

BIOCRYST PHARMACEUTICALS INC

Form S-3/A

January 23, 2009

**Table of Contents**

**As filed with the United States Securities and Exchange Commission on January 23, 2009**

Registration No. 333-153084

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549  
Amendment No. 1  
to  
FORM S-3  
REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933  
BioCryst Pharmaceuticals, Inc.  
(Exact name of registrant as specified in its charter)**

**Delaware**

*(State or other jurisdiction of incorporation or organization)*

**62-1413174**

*(I.R.S. Employer Identification Number)*

**2190 Parkway Lake Drive  
Birmingham, Alabama 35244  
(205) 444-4600**

*(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)*

**Jon P. Stonehouse  
President and Chief Executive Officer**

**2190 Parkway Lake Drive  
Birmingham, Alabama 35244  
(205) 444-4600**

*(Name, address, including zip code and telephone number, including area code, of agent for service)*

*With a copy to:*

**Brian Lane, Esq.  
Gibson, Dunn & Crutcher LLP  
1050 Connecticut Avenue, NW  
Washington, DC 20036  
(202) 955-8500**

**Approximate date of commencement of proposed sale to the public:** From time to time after the effective date of this Registration Statement, as determined by market conditions.

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

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

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

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

If this Form is a registration statement pursuant to General Instruction I.D. or a post effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer  Accelerated filer  Non-accelerated filer  Smaller Reporting Company   
(Do not check if a smaller reporting company)

**The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with section 8(a) of the Securities Act of 1933, as amended, or until this Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.**

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**Table of Contents**

**SUBJECT TO COMPLETION, DATED JANUARY 23, 2009**

**The information in this prospectus is not complete and may be changed. The selling stockholders may not sell these securities until the Registration Statement filed with the Securities and Exchange Commission becomes effective. This prospectus is not an offer to sell these securities and it is not soliciting offers to buy these securities in any state where the offer or sale is not permitted.**

**PROSPECTUS**

**3,335,408 Shares of Common Stock**

**3,159,895 Warrants to Purchase Common Stock**

This prospectus relates to the disposition from time to time of up to (i) 3,335,408 shares of our outstanding common stock in the aggregate, 175,513 of which are owned by the selling stockholders named on page 22 of this prospectus on the date hereof, and 3,159,895 of which are issuable upon exercise of warrants to purchase shares of our common stock (the warrants) owned by the selling stockholders on the date hereof, (ii) the disposition from time to time of up to 3,159,895 warrants owned by the selling stockholders on the date hereof, and (iii) the initial issuance of shares of our common stock upon the exercise of the warrants acquired from the selling stockholders pursuant to this prospectus.

We will not be paying any underwriting discounts or commissions in this offering. All of our securities offered hereby are being sold by the selling stockholders named in this prospectus. We will not receive any proceeds from sale of the securities included in this prospectus. To the extent that any of the warrants to purchase common stock are exercised, we will receive the exercise price paid for the shares of common stock purchased thereunder. The exercise price of the warrants is \$10.25 per share.

Our common stock, par value \$0.01 per share, trades on the Nasdaq Global Market under the symbol BCRX. On January 21, 2009, the reported last sale price of our common stock on the Nasdaq Global Market was \$2.09 per share.

The selling stockholders or their pledges, assignees or successors-in-interest may offer and sell or otherwise dispose of the shares of common stock and warrants described in this prospectus from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices. See Plan of Distribution beginning on page 24 for more information about how the selling stockholders may sell or dispose of their shares of common stock and warrants.

The selling stockholders may resell the common stock and warrants to or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions. The selling stockholders will bear all commissions and discounts, if any, attributable to the sales of shares. We will bear all costs, expenses and fees in connection with the registration of the shares.

**Investing in these securities involves a high degree of risk. See Risk Factors beginning on page 6 of this prospectus.**

**Neither the Securities and Exchange Commission nor any state securities regulators have 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 \_\_\_\_\_, 2009.

**TABLE OF CONTENTS**

	Page
<u>ABOUT THIS PROSPECTUS</u>	i
<u>PROSPECTUS SUMMARY</u>	1
<u>RISK FACTORS</u>	6
<u>INFORMATION REGARDING FORWARD-LOOKING STATEMENTS</u>	18
<u>USE OF PROCEEDS</u>	19
<u>DESCRIPTION OF SECURITIES</u>	20
<u>SELLING STOCKHOLDERS</u>	22
<u>PLAN OF DISTRIBUTION</u>	24
<u>LEGAL MATTERS</u>	26
<u>EXPERTS</u>	26
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	27
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	27
<u>EX-23.1</u>	

**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 shelf process, certain selling stockholders may from time to time sell the shares of common stock and warrants described in this prospectus in one or more offerings.

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. Reference to selling stockholders refers to those stockholders listed herein under Selling Stockholders beginning on page 22 of this prospectus, who may sell shares from time to time as described in this prospectus. All trade names used in this prospectus are either our registered trademarks or trademarks of their respective holders.

**You should rely only on the information contained or incorporated by reference into this prospectus or any applicable prospectus supplement. We have not, and the selling stockholders have not, authorized anyone to provide you with different information. The selling stockholders are offering to sell, and seeking offers to buy, shares of our common stock and warrants only in jurisdictions where it is lawful to do so. The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock or warrants.**

**Table of Contents**

**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.

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

**Table of Contents**

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. 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.

