

BIOCRYST PHARMACEUTICALS INC

Form 424B5

May 27, 2014

Table of Contents

Filed Pursuant to Rule 424(b)(5)

Registration No. 333-192117

The information in this preliminary prospectus supplement and accompanying prospectus 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.

Subject to completion, dated May 27, 2014

Prospectus supplement

(To prospectus dated November 15, 2013)

\$100,000,000

Common stock

BioCryst Pharmaceuticals, Inc. is offering \$100,000,000 of shares of its common stock.

Our common stock is listed on the Nasdaq Global Select Market under the symbol BCRX. On May 23, 2014, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$9.01 per share.

	Per share	Total
Public offering price	\$	\$
Underwriting discounts and commissions	\$	\$
Proceeds to BioCryst, before expenses	\$	\$

We have granted the underwriters an option for a period of 30 days to purchase up to \$15,000,000 of additional shares of our common stock at the public offering price less the underwriting discounts and commissions.

Investing in our common stock involves risks. See Risk Factors on page S-5 of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of the factors you should carefully consider before deciding to purchase shares of our common stock.

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

The underwriters expect to deliver the shares on or about June , 2014.

Sole book-running manager

J.P. Morgan

Sole lead manager

Piper Jaffray

, 2014

Table of Contents

Table of contents

Prospectus Supplement	Page
<u>About this prospectus supplement</u>	S-ii
<u>Forward-looking statements</u>	S-iii
<u>Prospectus supplement summary</u>	S-1
<u>Risk factors</u>	S-5
<u>Use of proceeds</u>	S-23
<u>Dilution</u>	S-24
<u>Price range of common stock and dividend policy</u>	S-26
<u>Description of capital stock</u>	S-27
<u>Underwriting</u>	S-28
<u>Legal matters</u>	S-32
<u>Experts</u>	S-32
<u>Where you can find more information</u>	S-33
<u>Incorporation of certain documents by reference</u>	S-33

Prospectus	Page
<u>About this prospectus</u>	i
<u>Prospectus summary</u>	1
<u>Risk factors</u>	2
<u>Information regarding forward-looking statements</u>	3
<u>Use of proceeds</u>	5
<u>Description of common stock, preferred stock and depositary shares</u>	6
<u>Description of stock purchase contracts</u>	9
<u>Description of warrants</u>	10
<u>Description of units</u>	11
<u>Plan of distribution</u>	12
<u>Legal matters</u>	15
<u>Experts</u>	15
<u>Where you can find more information</u>	16
<u>Incorporation of certain documents by reference</u>	16

Table of Contents

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, dated November 15, 2013, 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 **BioCryst**, the **Company**, **we**, **us** and **our** refer to **BioCryst Pharmaceuticals, Inc.** together with its consolidated subsidiaries.

Table of Contents

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 (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. These forward-looking statements can generally be identified by the use of words such as may, will, intends, plans, believes, anticipates, expects, estimates, predicts, 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 contracts with the Biomedical Advanced Research and Development Authority within the United States Department of Health and Human Services (BARDA/HHS) for the development and support of the New Drug Application (NDA) filing for peramivir and the potential funding from our contract with the National Institute of Allergy and Infectious Diseases (NIAID/HHS) for the development of BCX4430;

the U.S. Food and Drug Administration (FDA) approval of peramivir;

peramivir approval and/or supply, which could be limited or delayed due to regulatory issues at our manufacturer;

the potential for a stockpiling order or profit from any order of peramivir;

the potential use of peramivir as a treatment for H1N1, H5N1 and H7N9 or other strains of influenza;

the further preclinical or clinical development and commercialization of our product candidates, including our oral hereditary angioedema (HAE) kallikrein inhibitors, as well as peramivir, BCX4430 and small molecule drug discovery programs;

the implementation of our business model, strategic plans for our business, product candidates and technology;

our ability to establish and maintain collaborations or licenses related to our drug candidates;

plans, programs, progress and potential success of our collaborations, including Mundipharma International Holdings Limited (Mundipharma) for forodesine and Shionogi & Co., Ltd. (Shionogi) and Green Cross Corporation (Green Cross) for peramivir in their territories;

the ability of our wholly-owned subsidiary, JPR Royalty Sub LLC (Royalty Sub), which was formed in connection with our \$30.0 million financing transaction completed on March 9, 2011, to service its payment obligations in respect of its Pharma Senior Secured 14.0% Notes due 2020 (the Pharma Notes) issued in that financing transaction, and our ability to benefit from our equity interest in Royalty Sub;

