bound by the restrictions set forth above and (ii) no filing under Section 16(a) of the Exchange Act, reporting a reduction in beneficial ownership of shares of common stock, is required or voluntarily made during the restricted period; (4) the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that the plan does not provide for the transfer of common stock during the restricted period; (5) transactions pursuant to a trading plan pursuant to Rule 10b5-1 under the Exchange Act established prior to the date of this prospectus supplement or (6) in the case of restricted common stock that vests during the restricted period, the sale of such common stock by the holder or disposition of shares of such common stock to us to pay withholding tax obligations upon vesting.

In addition, the restrictions described above do not apply (l) in the case of entities affiliated with our significant stockholder, Baker Brothers Investments, to an aggregate of 1,000,000 shares of common stock held by such entities and (2) in the case of an entity affiliated with our director, William W. Featheringill, to an aggregate of 600,000 shares of common stock held by such entity. As of September 30, 2009, affiliates of Baker Brothers Investments beneficially owned approximately 14.4% of our outstanding common stock prior to this offering and Mr. Featheringill beneficially

owned approximately 9.2% of our outstanding common stock prior to this offering.

The 45 day restricted period described in the preceding paragraph will be extended if:

during the last 17 days of the 45 day restricted period we issue an earnings release or material news event relating to us occurs, or

prior to the expiration of the 45 day restricted period, we announce that we will release earnings results during the 16 day period beginning on the last day of the 45 day period,

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in which case the restrictions described in the preceding paragraph will continue to apply until the expiration of the 18 day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the over-allotment option. The underwriters can close out a covered short sale by exercising the over-allotment option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the over-allotment option. The underwriters may also sell shares in excess of the over-allotment option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. These transactions may be effected on The Nasdaq Global Market, in the over-the-counter market or otherwise. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus supplement or accompanying prospectus in electronic format may be made available on the web sites maintained by one or more of the underwriters, and one or more of the underwriters may distribute prospectuses electronically. Other than the prospectus supplement or accompanying prospectus in electronic format, the information on any of these websites and any other information contained on a website maintained by an underwriter or syndicate member is not part of this prospectus supplement or accompanying prospectus. The underwriters may agree to allocate a number of shares of common stock to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representative to the underwriters that may make Internet distributions on the same basis as other allocations.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive, each Manager has represented and agreed that with effect from and including the date on which the Prospectus Directive is implemented in that Member State it has not made and will not make an offer of our shares of common stock to the public in that Member State, except that it may, with effect from and including such date, make an offer of our shares of common stock to the public in that Member State:

(a) at any time to legal entities which are authorised or regulated to operate in the financial markets or, if not so authorised or regulated, whose corporate purpose is solely to invest in securities;

(b) at any time to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than 43,000,000 and (3) an annual net turnover of more than 50,000,000, as shown in its last annual or consolidated accounts; or

(c) at any time in any other circumstances which do not require the publication by us of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of the above, the expression an offer of our shares of common stock to the public in relation to any our shares of common stock in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the our shares of common stock to be offered so as to enable an investor to decide to purchase or subscribe the our shares of common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression

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Prospectus Directive means Directive 2003/71/EC and includes any relevant implementing measure in that Member State.

United Kingdom

Each underwriter has represented and agreed that it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000) in connection with the issue or sale of the our shares of common stock in circumstances in which Section 21(1) of such Act does not apply to us and it has complied and will comply with all applicable provisions of such Act with respect to anything done by it in relation to any our shares of common stock in, from or otherwise involving the United Kingdom.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus supplement will be passed upon for us by Gibson, Dunn & Crutcher LLP. Certain legal matters in connection with this offering will be passed upon for the underwriters by Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2008, and the effectiveness of our internal control over financial reporting as of December 31, 2008, as set forth in their reports, which are incorporated by reference in this prospectus supplement and elsewhere in the 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.

WHERE YOU CAN FIND MORE INFORMATION

We file electronically with the Securities and Exchange Commission our annual reports on Form 10-K, quarterly interim reports on Form 10-Q, current reports on Form 8-K, proxy statements and other information. We make available on or through our website, http://www.biocryst.com, free of charge, copies of these filings as soon as reasonably practicable after we electronically file them with or furnish them to the SEC. The information on our website is not incorporated by reference into this prospectus supplement. You can also request copies of such documents by contacting our Investor Relations Department at 2190 Parkway Lake Drive, Birmingham, Alabama 35244 or sending an email to info@biocryst.com. You may read and copy any document we file at the SEC s Public Reference Room at 100 F Street, N.E. Washington, D.C. 20549. You can also obtain copies of this information by mail from the Public Reference Room of the SEC at prescribed rates. You may obtain information on the operation of the Public Reference Room by calling the SEC at (800) SEC-0330.

The SEC also maintains an Internet world wide web site that contains reports, proxy statements and other information about issuers, like BioCryst, that file electronically with the SEC. The address of that site is http://www.sec.gov. Unless specifically listed below under Incorporation of Certain Documents by Reference the information contained on the SEC website is not incorporated by reference into this prospectus supplement.

We have filed with the SEC a registration statement on Form S-3 that registers the securities we are offering. The registration statement, including the attached exhibits and schedules, contains additional relevant information about us and our securities. The rules and regulations of the SEC allow us to omit certain information included in the registration statement from this prospectus.

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INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference information into this prospectus supplement. This means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus supplement, except for any information that is superseded by information that is included directly in this document.

This prospectus supplement incorporates by reference the documents listed below that we have previously filed with the SEC and that are not included in or delivered with this document. They contain important information about us and our financial condition.

- Our Annual Report on Form 10-K for the year ended December 31, 2008, filed with the SEC on March 6, 2009 (including the sections of our proxy statement relating to our April 30, 2009 annual meeting of stockholders that are incorporated by reference therein);

- Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2009 (filed with the SEC on May 8, 2009), June 30, 2009 (filed with the SEC on July 31, 2009) and September 30, 2009 (filed with the SEC on November 6, 2009);

- Our Current Reports on Form 8-K filed with the SEC on January 28, 2009 and September 23, 2009;

- The description of our common stock which is contained in our Registration Statement on Form 8-A (File No. 000-23186) filed with the SEC on January 8, 1994, including any amendment or reports filed for the purpose of updating such description; and

- The description of our preferred stock purchase rights which is contained in our Registration Statement on Form 8-A (File No. 000-23186) filed with the SEC on June 17, 2002, including any amendment or reports filed for the purpose of updating such description.

All documents filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement and prior to the termination of this offering shall be deemed to be incorporated by reference herein and to be a part of this prospectus supplement from the date of filing of such documents, excluding any information furnished under Item 2.02 or Item 7.01 of any Current Report on Form 8-K and exhibits filed on such form that are related to such items. Any statement contained in a document incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement.

You can obtain any of the documents incorporated by reference in this prospectus supplement from us without charge, excluding any exhibits to those documents unless the exhibit is specifically incorporated by reference as an exhibit to this prospectus supplement by requesting them in writing or by telephone from us at the following address and telephone number:

Investor Relations
BioCryst Pharmaceuticals, Inc.
2190 Parkway Lake Drive

Birmingham, Alabama 35244
(205) 444-4600

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PROSPECTUS

$70,000,000

Common Stock
Preferred Stock
Depositary Shares
Stock Purchase Contracts
Warrants
Units

By this prospectus, we may from time to time offer securities to the public. We will provide specific terms of these securities in supplements to this prospectus. You should read this prospectus, each applicable prospectus supplement, and the information incorporated by reference in this prospectus and each applicable prospectus supplement carefully before you invest.

Our common stock, par value $0.01 per share, trades on the Nasdaq Global Market under the symbol BCRX.

You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone else to provide you with different information or to make additional representations. We are not making or soliciting an offer of any securities other than the securities described in this prospectus and any prospectus supplement. We are not making or soliciting an offer of these securities in any state or jurisdiction where the offer is not permitted or in any circumstances in which such offer or solicitation is unlawful. You should not assume that the information contained or incorporated by reference in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front of those documents.

Investing in these securities involves a high degree of risk. See Risk Factors beginning on page 5 of this prospectus and in the prospectus supplement we will deliver with 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, or through a combination of these methods. 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 securities unless accompanied by a prospectus supplement.

The aggregate market value of our outstanding common equity held by non-affiliates as of September 29, 2008 was approximately $87 million. We have not issued any securities under Form S-3 during the last 12 months.

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

The date of this prospectus is January 27, 2009.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration or continuous offering process. Under this registration statement, we may sell any combination of the securities described in this prospectus from time to time, either separately or in units, in one or more offerings. Together, these offerings may total up to $70,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement containing specific information about the terms of that offering. That prospectus supplement will also include the following information:

- the type and amount of securities that we propose to sell;
- the public offering price of the securities;
- the names of any underwriters, agents or dealers through or to which the securities will be sold;
- any compensation of those underwriters, agents or dealers;
- information about any securities exchanges or automated quotation systems on which the securities will be listed or traded;
- any risk factors applicable to the securities that we propose to sell; and
- any other material information about the offering and sale of the securities.