**Table of Contents**

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.

***Summary of 2007 Private Placement***

On August 9, 2007, we sold to a group of existing stockholders in a private placement:

8,315,513 shares of the Company's common stock at a purchase price of \$7.80 per share, the closing Nasdaq composite bid price on August 3, 2007, the last trading date prior to the agreement reached prior to the opening of trading on August 6, 2007; and

warrants (exercisable at \$10.25 per share) to purchase 3,159,895 shares of the Company's common stock, for a purchase price of \$0.125 per warrant share.

The aggregate purchase price was approximately \$65.3 million. The investors included funds managed by Baker Brothers Investments, Kleiner Perkins Caufield & Byers, EHS Holdings, OrbiMed Advisors, TPG Biotechnology, and Stephens Investment Management, all of whom are current stockholders.

We relied upon the exemptions from registration provided by Section 4(2) of the Securities Act and Regulation D promulgated under that section. Each investor represented that it was an accredited investor, as such term is defined in Regulation D under the Securities Act, and that it was acquiring the common stock and warrants for its own account and not with a view to or for sale in connection with any distribution thereof, and appropriate legends are affixed to the common stock and warrants.

We have filed with the SEC all of our agreements regarding the private placement with the selling stockholders, with our Current Report on Form 8-K filed August 7, 2007 and our Quarterly Report on Form 10-Q filed August 9, 2007. We made no other agreements, plans or arrangements with the selling stockholders in connection with the private placement.

We paid no investment banking fees or commissions in connection with the private placement. We estimate the aggregate market value of our common stock held by non-affiliates (based upon the Nasdaq Global Market closing sales price on August 15, 2008) was approximately \$61.3 million.

The shares and warrants included in the private placement were not registered under the Securities Act of 1933, as amended. Under the purchase agreement for the private placement, we agreed to register for resale under the Securities Act the shares, the warrants and the shares issuable upon exercise of the warrants sold to the selling stockholders. If registration statements covering such shares, warrants and shares issuable upon exercise of the warrants are not filed by us or declared effective by the SEC within the periods specified in the purchase agreement, or if effectiveness of a registration statement is suspended for longer than the periods specified in the purchase agreement, we must pay to each investor, as liquidated damages and not as a penalty, a cash payment equal to 1.5% of the aggregate purchase price per month, up to a maximum of 12%, paid by such investor to us with respect to the shares then held by such selling stockholder which are not then registered under an effective registration statement, until such event has been cured. No such amounts shall be payable by us in respect of the warrants or the shares issuable upon exercise of the warrants. We have agreed to maintain the effectiveness of the registration statements covering such securities for each selling stockholder until the earlier of August 9, 2009, the date all of such shares, including shares underlying the warrants, may be sold by the selling stockholder without restriction by the volume limitations of Rule 144(e) of the Securities Act or the date all of such shares have been sold pursuant to the registration statement.

On August 22, 2007, we filed a registration statement covering the resale of 8,140,000 shares of common stock as required by the purchase agreement, which was declared effective on August 30, 2007.



**Table of Contents**

This registration statement covers the resale by the selling stockholders of the balance of 175,513 shares of common stock purchased, the warrants to buy approximately 3,159,895 shares of common stock, and the 3,159,895 shares to be issued upon exercise of the warrants. We will not receive any proceeds from the resale of the common stock or warrants by the investors.

The private placement:

increases our concentration of stock ownership, which could limit the influence of other stockholders and delay, defer or prevent a change in our control;

upon registration of the shares covered by this prospectus, increases the number of shares of our common stock eligible for sale, which could depress our stock price and adversely affect the trading market for our stock; and

exercise of the warrants above their exercise price of \$10.25 will result in dilution to our other stockholders and more shares eligible for sale, which could depress our stock price.

Please review the risk factors under the heading **Risks Relating to Our Common Stock** for more information on these risks.

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.

**Table of Contents**

**The Offering**

Issuer	BioCryst Pharmaceuticals, Inc.
Selling Stockholders	The selling stockholders identified in the table on page 22. They purchased our common stock and warrants in August 2007.
Securities Offered	up to 3,335,408 shares of our common stock, including 3,159,895 shares issuable upon exercise of the warrants;  up to 3,159,895 warrants to purchase our common stock; and  the initial issuance of shares of our common stock upon the exercise of the warrants acquired from the selling stockholders pursuant to this prospectus.
Use of Proceeds	We will not receive any proceeds from sales of the shares of common stock sold from time to time under this prospectus by the selling stockholders. We will not receive any proceeds from the resale of the warrants, including the sale of the shares of common stock issuable upon exercise of the warrants. To the extent that any of the warrants to purchase common stock are exercised, we will receive the exercise price paid for the shares of common stock purchased thereunder.
Risk Factors	An investment in our common stock involves a high degree of risk. See Risk Factors beginning on page 6 for a discussion of certain factors that you should consider when evaluating an investment in our common stock.
Nasdaq Global Market Symbol	BCRX

**Table of Contents**

**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. 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;

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

**Table of Contents**

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 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.



**Table of Contents**

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, 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;

8

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**Table of Contents**

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 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;

**Table of Contents**

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 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;

**Table of Contents**

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;

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.



## **Table of Contents**

These contract manufacturers may not be able to manufacture the materials required for 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 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

**Table of Contents**

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, 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

13

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**Table of Contents**

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.

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