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the foreign currency hedge agreement entered into by us in connection with the issuance by Royalty Sub of the PhaRMA Notes;

the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;

S-iii

Table of Contents

our ability to operate our business without infringing the intellectual property rights of others;

estimates of our expenses, revenues, capital requirements and our needs for additional financing, including our financial outlook for the remainder of 2014;

the timing or likelihood of regulatory filings and approvals;

our ability to raise additional capital to fund our operations;

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 Securities and Exchange Commission (the **SEC**).

Table of Contents

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-5 and the consolidated 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 the pathogenesis of diseases. We focus on rare and infectious diseases in which unmet medical needs exist and that are aligned with our capabilities and expertise. 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-guided drug design.

Drugs and drug candidates

Set forth below is a description of our main drugs and drug candidates in development.

Rare disease programs

BCX4161 for hereditary angioedema (HAE)

BCX4161 is positioned to be the first targeted oral prophylactic drug for the treatment of HAE attacks. BCX4161 is a novel, selective inhibitor of plasma kallikrein in development as an orally administered treatment for the prevention of attacks in patients with HAE. By inhibiting plasma kallikrein, BCX4161 suppresses bradykinin production. Bradykinin is the mediator of acute swelling attacks in HAE patients. HAE is a rare, severely debilitating and potentially fatal genetic condition that occurs in about 1 in 10,000 to 1 in 50,000 people. HAE symptoms include recurrent episodes of edema in various locations, including the hands, feet, face, genitalia, intestine and airway. Airway swelling is particularly dangerous and can lead to death by asphyxiation. In addition, patients often have bouts of excruciating abdominal pain, nausea and vomiting that are caused by swelling in the intestinal wall.

In November 2013, we enrolled the first patient in a proof of concept Phase 2a clinical trial in patients with HAE (which we refer to as OPuS-1). This clinical trial evaluated 400 mg of BCX4161 administered three times a day for 28 days in a randomized, placebo-controlled, two-period cross-over design. This trial was designed to provide proof of concept for oral kallikrein inhibition as a treatment strategy for HAE. Twenty-four HAE patients who have a high frequency of attacks (more than one per week) were enrolled. The primary goals for the trial were to estimate the degree efficacy of BCX4161 in reducing the frequency of angioedema attacks, and to evaluate the safety and tolerability of 28 days of BCX4161 treatment.

On May 27, 2014, we announced that the OPuS-1 trial met its primary efficacy endpoint, several secondary endpoints and all other objectives established for the trial. Each of the twenty-four patients dosed in the study completed the trial. The primary efficacy endpoint for the trial was the by-subject difference in mean angioedema attack rate on BCX4161 compared to placebo. Treatment with BCX4161 demonstrated a statistically significant mean attack rate reduction of 0.45 attacks per week versus placebo, $p < 0.001$. The mean attack rate per week was 0.82 on BCX4161 treatment, compared to 1.27 on placebo.

Table of Contents

Oral administration of BCX4161 was generally safe and well tolerated, with an adverse event profile similar to that observed for placebo. There was one serious adverse event reported, an abdominal HAE attack during the placebo period. Patient dosing compliance was 98 percent. The mean number of attack-free days during each 28-day treatment period improved from 19 for placebo to 22 for BCX4161, $p=0.008$. Three subjects were attack-free during the BCX4161 period, compared to none during the placebo period. In OPuS-1, higher drug exposure was associated with a better clinical outcome. Quality of life was measured by the Angioedema Quality of Life questionnaire, AeQoL. For BCX4161, the mean total AeQoL score improved by 8.4 units from baseline compared to 0.5 for placebo, $p=0.004$.