If there is any inconsistency between the information in this prospectus and any prospectus supplement, you should rely on the information in the prospectus supplement. You should read both this prospectus and any prospectus

supplement together with the additional information described under the heading Where You Can Find More Information. The registration statement containing this prospectus, including the exhibits to the registration statement, provides additional information about us and the securities offered under this prospectus. The registration statement, including the exhibits, can be read at the SEC s website or at the SEC s offices mentioned under the heading Where You Can Find More Information.

All references to Company we, our or us refer solely to BioCryst Pharmaceuticals, Inc. and not to the persons who manage us or sit on our Board of Directors. All trade names used in this prospectus are either our registered trademarks or trademarks of their respective holders.

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PROSPECTUS SUMMARY

This summary highlights information contained elsewhere or incorporated by reference into this prospectus. Because it is a summary, it does not contain all of the information that you should consider before investing in our securities. You should read this entire prospectus carefully, including the section entitled Risk Factors and the documents that we incorporate by reference into this prospectus, before making an investment decision.

Business of BioCryst Pharmaceuticals, Inc.

Overview

BioCryst Pharmaceuticals, Inc. is a biotechnology company that designs, optimizes and develops novel drugs that block key enzymes involved in cancer, viral infections, and autoimmune diseases. We integrate the necessary disciplines of biology, crystallography, medicinal chemistry and computer modeling to effectively use structure-based drug design to discover and develop small molecule pharmaceuticals.

Our business strategy is to maximize sustainable value by moving our drug candidate portfolio through clinical development, registration and ultimately to the market. We believe this is best achieved by retaining full product rights to our drug candidates within specialty markets, while relying on collaborative arrangements with third parties for drug candidates within larger markets or outside our area of expertise.

Clinical Development Projects

Currently we have a well advanced and relatively full pipeline. We have one pivotal trial and two other phase II trials currently ongoing. In addition we have a number of potential preclinical candidates to be evaluated for clinical study.

Peramivir

Peramivir, a neuraminidase inhibitor, is in development for the treatment of influenza with two parenteral formulations, intramuscular (i.m.) and intravenous (i.v.).

We completed a double-blind placebo-controlled Phase II clinical trial with i.m. peramivir testing two different dose levels of peramivir (150mg and 300mg) versus placebo in adults with acute uncomplicated influenza. While the trial did not demonstrate statistically significant differences for its primary endpoint of time to alleviation of symptoms, the preliminary analysis of the virologic data indicated that peramivir demonstrated statistically significant reductions in influenza virus shedding in both peramivir treatment groups compared to placebo, with greater reductions in the 300mg dose. With this information and the additional pharmacokinetic information we have obtained subsequent to the trial, we initiated a Phase II placebo-controlled trial of 600 mg i.m. peramivir for the treatment of seasonal influenza. This trial uses a new, more concentrated 150 mg/ml formulation of peramivir.

In addition, in July 2007, we announced the initiation of a Phase II clinical trial in hospitalized patients using an i.v. formulation of peramivir to compare the efficacy and safety of i.v. peramivir to orally administered oseltamivir in patients who require hospitalization due to acute influenza. In October, 2008 BioCryst reported results of an exploratory Phase 2 trial of i.v. peramivir in subjects hospitalized for acute serious or potentially life-threatening influenza. The Phase 2 trial compared the efficacy and safety of five days of therapy with either 200 mg i.v. peramivir per day, 400 mg i.v. peramivir per day or 75 mg oral oseltamivir twice a day for five days, in subjects who required hospitalization related to influenza. The primary objective of the study was to evaluate a novel composite endpoint,

time to clinical stability, which is comprised of normalization of temperature, oxygen saturation, respiratory rate, systolic blood pressure and heart rate. Secondary objectives of the study included evaluation of viral shedding, mortality, clinical relapse and time to resumption of usual activities. In the primary efficacy population, for all groups combined, the study demonstrated a median of 25.3 hours to clinical stability, a median of 2.0 log reduction in time weighted change from baseline in viral titer, zero mortality, no clinical relapse and a median of 10.8 days of time to resumption of usual activities. There were no statistically significant differences in any of the efficacy endpoints between the three treatment arms. Peramivir was generally safe and well-tolerated at these dose levels.

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In January 2007, we announced the United States Department of Health and Human Services, HHS, had awarded us a $102.6 million, four-year contract for the advanced development of peramivir. In January 2008, we announced that the development plan for peramivir had changed and that we would no longer pursue the Phase III i.m. program in peramivir for the current influenza season, but would move forward in evaluating higher doses than used in previous studies. Also in January, we announced that the program would cost in excess of the $102.6 million contract and that any funding above the $102.6 million may be the responsibility of the Company. Since then, HHS and BioCryst have been working in collaboration through various contract modifications to maximize resources by stopping work on some projects (e.g. the Phase III i.m. program) and capping expenditures on other projects in order to maximize remaining funds. HHS and BioCryst executed a contract modification that fully funds BioCryst through the completion of both the phase II studies in outpatients treated with intramuscular peramivir, the phase II study in hospitalized patients with intravenous peramivir, and certain manufacturing and toxicology components of the program. The modification also allows the Company and HHS to agree on additional development activities for peramivir within the confirmed $102.6 million funding. All temporary restraints, effected through a stop work order, have now been removed. Following completion of the phase II studies, the Company expects to continue the dialogue with HHS regarding additional funding beyond the $102.6 million for peramivir development through U.S. licensure. The original contract of $102.6 million and the four year term remain unchanged.

In March 2007, we announced our collaboration with Shionogi & Co., Ltd. (Shionogi) for the development and commercialization of peramivir in Japan. This exclusive license agreement for Japan included an upfront payment of $14 million and future clinical event milestone payments of up to $21 million. Shionogi recently completed a Phase II study of intravenous (i.v.) peramivir administered via a single dose injection in the outpatient setting for treatment of seasonal influenza. This trial met its primary endpoint of improvement in the median time to alleviation of symptoms in subjects with confirmed, acute, uncomplicated influenza infection, compared to placebo alone.

Forodesine HCl

Forodesine HCl is a transition-state analog inhibitor of the enzyme purine nucleoside phosphorylase, or PNP. In February 2006, we announced an exclusive licensing agreement with Mundipharma to develop and commercialize forodesine HCl in markets across Europe, Asia and Australia for use in oncology. We have retained full development and commercialization rights in the rest of the world, including North America.

An oral formulation of the compound is currently in a Phase IIb trial, which is planned to be a pivotal trial, for patients with Cutaneous T-cell Lymphoma, commonly called CTCL. The trial is being conducted under a special protocol assessment negotiated with the United States Food and Drug Administration, or the FDA. Additionally, forodesine HCl is currently being studied in a Phase II trial with an oral formulation in Chronic Lymphocytic Leukemia, commonly called CLL.

Forodesine HCl has been granted Orphan Drug status by the FDA for three indications:

T-cell non-Hodgkin lymphoma, including CTCL;

CLL and related leukemias including T-cell prolymphocytic leukemia, adult T-cell leukemia, and hairy cell leukemia; and

B-cell acute lymphoblastic leukemia, commonly called B-ALL.

In December 2007, we announced the presentation of data related to the Phase I/II clinical study of forodesine HCl in subjects with refractory CTCL and a poster detailing the in vitro activity of forodesine HCl as a single agent and the synergistic in vitro activity of forodesine HCl in combination with bendamustine in primary cells from 29 patients

with CLL. These data were presented at the 2007 American Society of Hematology meeting. Use of single agent forodesine HCl is being explored in various cancer settings, and combination studies are being planned.

In December 2008, we announced interim data from the ongoing forodesine HCl Phase II program in patients with CLL and data from a healthy subject pharmacokinetic and pharmacodynamic study. The CLL study will continue with an amendment to study a new dosing regimen of oral forodesine, 200 mg twice-daily.

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An interim analysis was conducted on data from an exploratory Phase II single-arm, open-label program in patients with CLL whose previous treatment had failed. While this analysis showed that no partial or complete responses were observed, five out of 13 patients administered 200 mg of forodesine HCl once-daily had substantial reductions in malignant lymphocytes, and at the time of the analysis, seven patients were still on study. Forodesine HCl was generally safe and well-tolerated at the 200 mg once-daily dose. In a parallel, healthy subject, pharmacokinetic and pharmacodynamic study, we compared the effect of seven days of 200 mg forodesine HCl dosed once-daily with seven days of 200 mg forodesine HCl dosed twice-daily. The study demonstrated substantially increased drug exposure and pharmacodynamic effect in subjects administered forodesine HCl 200 mg twice-daily. Drug exposure, as measured by area under the (plasma-concentration/time) curve (AUC), increased by 63 percent ($P<0.001$) for twice-daily dosing compared to once-daily dosing. Serum uric acid levels were reduced at steady state compared to baseline by 50.0 percent for twice-daily dosing compared to 23.5 percent for once-daily dosing ($p<0.001$), indicating increased PNP enzyme inhibition with twice-daily dosing.

BCX-4208

BCX-4208 is another PNP inhibitor in clinical development. In November 2005, BioCryst announced it was entering into an exclusive worldwide development and commercialization agreement with Roche. In the third quarter of 2007, we announced that Roche had initiated a Phase II clinical trial with oral doses of BCX-4208/R3421, which is designed to evaluate the drug candidate in patients with moderate to severe plaque psoriasis. The efficacy assessment of the study has been completed. Consistent with interim findings reported by the Company in May 2008, the Phase II clinical study of BCX-4208, a potent, rationally designed, orally available PNP inhibitor, met its primary objectives of safety and tolerability. In addition, BCX-4208 displayed dose-dependent reductions in peripheral blood lymphocyte counts, including subsets measuring B cells (CD20), total T cells (CD3), T helper cells (CD4) and T suppressor/cytotoxic cells (CD8). Further, plasma levels of BCX-4208 increased with dose, and plasma uric acid levels showed dose-related reductions with BCX-4208. In addition, consistent with interim results previously reported by the Company, no evidence of clinical efficacy, a secondary objective, was observed in psoriasis patients with doses and duration of administration tested.

In the Phase IIa trial, BCX-4208 was generally safe and well-tolerated at doses up to 120 mg daily. Most adverse events reported were considered mild or moderate, and low in frequency. No opportunistic infections were observed. In addition, detailed laboratory and clinical monitoring did not indicate any patterns suggestive of off-target adverse findings.

Also in May 2008, we announced that we received notice that Roche was exercising the no cause termination right under the license agreement for BCX-4208. As a result, BioCryst regained worldwide rights to BCX-4208.

Additional Products

In addition to our clinical programs shown above, we also retain exclusive world wide rights to potent inhibitors of hepatitis C nucleoside polymerase, parainfluenza neuraminidase, and additional PNP inhibitors. We will continue to evaluate and test each of these compounds to determine which should be taken into clinical testing.

Because none of our products have been approved by regulatory authorities, we may not be able to generate significant revenue or attain profitability. Since our inception, we have not generated any product sales from our drug discovery and development efforts and we have a history of significant losses. Given that we expect to incur substantial net losses to develop our potential products, it is unclear when, if ever, we will become profitable. See Risk Factors for a full discussion of these and other risks relating to our business and owning our capital stock.

Alliances

As our part of our strategy we will consider potential third party alliances in large primary care markets and in areas where do not have the resources or expertise to move candidates forward on our own. These alliances could include preclinical development, clinical development, regulatory approval, marketing, sales and distribution of our drug candidates.

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We have established collaborative relationships for development and commercialization of product candidates in their respective territories as follows:

Mundipharma Internal Holdings Limited, for forodesine HCl in Europe, Asia and Australia;

Shionogi & Co. Ltd.; and

Green Cross Corporation.

The process of establishing and implementing collaborative relationships is difficult, time-consuming and involves significant uncertainty. See Risk Factors for further details.

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.

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RISK FACTORS

An investment in our securities 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 securities. It is anticipated that the prospectus supplement will contain a description of the risks relating to the securities we may offer with the prospectus supplement. 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 securities.

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. To become profitable, we must successfully manufacture and develop drug product candidates, receive regulatory approval, and successfully commercialize or enter into profitable agreements with other parties. It could be several years, if ever, before we receive royalties from any current or future license agreements or revenues directly from product sales.

Because of the numerous risks and uncertainties associated with developing our product candidates and their potential for commercialization, we are unable to predict the extent of any future losses. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. If we are unable to achieve and sustain profitability, the market value of our common stock will likely decline.

Our success depends upon our ability to advance our products through the various stages of development, especially through the clinical trial process.

To receive the regulatory approvals necessary for the sale of our product candidates, we or our partners must demonstrate through preclinical studies and clinical trials that each product candidate is safe and effective. 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 unlikely to show good results in the trials, unlikely to help advance a product to the point of a meaningful collaboration, or unlikely to have a reasonable commercial potential. We may suffer significant setbacks in pivotal clinical trials, even after earlier clinical trials show promising results. Clinical trials may not be adequately designed or executed, which could affect the potential outcome and analysis of study results. Any of our product 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 product candidate. These side effects could also result in the FDA or foreign regulatory authorities refusing to approve the product candidate for any targeted indications. We, our partners, 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 product candidates are safe or effective and have acceptable commercial viability.

Our ability to successfully complete clinical trials is dependent upon many factors, including but not limited to:

our ability to find suitable clinical sites and investigators to enroll patients;

the availability of and willingness of patients to participate in our clinical trials;

difficulty in maintaining contact with patients to provide complete data after treatment;

our product candidates may not prove to be either safe or effective;

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clinical protocols or study procedures may not be adequately designed or followed by the investigators;

manufacturing or quality problems could affect the supply of drug product for our trials; and

delays or changes in requirements by governmental agencies.

Clinical trials are lengthy and expensive. We or our partners 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 partners successfully complete clinical trials for our product candidates, we or our partners might not file the required regulatory submissions in a timely manner and may not receive regulatory approval for the product candidate.

Our later stage clinical trials may not adequately show our drugs are safe or effective.

Progression of our drug products through the clinical development process is dependent upon our trials indicating our drugs have adequate safety profiles and show positive therapeutic effects in the patients being treated by achieving pre-determined endpoints according to the trial protocols. Failure to achieve either of these could result in delays in our trials or even require the performance of additional unplanned trials. This could result in delays in the development of our drug candidates and could result in significant unexpected costs.

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.

As our clinical programs continue to grow and patient enrollment increases, our costs will increase. Our current and planned clinical trials plus the related development, manufacturing, regulatory approval process requirements, and additional personnel resources and testing required for supporting the development of our drug candidates will consume significant capital resources. Our expenses, revenues and burn rate could vary significantly depending on many factors, including our ability to raise additional capital, the development progress of our collaborative agreements for our drug candidates, the amount of funding we receive from HHS for peramivir, the amount of funding or assistance, if any, we receive from other governmental agencies or other new partnerships with third parties for the development of our drug candidates, the progress and results of our current and proposed clinical trials for our most advanced drug products, the progress made in the manufacturing of our lead products and the progression of our other programs.

We expect that 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, including governmental agencies, in general and from the HHS contract specifically, 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.

If HHS were to eliminate, reduce or delay funding from our contract or dispute some of our incurred costs, this would have a significant negative impact on our revenues, cash flows and the development of peramivir.

Our projections of revenues and incoming cash flows are substantially dependent upon HHS reimbursement for the costs related to our peramivir program. If HHS were to eliminate, reduce or delay the funding for this program or disallow some of our incurred costs, we would have to obtain additional funding for development of this drug candidate or significantly reduce or stop the development effort. For example, in

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January 2008, we announced that the development plan for peramivir had changed and that we would no longer pursue the Phase III i.m. program in peramivir for the current influenza season, but would move forward in evaluating higher doses than used in previous studies. Also in January, we announced that the program would cost in excess of the $102.6 million contract and that any funding above the $102.6 million may be the responsibility of the Company. Since then, HHS and BioCryst have been working in collaboration through various contract modifications to maximize resources by stopping work on some projects (e.g. the Phase III i.m. program) and capping expenditures on other projects in order to maximize remaining funds. HHS and BioCryst executed a contract modification that fully funds BioCryst through the completion of both the phase II studies in outpatients treated with intramuscular peramivir, the phase II study in hospitalized patients with intravenous peramivir, and certain manufacturing and toxicology components of the program. The modification also allows the Company and HHS to agree on additional development activities for peramivir within the confirmed $102.6 million funding. All temporary restraints, effected through a stop work order, have now been removed. Following completion of the phase II studies, the Company expects to continue the dialogue with HHS regarding additional funding beyond the $102.6 million for peramivir development through U.S. licensure. The original contract of $102.6 million and the four year term remain unchanged. In July 2008, HHS indicated that it does not intend to reimburse us all of the costs incurred related to the terminated Phase III studies. We continue to pursue reimbursement of these costs. During the second quarter of 2008, we recorded a $4.9 million reserve against revenue for amounts we previously expected to receive from HHS related to the costs incurred in this program. Approximately $4.6 million of the reserve relates to revenues recognized in the first quarter of 2008, while approximately $0.3 million of the reserve relates to revenues recognized in 2007.

In contracting with HHS, we are subject to various U.S. government contract requirements, including general clauses for a cost-reimbursement research and development contract, which may limit our reimbursement or if we are found to be in violation could result in contract termination. U.S. government contracts typically contain unfavorable termination provisions and are subject to audit and modification by the government at its sole discretion. The U.S. government may terminate its contract with us either for its convenience or if we default by failing to perform in accordance with the contract schedule and terms, which would have a significant negative impact on our cash flows and operations.

Our contract with HHS has special contracting requirements, which create additional risks of reduction or loss of funding.

We have entered into a contract with HHS for the advanced development of our neuraminidase inhibitor, peramivir. In contracting with HHS, we are subject to various U.S. government contract requirements, including general clauses for a cost-reimbursement research and development contract. U.S. government contracts typically contain unfavorable termination provisions and are subject to audit and modification by the government at its sole discretion, which subjects us to additional risks. These risks include the ability of the U.S. government to unilaterally:

terminate or reduce the scope of our contract; and

audit and object to our contract-related costs and fees, including allocated indirect costs.