We plan to start OPuS-2, a 12-week trial of BCX4161 in HAE patients, during 2014 and expect to announce data from this trial in the second half of 2015.

Second generation HAE compounds

In December 2013, we announced the selection of two optimized plasma kallikrein inhibitors to advance into preclinical development as potential once-daily, oral treatments for the prevention of HAE attacks. The second generation discovery program's goals of improving bioavailability and selectivity while maintaining potency compared to BCX4161 were all met. Nonclinical pharmacokinetics of these drug candidates continues to support the opportunity for once-daily dosing for the prevention of HAE attacks. Nonclinical development including pharmacology and IND-enabling toxicology studies continues to progress as planned, with the goal of starting phase 1 clinical studies in the first half of 2015, announcing data from these studies and initiating a 12-week trial of one such compound in the second half of 2015.

Small molecule discovery program for rare diseases

In 2014, our research team started small molecule drug discovery programs addressing two rare-disease targets. These programs are intended to refill our clinical development pipeline in the timeframe our second generation HAE compounds reach the commercialization stage.

Infectious disease programs

Peramivir for influenza

Peramivir is a neuraminidase inhibitor for the treatment of patients with influenza. Influenza is a seasonal virus with highest infection rates generally observed in colder months. Intravenous (i.v.) peramivir has been approved in Japan and Korea for the treatment of patients with influenza. In these countries and in the United States, influenza occurs primarily during the September to April timeframe. Peramivir has been developed under a \$234.8 million contract with BARDA/HHS.

In December 2013, we submitted a NDA filing for peramivir to the FDA seeking an indication as the first i.v. neuraminidase inhibitor approved in the United States for the treatment of acute uncomplicated influenza in adults. The NDA submission includes results in over 2,700 subjects treated with peramivir in 27 clinical trials. On February 24, 2014, the FDA notified us that our NDA filing was accepted for review. The FDA is expected to take action on our application by December 23, 2014. The BARDA/HHS contract funding peramivir development expires on May 31, 2014, as substantially all work under the contract has been completed in association with the regulatory filing of the NDA.

Following the issuance of a Warning Letter, and a recent re-inspection by the FDA, our contract manufacturer for peramivir drug product received a Form 483, which contained a number of observations that need to be addressed. It is unclear how these findings may impact the peramivir NDA or supply of peramivir drug product. BioCryst and the contract manufacturer are working with the FDA to meet the requirements for approval of the peramivir NDA.

Table of Contents

BCX4430 broad spectrum anti-viral

In September 2013, NIAID/HHS contracted with us for the development of BCX4430 as a treatment for Marburg virus disease. NIAID/HHS, part of the National Institutes of Health, awarded us a contract for up to \$22.0 million, if all contract options are exercised. The goals of this contract are to file Investigational New Drug (IND) applications for intravenous and intramuscular administration of BCX4430 for the treatment of Marburg virus disease and to conduct an initial Phase 1 human clinical trial, which we currently expect to occur in the first half of 2015. As of March 31, 2014, a total of \$7.5 million of contract options has been awarded under this contract.

In March 2014, we announced the publication in the online version of the journal *Nature* of compelling BCX4430 efficacy results in animal models of infection with Marburg virus and Ebola virus, two highly virulent pathogens responsible for viral hemorrhagic fever diseases. The *Nature* publication, *Protection against filovirus diseases by a novel broad-spectrum nucleoside analog BCX4430*, represents the first report of protection of non-human primates from filovirus disease by a small molecule drug.

Financial outlook for 2014

Based upon the successful outcome of our OPuS-1 clinical trial, we plan to accelerate the development of BCX4161 and our second generation HAE compounds, and as a result we expect our total 2014 operating expenses to be in the upper half of the previously announced range of \$48 to \$59 million. Our operating expense range excludes equity-based compensation expense due to the difficulty in projecting this expense, as it is impacted by the volatility and price of our common stock, as well as by the vesting of our outstanding performance-based stock options. Our ability to remain within our operating expense target ranges is subject to multiple factors, including unanticipated or additional general development and administrative costs and other factors described under the Risk Factors section located elsewhere in this prospectus supplement and in the documents incorporated herein by reference.