The U.S. government may terminate its contract with us either for its convenience or if we default by failing to perform in accordance with the contract schedule and terms. Termination for convenience provisions generally enable us to recover only our costs incurred or committed, and settlement expenses and profit on the work completed prior to termination. Termination for default provisions does not permit these recoveries.

As a U.S. government contractor, we are required to comply with applicable laws, regulations and standards relating to our accounting practices and are subject to periodic audits and reviews. As part of any such audit or review, the U.S. government may review the adequacy of, and our compliance with, our internal control systems and policies,

including those relating to our purchasing, property, estimating, compensation and management information systems. Based on the results of its audits, the U.S. government may adjust our contract-related costs and fees, including allocated indirect costs. In addition, if an audit or review uncovers any improper or illegal activity, we may be subject to civil and criminal penalties and administrative sanctions,

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including termination of our contracts, forfeiture of profits, suspension of payments, fines and suspension or prohibition from doing business with the U.S. government. We could also suffer serious harm to our reputation if allegations of impropriety were made against us. In addition, under U.S. government purchasing regulations, some of our costs may not be reimbursable or allowed under our contracts. Further, as a U.S. government contractor, we are subject to an increased risk of investigations, criminal prosecution, civil fraud, whistleblower lawsuits and other legal actions and liabilities as compared to private sector commercial companies.

If we fail to successfully commercialize or establish collaborative relationships to commercialize certain of our drug product candidates or if any partner terminates or fails to perform its obligations under agreements with us, potential revenues from commercialization of our product candidates could be reduced, delayed or eliminated.

Our business strategy is to increase the asset value of our drug candidate portfolio. We believe this is best achieved by retaining full product rights or through collaborative arrangements with third parties as appropriate. As needed, potential third party alliances could include preclinical development, clinical development, regulatory approval, marketing, sales and distribution of our drug product candidates.

Currently, we have established collaborative relationships with certain pharmaceutical companies, Roche (recently terminated), Mundipharma, and both Shionogi and Green Cross for the development and commercialization of BCX-4208, forodesine HCl and peramivir, respectively. The process of establishing and implementing collaborative relationships is difficult, time-consuming and involves significant uncertainty, including:

- our partners may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, a change in business strategy, a change of control or other reasons;
- our contracts for collaborative arrangements may expire;
- 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;
- we do not have day to day control over the activities of our partners and have limited control over their decisions;
- our ability to generate future event payments and royalties from our partners depends upon their abilities to establish the safety and efficacy of our drug candidates, obtain regulatory approvals and achieve market acceptance of products developed from our drug candidates;
- we or our partners may fail to properly initiate, maintain or defend our intellectual property rights, where applicable, or a party may utilize our proprietary information in such a way as to invite litigation that could jeopardize or potentially invalidate our proprietary information or expose us to potential liability;
- our partners may not devote sufficient capital or resources towards our product candidates; and
- our partners may not comply with applicable government regulatory requirements.

If any partner fails to fulfill its responsibilities in a timely manner, or at all, our commercialization efforts related to that collaboration could be reduced, delayed or terminated, or it may be necessary for us to assume responsibility for activities that would otherwise have been the responsibility of our partner. If we are unable to establish and maintain collaborative relationships on acceptable terms, we may have to delay or discontinue further development of one or

more of our product candidates, undertake commercialization activities at our own expense or find alternative sources of funding. Any delay in the development or commercialization of our compounds would severely affect our business, because if our compounds do not progress through the development process or reach the market in a timely manner, or at all, we may not receive additional future event payments and may never receive product or royalty payments.

For example, in May 2008, we received notice that Roche was exercising the no cause termination right under the license agreement for BCX-4208. In the third quarter of 2007, we announced that Roche had

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initiated a Phase II clinical trial with oral doses of BCX-4208/R3421, which is designed to evaluate the drug candidate in patients with moderate to severe plaque psoriasis. The efficacy assessment of the study has been completed. Consistent with interim findings reported by the Company in May 2008, this study of BCX-4208, a potent, rationally designed, orally available PNP inhibitor, met its primary objectives of safety and tolerability. In addition, BCX-4208 displayed dose-dependent reductions in peripheral blood lymphocyte counts, including subsets measuring B cells (CD20), total T cells (CD3), T helper cells (CD4) and T suppressor/cytotoxic cells (CD8). Further, plasma levels of BCX-4208 increased with dose, and plasma uric acid levels showed dose-related reductions with BCX-4208. In addition, consistent with interim results previously reported by the Company, no evidence of clinical efficacy, a secondary objective, was observed in psoriasis patients with doses and duration of administration tested.

In the Phase IIa trial, BCX-4208 was generally safe and well-tolerated at doses up to 120 mg daily. Most adverse events reported were considered mild or moderate, and low in frequency. No opportunistic infections were observed. In addition, detailed laboratory and clinical monitoring did not indicate any patterns suggestive of off-target adverse findings.

In May 2008, we announced that we received notice that Roche was exercising the no cause termination right under the license agreement for BCX-4208. As a result, BioCryst regained worldwide rights to BCX-4208.

We are currently in dispute with Mundipharma regarding the contractual obligations of the parties with respect to certain costs related to the manufacturing and development of forodesine HCl. Notwithstanding, we do not believe that we are responsible for any of the disputed amounts. We are engaged in ongoing discussion to resolve this dispute. The maximum potential exposure to us is estimated to be approximately $2.5 million. Because of the preliminary nature of the discussions, no amounts have been accrued as of September 30, 2008.

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

We have not commercialized any products or technologies, and we may never be able to do so. We currently have no marketing capability and no direct or third-party sales or distribution capabilities and may be unable to establish these capabilities for products we plan to commercialize. In addition, 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 event or other collaborative payments.

Our ability to receive revenue from products we commercialize presents several risks, including:

- we or our collaborators may fail to successfully complete clinical trials sufficient to obtain FDA marketing approval;
- many competitors are more experienced and have significantly more resources and their products could be more cost effective or have a better efficacy or tolerability profile than our product candidates;
- we may fail to employ a comprehensive and effective intellectual property strategy which could result in decreased commercial value of our company and our products;
- we may fail to employ a comprehensive and effective regulatory strategy which could result in a delay or failure in commercialization of our products;
- our ability to successfully commercialize our products are affected by the competitive landscape, which cannot be fully known at this time;

reimbursement is constantly changing which could greatly affect usage of our products; and

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.

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If our development collaborations with third parties, such as our development partners and contract research organizations, fail, the development of our drug product candidates will be delayed or stopped.

We rely heavily upon other parties for many important stages of our drug development programs, including but not limited to:

- discovery of compounds that cause or enable biological reactions necessary for the progression of the disease or disorder, called enzyme targets;
- licensing or design of enzyme inhibitors for development as drug product candidates;
- execution of some preclinical studies and late-stage development for our compounds and product candidates;
- management of our clinical trials, including medical monitoring and data management;
- execution of additional toxicology studies that may be required to obtain approval for our product candidates; and
- manufacturing the starting materials and drug substance required to formulate our drug products and the drug products to be used in both our clinical trials and toxicology studies.

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, conduct our toxicology studies, manufacture our starting materials, drug substance and drug products or manage our regulatory function breached their obligations to us or perform their services inconsistent with industry standards and not in accordance with the required regulations, this would delay or prevent the development of our product candidates.

If we lose our relationship with any one or more of these parties, we could experience a significant delay in both identifying another comparable provider and then contracting for its services. We may be unable to retain an alternative provider on reasonable terms, if at all. Even if we locate an alternative provider, it is likely that this provider may need additional time to respond to our needs and may not provide the same type or level of service as the original provider. In addition, any provider that we retain will be subject to current Good Laboratory Practices (cGLP), current Good Manufacturing Practices (cGMP), or current Good Clinical Practices (cGCP), and similar foreign standards and we do not have control over compliance with these regulations by these providers. Consequently, if these practices and standards are not adhered to by these providers, the development and commercialization of our product candidates could be delayed.

Our development of both intravenous and intramuscular dosing of peramivir for avian and seasonal influenza is subject to all disclosed drug development and potential commercialization risks and numerous additional risks. Any potential revenue benefits to us are highly speculative.

Further development and potential commercialization of peramivir is subject to all the risks and uncertainties disclosed in our other risk factors relating to drug development and commercialization. In addition, potential commercialization of peramivir is subject to further risks, including but not limited to the following:

the injectable versions of peramivir are currently in Phase II clinical development and have been tested in a limited number of humans and may not be safe or effective;

necessary government or other third party funding and clinical testing for further development of peramivir may not be available timely, at all, or in sufficient amounts;

the avian flu prevention or treatment concerns may not materialize at all, or in the near future;

advances in flu vaccines could substantially replace potential demand for an antiviral such as peramivir;

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any substantial demand for avian flu treatments may occur before peramivir can be adequately developed and tested in clinical trials;

injectable forms of peramivir may not prove to be accepted by patients and physicians as a treatment for seasonal influenza compared to the other currently marketed antiviral drugs, which would limit revenue from non-governmental entities;

numerous large and well-established pharmaceutical and biotech companies will be competing to meet the market demand for avian flu drugs and vaccines;

regulatory authorities may not make needed accommodations to accelerate the drug testing and approval process for peramivir; and

in the next few years, it is expected that a limited number of governmental entities will be the primary potential customers for peramivir and if we are not successful at marketing peramivir to these entities for any reason, we will not receive substantial revenues from stockpiling orders from these entities.

If any or all of these and other risk factors occur, we will not attain significant revenues or gross margins from peramivir and our stock price will be adversely affected.

Because we have limited manufacturing experience, we depend on third-party manufacturers to manufacture our drug product candidates and the materials for our product candidates. If we cannot rely on third-party manufacturers, we will be required to incur significant costs and potential delays in finding new third-party manufacturers.

We have limited manufacturing experience and only a small scale manufacturing facility. We currently rely upon third-party manufacturers to manufacture the materials required for our drug product candidates and most of the preclinical and clinical quantities of our product candidates. We depend on these third-party manufacturers to perform their obligations in a timely manner and in accordance with applicable governmental regulations. Our third-party manufacturers may encounter difficulties with meeting our requirements, including but not limited to problems involving:

inconsistent production yields;

product liability claims;

difficulties in scaling production to commercial and validation sizes;

interruption of the delivery of materials required for the manufacturing process;

scheduling of plant time with other vendors or unexpected equipment failure;

potential catastrophes that could strike their facilities;

potential impurities in our drug substance or drug products that could affect availability of product for our clinical trials or future commercialization;

poor quality control and assurance or inadequate process controls; and

lack of compliance with regulations and specifications set forth by the FDA or other foreign regulatory agencies.

These contract manufacturers may not be able to manufacture the materials required or our drug product candidates at a cost or in quantities necessary to make them commercially viable. We also have no control over whether third-party manufacturers breach their agreements with us or whether they may terminate or decline to renew agreements with us. To date, our third party manufacturers have met our manufacturing requirements, but they may not continue to do so. Furthermore, changes in the manufacturing process or procedure, including a change in the location where the drug is manufactured or a change of a third-party manufacturer, may require prior review and approval in accordance with the FDA s cGMPs, and comparable foreign requirements. This review may be costly and time-consuming and could delay or prevent the launch of a product. The FDA or similar foreign regulatory agencies at any time may also implement new standards, or

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change their interpretation and enforcement of existing standards for manufacture, packaging or testing of products. If we or our contract manufacturers are unable to comply, we or they may be subject to regulatory action, civil actions or penalties.

If we are unable to enter into agreements with additional manufacturers on commercially reasonable terms, or if there is poor manufacturing performance on the part of our third party manufacturers, we may not be able to complete development of, or market, our product candidates.

Our raw materials, drug substances, and drug products are manufactured by a limited group of suppliers and some at a single facility. If any of these suppliers were unable to produce these items, this could significantly impact our supply of drugs for further preclinical testing and clinical trials.

If we or our partners 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 partners must obtain regulatory approval before marketing or selling our future drug products. If we or our partners 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 process of preparing for and obtaining FDA approval may be lengthy and expensive, and approval is never certain. Products distributed abroad are also subject to foreign government regulation. Neither the FDA nor foreign regulatory agencies have approved any of our drug product candidates. Because of the risks and uncertainties in biopharmaceutical development, our product 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 product 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 product candidate, the approval may limit the indicated uses for a product 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, our clinical data and our manufacturing data at our facility. While we do store duplicate copies of most of our clinical data offsite and a significant portion of our data is included in regular backups of our systems, we could lose important 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 partners 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 CTCL and psoriasis. In November 1995, the FDA issued 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 CTCL 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. We are 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.

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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 product 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 and our partners are performing research on or developing products for the treatment of several disorders including T-cell mediated disorders (T-cell cancers, transplant rejection, psoriasis and other autoimmune indications), oncology, influenza, and hepatitis C. 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. Such is the case with Eisai s Targretin for CTCL and the current neuraminidase inhibitors marketed by Glaxo Smith Kline and Roche for influenza. In addition, several 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, influenza, hepatitis C, and in other therapeutic areas where we have discovery efforts ongoing. 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 partners to obtain, protect and enforce viable intellectual property rights including but not limited to trade name, trade mark and patent protection for our company and its products, methods, processes and other technologies we may license or develop, to preserve our trade secrets, and to operate without infringing the proprietary rights of third parties both domestically and abroad. The patent position of biotechnology and pharmaceutical companies is generally highly uncertain, involves complex legal and factual questions and has recently been the subject of much litigation. Neither the United States Patent and Trademark Office (USPTO), the Patent Cooperation Treaty offices, nor the courts of the United States and other jurisdictions have consistent policies nor predictable rulings regarding the breadth of claims allowed or the degree of protection afforded under many biotechnology and pharmaceutical patents. The validity, scope, enforceability and commercial value of these rights, therefore, is highly uncertain.

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Our success depends in part on avoiding the infringement of other parties patents and other intellectual property rights as well as avoiding the breach of any licenses relating to our technologies and products. In the U.S., patent applications filed in recent years are confidential for 18 months, while older applications are not published until the patent issues. As a result, avoiding patent infringement may be difficult and we may inadvertently infringe third-party patents or proprietary rights. These third parties could bring claims against us, our partners or our licensors that even if resolved in our favor, could cause us to incur substantial expenses and, if resolved against us, could additionally cause us to pay substantial damages. Further, if a patent infringement suit were brought against us, our partners or our licensors, we or they could be forced to stop or delay research, development, manufacturing or sales of any infringing product in the country or countries covered by the patent we infringe, unless we can obtain a license from the patent holder. Such a license may not be available on acceptable terms, or at all, particularly if the third party is developing or marketing a product competitive with the infringing product. Even if we, our partners or our licensors were able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property.

If we or our partners are unable or fail to adequately, initiate, protect, defend or enforce our intellectual property rights in any area of commercial interest or in any part of the world where we wish to seek regulatory approval for our products, methods, processes and other technologies, the value of the drug product candidates to produce revenue would diminish. Additionally, if our products, methods, processes, and other technologies or our commercial use of such products, processes, and other technologies, including but not limited to any tradename, trademark or commercial strategy infringe the proprietary rights of other parties, we could incur substantial costs. The USPTO and the patent offices of other jurisdictions have issued to us a number of 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 USPTO. We have filed a number of corresponding foreign patent applications and intend to file additional foreign and U.S. patent applications, as appropriate. We have also filed certain trademark and tradename applications worldwide. 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;
- if patents do issue we can not be sure that we will be able to adequately defend such patents and whether or not we will be able to adequately enforce such patents; or
- whether or not others will obtain patents claiming aspects similar to those covered by our patent applications.

If the USPTO or other foreign patent office upholds patents issued to others or if the USPTO 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 USPTO or other foreign patent 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 partners 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

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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 or commercialize our product candidates and any such events would significantly impair the value of such product candidates.

There is a substantial risk of product liability claims in our business. If we are unable to obtain sufficient insurance, a product liability claim against us could adversely affect our business.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face even greater risks upon any commercialization by us of our product candidates. We have product liability insurance covering our clinical trials in the amount of $11 million. Clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance or increase our existing coverage at a reasonable cost to protect us against losses that could have a material adverse effect on our business. An individual may bring a product liability claim against us if one of our products or product candidates causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any product liability claim brought against us, with or without merit, could result in:

- liabilities that substantially exceed our product liability insurance, which we would then be required to pay from other sources, if available;
- an increase of our product liability insurance rates or the inability to maintain insurance coverage in the future on acceptable terms, or at all;
- withdrawal of clinical trial volunteers or patients;
- damage to our reputation and the reputation of our products, resulting in lower sales;
- regulatory investigations that could require costly recalls or product modifications;
- litigation costs; and
- the diversion of management s attention from managing our business.

If our facility incurs damage or power is lost for a significant length of time, our business will suffer.

We currently store numerous clinical and stability samples at our facility that could be damaged if our facility incurred physical damage or in the event of an extended power failure. We have backup power systems in addition to backup generators to maintain power to all critical functions, but any loss of these samples could result in significant delays in our drug development process.

In addition, we currently store most of our preclinical and clinical data at our facility. Duplicate copies of most 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 we fail to retain our existing key personnel or fail to attract and retain additional key personnel, the development of our drug product 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.

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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, 2008, the 52-week range of the market price of our stock was from $2.40 to $8.33 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;

additional dilution through sales of our common stock or other derivative securities;

status of new or existing licensing or collaborative agreements and government contracts;

announcements relating to the status of our programs;

we or our partners achieving or failing to achieve development milestones;

publicity regarding actual or potential medical results relating to products under development by us or our competitors;

publicity regarding certain public health concerns for which we are or may be developing treatments;

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;

changes in the structure of healthcare payment systems, including developments in price control legislation;

announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;

additions or departures of key personnel or members of our board of directors;

purchases or sales of substantial amounts of our stock by existing stockholders, including officers or directors;

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 limited influence on stockholder decisions.