In addition, the successful results achieved in our OPuS-1 clinical trial satisfy a vesting criterion associated with previously issued performance-based stock options. In association with this vesting, the Company will incur approximately \$2.2 million of non-cash stock compensation expense.

With the funds available at March 31, 2014, together with the net proceeds of this offering and future amounts that are expected to be received under our contracts with BARDA/HHS and NIAID/HHS, we currently believe we will have sufficient resources to fund our operations beyond 2015. However, this is a forward-looking statement and there may be changes that would consume available resources significantly before such time. See Forward-Looking Statements in this prospectus supplement.

We are a Delaware corporation originally founded in 1986. Our principal executive offices are located at 4505 Emperor Blvd., Suite 200, Durham, North Carolina 27703, and our telephone number is (919) 859-1302. Our website is located at <http://www.biocryst.com>. The information on our website is not incorporated by reference into this prospectus supplement or the accompanying prospectus.

Table of Contents

The offering

Common stock offered \$100,000,000 of shares of common stock

Common stock to be outstanding after the offering 71,173,616 shares

Option to purchase additional shares Up to \$15,000,000 of shares of common stock

Use of proceeds We intend to use the net proceeds of this offering for general corporate purposes, including funding clinical development of BCX4161, the continued development of both second generation HAE compounds, commercialization activities relating to peramivir and the advancement of other preclinical rare disease programs. See Use of Proceeds.

Nasdaq global select market symbol BCRX

Risk factors See Risk Factors beginning on page S-5 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 60,074,837 shares outstanding as of May 19, 2014 and assumes the sale of \$100,000,000 of shares of common stock at \$9.01 per share, the last reported sale price of our common stock on the NASDAQ Global Select Market on May 23, 2014. A 5% increase or decrease in the assumed public offering price of \$9.01 per share would increase or decrease the number of shares of our common stock issued in this offering by approximately 5%.

The number of shares of our common stock to be outstanding after this offering set forth above excludes:

8,519,807 shares of common stock issuable upon the exercise of stock options outstanding under our stock incentive plan as of May 19, 2014, at a weighted average exercise price of \$5.24 per share; and

4,710,478 additional shares of common stock reserved for issuance under our stock incentive plan and 559,176 additional shares of common stock reserved for issuance under our employee stock purchase plan as of May 19, 2014.

Except as otherwise noted, all information in this prospectus supplement assumes the underwriters do not exercise their option to purchase additional shares.

Table of Contents

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.

Risks relating to our business

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

Since our inception, we have not achieved profitability. We expect to incur additional losses for the foreseeable future, and our losses could increase as our research and development efforts progress. We expect that such losses will fluctuate from quarter to quarter and losses and fluctuations may be substantial.

To become profitable, we, or our collaborative partners, must successfully manufacture and develop product candidates, receive regulatory approval, and successfully commercialize and/or enter into profitable agreements with other parties. It could be several years, if ever, before we receive significant 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 clinical 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. Regulatory authorities may interrupt, delay or halt clinical trials for a product candidate for any number of reasons.

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;

Table of Contents

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.

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 we 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. Lack of adequate drug supply or delays in patient enrollment, including in our planned clinical trials for HAE, 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, including with respect to our NDA filing for peramivir.

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 and efficacy in the patients being treated by achieving pre-determined safety and efficacy endpoints according to the trial protocols. Failure to achieve either of these in any of our programs, including BCX4161, could result in delays in our trials or 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 or the termination of programs.

If we fail to reach milestones or to make annual minimum payments or otherwise breach our obligations under our license agreements, our licensors may terminate our agreements with them and seek additional remedies.

If we are unable or fail to meet payment obligations, performance milestones relating to the timing of regulatory filings, or development and commercial diligence obligations, are unable or fail to make milestone payments or material data use payments in accordance with applicable provisions, or fail to pay the minimum annual payments under our respective licenses, our licensors may terminate the applicable license or seek other available remedies. As a result, our development of the respective product candidate or commercialization of the product would cease.