As of September 30, 2008, our directors, executive officers and our stockholders who hold 5% or greater of our outstanding common stock, beneficially owned a significant portion of our outstanding common stock and common stock equivalents. As a result, these holders will likely be able to significantly influence our operations and matters requiring stockholder approval, including the election of directors. The interests of these stockholders may be different from the interests of other stockholders and they could take actions that might not be considered by other stockholders to be in their best interests. 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 4,905,000 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 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 beneficially owned approximately 10.3% as of September 30, 2008, but owned more than 15% at the time the Rights were put in place) of our common stock on terms not approved by the board of directors. In August 2007, this plan was amended for a transaction involving funds managed by or affiliated with Baker Brother Investments such that they could purchase up to 25% without triggering the Rights. At September 30, 2008, such group beneficially owned approximately 18.8% of our stock.

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.

Public sales of our common stock could depress the market price of our stock and adversely affect the liquidity of the trading market for our stock.

As of September 30, 2008, we had approximately 38.2 million shares of common stock outstanding. The approximately 11.5 million shares of common stock, including shares of common stock issuable upon the exercise of outstanding warrants, that may be sold by the selling stockholders under our most recent resale registration statements on Form S-3 are freely tradable without restriction or further registration under the federal securities laws unless purchased by our affiliates. Additionally, at September 30, 2008, we had outstanding options to purchase

approximately 5.6 million shares of common stock. If these or other stockholders sell substantial amounts of our common stock in the public market, or if the market perceives that these sales may occur, the market price of our common stock might decline. We are unable to estimate the amount, timing or nature of future sales of outstanding common stock.

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The additional volume of shares available for trading could increase selling demand on our stock on the Nasdaq Global Market, and outstrip buying demand. This may make it difficult to sell substantial amounts of our stock without adversely impacting the stock price, and could depress the market price for our stock.

Exercise of outstanding options and warrants will dilute stockholders and could decrease the market price of our common stock.

As of September 30, 2008, we had issued and outstanding approximately 38.2 million shares of common stock, outstanding options to purchase approximately 5.6 million additional shares of common stock and warrants (exercisable at $10.25 per share) to purchase an additional 3,159,895 shares of our common stock. The existence of the outstanding options and warrants may adversely affect the market price of our common stock and the terms under which we could obtain additional equity capital.

INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the information we incorporate by reference, contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, referred to as the Exchange Act, which are subject to the safe harbor created in Section 21E. All statements other than statements of historical facts contained in this prospectus are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as may, could, will, should, expect, plan, anticipate, believe, estimate seek, potential or continue or 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. These forward-looking statements include, but are not limited to, statements about:

- the initiation, timing, progress and results of our preclinical testing, clinical trials, and other research and development efforts;
- the potential funding from our contract with HHS for the development of peramivir;
- the further preclinical or clinical development and commercialization of our product candidates, including peramivir, forodesine HCl and other PNP inhibitor and hepatitis C development programs;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- our ability to establish and maintain collaborations;
- plans, programs, progress and potential success of our collaborations, including Mundipharma for forodesine HCl and Shionogi and Green Cross for peramivir;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our ability to operate our business without infringing the intellectual property rights of others;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the timing or likelihood of regulatory filings and approvals;
- our financial performance; and

competitive companies, technologies and our industry.

These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Risk Factors and elsewhere in this prospectus. Any forward-looking statement in this prospectus reflects our current views with respect to future events and is subject to

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these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future growth. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

Discussions containing these forward-looking statements are also contained in 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, our Current Reports on Form 8-K, as well as any amendments we make to those filings with the SEC.

USE OF PROCEEDS

Except as otherwise described in the applicable prospectus supplement, the net proceeds we expect to receive from the sale of the securities 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;
- increased manufacturing of compounds for clinical trials, toxicology studies and validation of both the manufacturing and formulation processes;
- 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 invest the net proceeds of this offering in investment grade, interest-bearing securities.

DESCRIPTION OF COMMON STOCK, PREFERRED STOCK AND DEPOSITARY SHARES

The following summary description of our capital stock summarizes general terms and provisions that apply to the capital stock. Because this is only a summary, it does not contain all of the information that may be important to you. This summary is subject to and qualified in its entirety by reference to our restated certificate of incorporation, as amended, by-laws, as amended, and the rights agreement, as amended, each of which are on file with the SEC. See Where You Can Find More Information.

Authorized and Outstanding Capital Stock

Our authorized capital stock consists of 95,000,000 shares of common stock, par value $0.01 per share, and 5,000,000 shares of preferred stock, par value $0.01 per share, of which 95,000 shares are designated Series B Junior Participating Preferred Stock with a par value of $0.001 per share. On November 24, 2008, there were 38,257,681 shares of common stock outstanding and no shares of preferred stock outstanding.

Common Stock

Holders of our common stock are entitled to one vote per share on all matters submitted to a vote of stockholders and may not cumulate votes for the election of directors. Common stockholders have the right to receive dividends as and when declared by the Board of Directors from funds legally available therefor, subject to any preferential dividend rights of any preferred stock then outstanding. Upon our dissolution or liquidation, common stockholders are entitled to receive all assets legally available for distribution to

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stockholders, subject to any preferential rights of any preferred stock then outstanding. Holders of common stock have no preemptive rights and have no rights to convert their common stock into any other securities.

Preferred Stock

Preferred stock may be issued from time to time in one or more series, each such series to have such terms as determined by our Board of Directors. Our Board of Directors has the authority to determine and fix such voting powers, full or limited, or no voting powers, and such designations, preferences and relative participating, optional or other special rights, and qualifications, limitations or restrictions thereof, including without limitation dividend rights, conversion rights, redemption privileges and liquidation preferences, without further vote or action by our stockholders. We will distribute a prospectus supplement with regard to each particular series of preferred stock that will describe the terms and provisions of that series of preferred stock. The rights of the holders of any preferred stock that may be issued 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.

Preferred Stock Purchase Rights

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 beneficially owned approximately 10.3% as of September 30, 2008 but owned more than 15% at the time the Rights were put in place) of our common stock on terms not approved by the board of directors. In August 2007, this plan was amended for a transaction involving funds managed by or affiliated with Baker Brother Investments such that they could purchase up to 25% without triggering the Rights. On September 30, 2008, such group beneficially owned approximately 18.8% of our stock. The rights are not exercisable until the distribution date, as defined in the Rights Agreement, dated June 17, 2002, by and between the Company and American Stock Transfer & Trust Company, as Rights Agent, as amended. The Rights will expire at the close of business on June 24, 2012, unless that final expiration date is extended or unless the rights are earlier redeemed or exchanged by the Company.

Each Right entitles the registered holder to purchase from the Company one one-thousandth of a share of Series B Junior Participating Preferred Stock (Series B), par value $0.001 per share, at a purchase price of $26.00, subject to adjustment. Shares of Series B purchasable upon exercise of the Rights will not be redeemable. Each share of Series B will be entitled to a dividend of 1,000 times the dividend declared per share of common stock. In the event of liquidation, each share of Series B will be entitled to a payment of 1,000 times the payment made per share of common stock. Each share of Series B will have 1,000 votes, voting together with the common stock. Finally, in the event of any merger, consolidation, or other transaction in which shares of common stock are exchanged, each share of Series B will be entitled to receive 1,000 times the amount received per share of common stock.

Anti-Takeover Provisions

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.

Depositary Shares

We may, at our option, elect to offer fractional shares of preferred stock, rather than full shares of preferred stock. If we exercise this option, we will issue to the public receipts for depositary shares, and each

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of these depositary shares will represent a fraction, to be set forth in the applicable prospectus supplement, of a share of a particular series of preferred stock.

The shares of any series of preferred stock underlying the depositary shares will be deposited under a deposit agreement between us and a bank or trust company selected by us. The depositary will have its principal office in the United States and a combined capital and surplus of at least $50,000,000. Subject to the terms of the deposit agreement, each owner of a depositary share will be entitled, in proportion to the applicable fraction of a share of preferred stock underlying the depositary share, to all the rights and preferences of the preferred stock underlying that depositary share. Those rights may include dividend, voting, redemption, conversion and liquidation rights.

The depositary shares will be evidenced by depositary receipts issued under a deposit agreement. Depositary receipts will be distributed to those persons purchasing the fractional shares of preferred stock underlying the depositary shares, in accordance with the terms of the offering. The following description of the material terms of the deposit agreement, the depositary shares and the depositary receipts is only a summary and you should refer to the forms of the deposit agreement and depositary receipts that will be filed with the SEC in connection with the offering of the specific depositary shares.

Pending the preparation of definitive engraved depositary receipts, the depositary, upon our written order, may issue temporary depositary receipts substantially identical to the definitive depositary receipts but not in definitive form. These temporary depositary receipts would entitle their holders to all the rights of definitive depositary receipts. Temporary depositary receipts would be exchangeable for definitive depositary receipts at our expense.

Dividends and Other Distributions. The depositary will distribute all cash dividends or other cash distributions received with respect to the underlying stock to the record holders of depositary shares in proportion to the number of depositary shares owned by those holders.

If there were a distribution other than in cash, the depositary would distribute property received by it to the record holders of depositary shares that are entitled to receive the distribution, unless the depositary determines that it is not feasible to make the distribution. If this occurs, the depositary, with our approval, would sell the property and distribute the net proceeds from the sale to the applicable holders.