If we fail to obtain additional financing or acceptable partnership arrangements, we may be unable to complete the development and commercialization of our product candidates or continue operations.

As our programs advance, our costs are likely to 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 cash utilization 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 BARDA/HHS for peramivir, NIAID/HHS or other government agencies for BCX4430 or from other new partnerships with third parties for the development of our product candidates, including ulodesine or BCX4161; the amount or profitability of any orders for peramivir or BCX4430 by any government agency or other party; the progress and results of our current and proposed clinical trials for our most advanced drug product candidates, including BCX4161; 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 enter into one or more acceptable partnership arrangements in order to complete the development of ulodesine for the treatment of gout.

Table of Contents

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. 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 BARDA/HHS or NIAID/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 or lack of an acceptable partnership may require us to delay, scale-back or eliminate certain of our research and development programs.

In order to continue future operations and continue our drug development programs, we will be required to raise additional capital. In addition to seeking strategic partnerships, transactions and government funding, we may decide to access the equity or debt markets or seek other sources to meet liquidity needs. Our ability to raise additional capital may be limited and may greatly depend upon the success of ongoing development related to our current drug development programs, including the NDA filing for peramivir, the Phase 2a clinical trial of BCX4161, progress of our second generation HAE compounds, and funding for and continued successful development of BCX4430. In addition, constriction and volatility in the equity and debt markets may restrict our future flexibility to raise capital when such needs arise. Furthermore, we have exposure to many different industries, financing partners and counterparties, including commercial banks, investment banks and partners (which include investors, licensing partners, and the U.S. Government) which may be unstable or may become unstable in the current economic and political environment. Any such instability may impact these parties' ability to fulfill contractual obligations to us or they might limit or place burdensome conditions upon future transactions with us. Also, it is possible that suppliers may be negatively impacted. Any such unfavorable outcomes in our current programs or unfavorable economic conditions could place severe downward pressure on the stock and credit markets, which could reduce the return available on invested corporate cash, which if severe and sustained could have a material and adverse impact on our results of operations and cash flows and limit our ability to continue development of our product candidates.

If BARDA/HHS and NIAID/HHS were to eliminate, reduce or delay funding from our contracts, this would have a significant negative impact on our revenues and cash flows.

Our projections of revenues and incoming cash flows are substantially dependent upon BARDA/HHS and NIAID/HHS reimbursement for the costs related to our peramivir and BCX4430 programs. If BARDA/HHS or NIAID/HHS were to eliminate, reduce or delay the funding for these programs or disallow some of our incurred costs, we would have to obtain additional funding for continued development or regulatory registration for these product candidates or significantly reduce or stop the development effort. Further, BARDA/HHS and NIAID/HHS may challenge actions that we have taken or may take under our contracts, which could negatively impact our operating results and cash flows.

In contracting with BARDA/HHS and NIAID/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 extraordinary provisions that 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. In addition, U.S. Government contracts are subject to an in-process review, where the U.S. Government will review the project and its options under the contract. As such, we may be at a disadvantage as

Table of Contents

compared to other commercial contracts. U.S. Government contracts are subject to audit and modification by the government at its sole discretion. If the U.S. Government terminates any of its contracts 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 government contracts with BARDA/HHS and NIAID/HHS have special contracting requirements, which create additional risks of reduction or loss of funding.

We have entered into a contract with BARDA/HHS for the advanced development of our neuraminidase inhibitor, peramivir. We also have entered into a contract with NIAID/HHS for the development of BCX4430 as a treatment for Marburg virus disease. In contracting with these government agencies, 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 extraordinary provisions that 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. In addition, U.S. Government contracts are subject to the in-process review described above. As such, we may be at a disadvantage as compared to competitors that do not rely on U.S. Government contracts.

U.S. Government contracts typically contain unfavorable termination provisions and are subject to audit and modification by the government at its sole discretion, each of 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 contracts 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 do not permit these recoveries. In the event of termination or upon expiration of a contract, the U.S. Government may dispute wind down and termination costs and may question prior expenses under the contract and deny payment of those expenses. Should we choose to challenge the U.S. Government for denying certain payments under a contract, such a challenge could subject us to substantial additional expenses which we may or may not recover. Further, if the U.S. Government terminates its contracts 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.