Withdrawal of Underlying Preferred Stock. Unless we provide otherwise in a prospectus supplement, holders may surrender depositary receipts at the principal office of the depositary and, upon payment of any unpaid amount due to the depositary, would be entitled to receive the number of whole shares of underlying preferred stock and all money and other property represented by the related depositary shares. We will not issue any partial shares of preferred stock. If the holder delivers depositary receipts evidencing a number of depositary shares that represent more than a whole number of shares of preferred stock, the depositary will issue a new depositary receipt evidencing the excess number of depositary shares to that holder.

Redemption of Depositary Shares. If a series of preferred stock represented by depositary shares were subject to redemption, the depositary shares would be redeemed from the proceeds received by the depositary resulting from the redemption, in whole or in part, of that series of underlying stock held by the depositary. The redemption price per depositary share would be equal to the applicable fraction of the redemption price per share payable with respect to that series of underlying stock. Whenever we redeem shares of underlying stock that are held by the depositary, the depositary will redeem, as of the same redemption date, the number of depositary shares representing the shares of underlying stock so redeemed. If fewer than all the depositary shares are to be redeemed, the depositary shares to be redeemed will be selected by lot or proportionately, as may be determined by the depositary.

Voting. Upon receipt of notice of any meeting at which the holders of the underlying stock are entitled to vote, the depositary will mail the information contained in the notice to the record holders of the depositary shares underlying the preferred stock. Each record holder of the depositary shares on the record date, which will be the same date as the record date for the underlying stock, will be entitled to instruct the depositary as to the exercise of the voting rights pertaining to the amount of the underlying stock represented by that holder s depositary shares. The depositary will then try, as far as practicable, to vote the number of shares of

preferred stock underlying those depositary shares in accordance with those instructions, and we will agree to take all actions which may be deemed necessary by the depositary to enable the depositary to do so. The depositary will not vote the underlying shares to the extent it does not receive specific instructions from the holders of depositary shares underlying the preferred stock.

Conversion of Preferred Stock. If the prospectus supplement relating to the depositary shares provides that the deposited preferred stock is convertible into or exchangeable for common stock or preferred stock of another series of BioCryst or securities of any third party, the following will apply. The depositary shares, as such, will not be convertible into or exchangeable for any securities of BioCryst or any third party. Rather, any holder of the depositary shares may surrender the related depositary receipts to the depositary with written instructions to instruct us to cause conversion or exchange of the preferred stock represented by the depositary shares into or for whole shares of common stock or shares of another series of preferred stock of BioCryst or securities of the relevant third party, as applicable. Upon receipt of those instructions and any amounts payable by the holder in connection with the conversion or exchange, we will cause the conversion or exchange using the same procedures as those provided for conversion or exchange of the deposited preferred stock. If only some of the depositary shares are to be converted or exchanged, a new depositary receipt or receipts will be issued for any depositary shares not to be converted or exchanged.

Amendment and Termination of the Depositary Agreement. The form of depositary receipt evidencing the depositary shares and any provision of the deposit agreement may be amended at any time by agreement between us and the depositary. However, any amendment which materially and adversely alters the rights of the holders of depositary shares will not be effective unless the amendment has been approved by the holders of at least a majority of the depositary shares then outstanding. The deposit agreement may be terminated by us or by the depositary only if (a) all outstanding depositary shares have been redeemed or converted or exchanged for any other securities into which the underlying preferred stock is convertible or exchangeable or (b) there has been a final distribution of the underlying stock in connection with our liquidation, dissolution or winding up and the underlying stock has been distributed to the holders of depositary receipts.

Charges of Depositary. We will pay all transfer and other taxes and governmental charges arising solely from the existence of the depositary arrangements. We will also pay charges of the depositary in connection with the initial deposit of the underlying stock and any redemption of the underlying stock. Holders of depositary receipts will pay other transfer and other taxes and governmental charges and those other charges, including a fee for any permitted withdrawal of shares of underlying stock upon surrender of depositary receipts, as are expressly provided in the deposit agreement to be for their accounts.

Reports. The depositary will forward to holders of depositary receipts all reports and communications from us that we deliver to the depositary and that we are required to furnish to the holders of the underlying stock.

Limitation on Liability. Neither we nor the depositary will be liable if either of us is prevented or delayed by law or any circumstance beyond our control in performing our respective obligations under the deposit agreement. Our obligations and those of the depositary will be limited to performance in good faith of our respective duties under the deposit agreement. Neither we nor the depositary will be obligated to prosecute or defend any legal proceeding in respect of any depositary shares or underlying stock unless satisfactory indemnity is furnished. We and the depositary may rely upon written advice of counsel or accountants, or upon information provided by persons presenting underlying stock for deposit, holders of depositary receipts or other persons believed to be competent and on documents believed to be genuine.

Resignation and Removal of Depositary. The depositary may resign at any time by delivering notice to us of its election to resign. We may remove the depositary at any time. Any resignation or removal will take effect upon the

appointment of a successor depositary and its acceptance of the appointment. The successor depositary must be appointed within 60 days after delivery of the notice of resignation or removal and must be a bank or trust company having its principal office in the United States and having a combined capital and surplus of at least $50,000,000.

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DESCRIPTION OF STOCK PURCHASE CONTRACTS

The following is a general description of the terms of the stock purchase contracts we may issue from time to time. Particular terms of any stock purchase contracts we offer will be described in the prospectus supplement relating to such stock purchase contracts. Material U.S. federal income tax considerations applicable to the stock purchase contracts will also be discussed in the applicable prospectus supplement. You should refer to the form of stock purchase contract and stock purchase certificate that we will file with the SEC in connection with the offering of the specific stock purchase contracts for more complete information.

We may issue stock purchase contracts, including contracts obligating holders to purchase from us, and obligating us to sell to holders, a specified number of shares of common stock, preferred stock or depositary shares at a future date. The consideration per share of common stock, preferred stock or depositary shares may be fixed at the time that the stock purchase contracts are issued or may be determined by reference to a specific formula set forth in the stock purchase contracts. Any stock purchase contract may include anti-dilution provisions to adjust the number of shares issuable pursuant to such stock purchase contract upon the occurrence of certain events.

The applicable prospectus supplement will describe the terms of any stock purchase contracts in respect of which this prospectus is being delivered, including, to the extent applicable, the following:

- whether the stock purchase contracts obligate the holder or us to purchase or sell, or both purchase and sell, the securities subject to purchase under the stock purchase contract, and the nature and amount of each of those securities, or the method of determining those amounts;
- whether the stock purchase contracts are to be prepaid or not;
- whether the stock purchase contracts will be issued as part of a unit and, if so, the other securities comprising the unit;
- whether the stock purchase contracts are to be settled by delivery, or by reference or linkage to the value, performance, or level of the securities subject to purchase under the stock purchase contract;
- any acceleration, cancellation, termination, or other provisions relating to the settlement of the stock purchase contracts; and
- whether the stock purchase contracts will be issued in full registered or global form.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase our preferred stock, depositary shares or common stock or any combination thereof. Warrants may be issued independently or together with any other securities in the form of units, and may be attached to, or separate from, such securities. The terms of any warrants to be issued and a description of the material provisions of the applicable warrant agreement will be set forth in the applicable prospectus supplement. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. You should refer to the form of warrant agreement and warrant that we file with the SEC in connection with the offering of the specific warrants for more complete information.

The prospectus supplement will describe the terms of any warrants being offered, including:

the title and the aggregate number of warrants;

the price or prices at which the warrants will be issued;

the currency or currencies in which the price of the warrants will be payable;

the securities or other rights, including rights to receive payment in cash or securities based on the value, rate or price of one or more specified commodities, currencies, securities or indices, or any combination of the foregoing, purchasable upon exercise of the warrants;

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the price at which, and the currency or currencies in which, the securities or other rights purchasable upon exercise of such warrants may be purchased;

the periods during which, and places at which, the warrants are exercisable;

the date or dates on which the warrants shall commence and the date or dates on which the warrants will expire;

the terms of any mandatory or optional call provisions;

the price or prices, if any, at which the warrants may be redeemed at the option of the holder or will be redeemed upon expiration;

whether the warrants will be sold separately or with other securities as part of a unit;

if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security;

if applicable, the date on and after which the warrants and the related securities will be separately transferable;

any provisions for the adjustment of the number or amount of securities receivable upon exercise of warrants;

the identity of the warrant agent;

the exchanges, if any, on which the warrants may be listed;

the maximum or minimum number of warrants which may be exercised at any time;

if applicable, a discussion of any material United States federal income tax considerations;

whether the warrants shall be issued in book-entry form; and

any other terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

DESCRIPTION OF UNITS

We may issue units consisting of one or more of the other securities described in this prospectus in any combination, as described in a prospectus supplement. We may issue units in one or more series, which will be described in a prospectus supplement. We will issue the units or hybrid securities under one or more unit agreements, each referred to as a unit agreement, to be entered into between us and a bank or trust company, as unit agent. You should refer to the form of unit agreement and unit certificate that we file with the SEC in connection with the offering of the specific units for more complete information.

The applicable prospectus supplement will describe:

the designation and the terms of the units and of the securities constituting the units, including whether and under what circumstances the securities comprising the units may be traded separately;

any additional terms of the governing unit agreement;

any additional provisions for the issuance, payment, settlement, transfer or exchange of the units or of the preferred stock, common stock, stock purchase contracts, depositary shares or warrants constituting the units; and

any applicable United States federal income tax consequences.

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PLAN OF DISTRIBUTION

We may sell the securities being offered hereby at prices and under terms then prevailing, at prices related to the then current market price or in negotiated transactions from time to time in one or more of the following ways:

- directly to one or more purchasers;
- through one or more underwriters on a firm commitment or best-efforts basis;
- through broker-dealers, who may act as agents or principals, including a block trade in which a broker or dealer so engaged will attempt to sell as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- through agents;
- through remarketing firms;
- in privately negotiated transactions; or
- in any combination of these methods of sale.

We will set forth in a prospectus supplement the terms of the offering of securities, including:

- the name or names of any underwriters, dealers or agents;
- the number of securities and purchase price of the securities being offered and the proceeds we will receive from the sale;
- any underwriting discounts and commissions or agency fees and other items constituting underwriters or agents compensation;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any delayed delivery arrangements;
- any discounts or concessions allowed or re-allowed or paid to dealers; and
- any securities exchange on which the securities may be listed.

The distribution of the securities may be effected from time to time in one or more transactions at a fixed price or prices, which may be changed, at market prices prevailing at the time of sale, at prices related to the prevailing market prices or at negotiated prices.

We may designate agents who agree to use their reasonable efforts to solicit purchases for the period of their appointment or to sell securities on a continuing basis. Agents may receive compensation in the form of commissions, discounts or concessions from us. Agents may also receive compensation from the purchasers of the securities for whom they sell as principals. Each particular agent will receive compensation in amounts negotiated in connection

with the sale, which might be in excess of customary commissions. Agents and any other participating broker-dealers may be deemed to be underwriters within the meaning of Section 2(11) of the Securities Act in connection with sales of the securities. Accordingly, any commission, discount or concession received by them and any profit on the resale of the securities purchased by them may be deemed to be underwriting discounts or commissions under the Securities Act. We have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of their securities. As of the date of this prospectus, there are no special selling arrangements between any broker-dealer or other person and us. No period of time has been fixed within which the securities will be offered or sold.

If required under applicable state securities laws, we will sell the securities only through registered or licensed brokers or dealers. In addition, in some states, we may not sell securities unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and complied with.

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If we use underwriters for a sale of securities, the underwriters will acquire the securities for their own account. The underwriters may resell the securities in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may change from time to time any initial public offering price and any discounts or concessions the underwriters allow or re-allow or pay to dealers. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement naming the underwriter the nature of any such relationship.

We may use a remarketing firm to offer to sell the securities in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own account or as agents for us. These remarketing firms will offer or sell the securities pursuant to the terms of the securities. A prospectus supplement will identify any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm s compensation. Remarketing firms may be deemed to be underwriters in connection with the securities they remarket.

If we offer and sell securities through a dealer, we or an underwriter will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale. Any such dealer may be deemed to be an underwriter of the securities so offered and sold. The name of the dealer and the terms of the transactions will be set forth in the applicable prospectus supplement.

We may also sell securities directly to one or more purchasers without using underwriters or agents. Underwriters, dealers and agents that participate in the distribution of the securities may be underwriters as defined in the Securities Act and any discounts or commissions they receive from us and any profit on their resale of the securities may be treated as underwriting discounts and commissions under the Securities Act.

We will identify in the applicable prospectus supplement any underwriters, dealers or agents and will describe their compensation. We may have agreements with the underwriters, dealers and agents to indemnify them against specified civil liabilities, including liabilities under the Securities Act. Underwriters, dealers and agents may engage in transactions with or perform services for us in the ordinary course of their businesses.

We may authorize agents, dealers or underwriters to solicit offers to purchase securities at the public offering price under delayed delivery contracts. The terms of these delayed delivery contracts, including when payment for and delivery of the securities sold will be made under the contracts and any conditions to each party s performance set forth in the contracts, will be described in the applicable prospectus supplement. The compensation received by underwriters, agents or dealers soliciting purchases of securities under delayed delivery contracts will be described in the applicable prospectus supplement.

We may enter into derivative or other hedging transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. We may also loan or pledge securities covered by this prospectus and the applicable prospectus supplement to third parties, who may sell the loaned securities or, in an event of default in the case of a pledge, sell the pledged securities pursuant to this prospectus and the applicable prospectus supplement.

Unless otherwise specified in the related prospectus supplement, all securities we offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We

may apply to list any series of securities on an exchange, but we are not obligated to do so. Therefore, no assurance can be given as to the liquidity of, or the trading market for, any series of securities.

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Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. These transactions may be effected on The Nasdaq Global Market or otherwise.

Any underwriters who are qualified market makers on The Nasdaq Global Market may engage in passive market making transactions in the common stock on The Nasdaq Global Market in accordance with Rule 103 of Regulation M, during the business day before the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker s bid, however, the passive market maker s bid must then be lowered when certain purchase limits are exceeded.

We will bear all costs, expenses and fees in connection with the registration of the securities, as well as the expense of all commissions and discounts, if any, attributable to sales of the securities by us.

LEGAL MATTERS

Certain legal matters will be passed upon for us by Gibson, Dunn & Crutcher LLP. Any agents or underwriters will be represented by their own legal counsel named in the applicable prospectus supplement.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2007, and the effectiveness of our internal control over financial reporting as of December 31, 2007, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the 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.

WHERE YOU CAN FIND MORE INFORMATION

We file electronically with the Securities and Exchange Commission our annual reports on Form 10-K, quarterly interim reports on Form 10-Q, current reports on Form 8-K, proxy statements and other information. We make available on or through our website, http://www.biocryst.com, free of charge, copies of these filings as soon as reasonably practicable after we electronically file them with or furnish them to the SEC. The information on our website is not incorporated by reference into this prospectus. You can also request copies of such documents by contacting our Investor Relations Department at 2190 Parkway Lake Drive, Birmingham, Alabama 35244 or sending an email to info@biocryst.com. You may read and copy any document we file at the SEC s Public Reference Room at 450 Fifth Street, N.W., Washington, D.C. 20549. You can also obtain copies of this information by mail from the Public Reference Room of the SEC at prescribed rates. You may obtain information on the operation of the Public Reference Room by calling the SEC at (800) SEC-0330.

The SEC also maintains an Internet world wide web site that contains reports, proxy statements and other information about issuers, like BioCryst, that file electronically with the SEC. The address of that site is http://www.sec.gov. Unless specifically listed below under Incorporation of Certain Documents by Reference the information contained on the SEC website is not incorporated by reference into this prospectus.

We have filed with the SEC a registration statement on Form S-3 that registers the securities we are offering. The registration statement, including the attached exhibits and schedules, contains additional relevant

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information about us and our securities. The rules and regulations of the SEC allow us to omit certain information included in the registration statement from this prospectus.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference information into this prospectus. This means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus, except for any information that is superseded by information that is included directly in this document.

This prospectus includes by reference the documents listed below that we have previously filed with the SEC and that are not included in or delivered with this document. They contain important information about us and our financial condition.

- Our Annual Report on Form 10-K for the year ended December 31, 2007, filed with the SEC on March 4, 2008;

- Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2008 (filed with the SEC on May 9, 2008), June 30, 2008 (filed with the SEC on August 8, 2008) and September 30, 2008 (filed with the SEC on October 31, 2008);

- Our Current Reports on Form 8-K filed with the SEC on January 10, 2008, May 8, 2008, May 21, 2008, May 28, 2008, June 18, 2008, July 10, 2008, July 28, 2008, October 24, 2008, November 4, 2008, November 10, 2008 and December 29, 2008;

- The description of our common stock which is contained in our Registration Statement on Form 8-A (File No. 000-23186) filed with the SEC on January 8, 1994, including any amendment or reports filed for the purpose of updating such description; and

- The description of our preferred share purchase rights which is contained in our Registration Statement on Form 8-A (File No. 000-23186) filed with the SEC on June 17, 2002, including any amendment or reports filed for the purpose of updating such description.

All documents filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and prior to the termination of this offering shall be deemed to be incorporated by reference herein and to be a part of this prospectus from the date of filing of such documents, excluding any information furnished under Item 2.02 or Item 7.01 of any Current Report on Form 8-K and exhibits filed on such form that are related to such items. Any statement contained in a document incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

You can obtain any of the documents incorporated by reference in this prospectus from us without charge, excluding any exhibits to those documents unless the exhibit is specifically incorporated by reference as an exhibit to this prospectus. You can obtain documents incorporated by reference in this prospectus at no cost by requesting them in writing or by telephone from us at the following address:

Investor Relations
BioCryst Pharmaceuticals, Inc.
2190 Parkway Lake Drive
Birmingham, Alabama 35244
(205) 444-4600

We have not authorized anyone to give any information or make any representation about us that is different from, or in addition to, that contained in this prospectus or in any of the materials that we have incorporated by reference into this document. Therefore, if anyone does give you information of this sort, you should not rely on it. If you are in a jurisdiction where offers to sell, or solicitations of offers to purchase, the securities offered by this document are unlawful, or if you are a person to whom it is unlawful to direct these types of activities, then the offer presented in this document does not extend to you.

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