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. Audits conducted by the U.S. Government for the BARDA/HHS contract have been performed and concluded through fiscal 2009; all subsequent fiscal years are still open and auditable. Based on the results of its audits, the U.S. Government may adjust our contract-related costs and fees, including allocated indirect costs. This adjustment could impact the amount of revenues reported on a historic basis and could impact our cash flows under the contracts prospectively. In addition, in the event BARDA/HHS or NIAID/HHS determines that certain costs and fees were unallowable or determines that the allocated indirect cost rate was higher than the actual indirect cost rate, BARDA/HHS or NIAID/HHS would be entitled to recoup any overpayment from us as a result. In addition, if an audit or review uncovers any improper or illegal activity, we

Table of Contents

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 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 product 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 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 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 we or our partners fail to fulfill our 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

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alternative sources of funding. Any delay in the development or commercialization of our product candidates would severely affect our business, because if our product candidates do not progress

S-9

Table of Contents

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 milestone, product sales 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 reach the market faster, 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 is 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 from product sales would depend on our ability to successfully complete clinical studies, obtain regulatory approvals, and 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 product candidates will be delayed or stopped.

We rely heavily upon other parties for many important stages of our product candidate development, 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 product candidates;

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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 (including peramivir) and the product candidates to be used in our clinical trials, toxicology studies and any potential commercial product.

S-10

Table of Contents

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 drug 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 both the development of our product candidates and the availability of any potential commercial product.

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 (cGLP), current Good Manufacturing Practices (cGMP) and current Good Clinical Practices (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.

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:

i.v. peramivir may not prove to be safe and sufficiently effective for market approval in the United States or other major markets;

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;

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

advances in flu vaccines or other antivirals, including competitive i.v. antivirals, could substantially replace potential demand for peramivir;

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

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;

Table of Contents

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 influenza, 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 us. 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 United States 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 additional 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 us. The sale of peramivir, emergency use or other use of peramivir in any country may create certain liabilities for us.

Because we have limited manufacturing experience, we depend on third-party manufacturers to manufacture our 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 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 or have an effect on infrastructure;

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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

S-12

Table of Contents

lack of compliance or cooperation with regulations and specifications or requests set forth by the FDA or other foreign regulatory agencies, particularly associated with our pending peramivir NDA.

For example, our drug product manufacturer for peramivir has been issued a Warning Letter and a Form 483 from the FDA, and failure to adequately address the observations made in the Form 483 may result in the unavailability or low supply of peramivir in the United States during the 2014-2015 influenza season in the event of an FDA approval of peramivir.

These contract manufacturers may not be able to manufacture the materials required for our 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 (including for peramivir), may require prior review and approval in accordance with the FDA's cGMP 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 maintain current manufacturing or other contract relationships, or enter into new agreements with additional manufacturers on commercially reasonable terms, or if there is poor manufacturing performance or failure to comply with any regulatory agency on the part of any of our third-party manufacturers, we may not be able to complete development of, seek timely approval 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 product candidate material for further preclinical testing and clinical trials.

Royalties and milestone payments from Shionogi under the Company's license agreement with Shionogi (the "Shionogi Agreement") will be required to be used by Royalty Sub to service its obligations under its PhaRMA Notes, and generally will not be available to us for other purposes until Royalty Sub has repaid in full its obligations under the PhaRMA Notes.

In March 2011, our wholly-owned subsidiary Royalty Sub issued \$30.0 million in aggregate principal amount of PhaRMA Notes. The PhaRMA Notes are secured principally by (i) certain royalty and milestone payments under the Shionogi Agreement, pursuant to which Shionogi licensed from us the rights to market peramivir in Japan and, if approved for commercial sale, Taiwan, (ii) rights to certain payments under a Japanese yen/U.S. dollar foreign currency hedge arrangement put into place by us in connection with the issuance of the PhaRMA Notes and (iii) the pledge by us of our equity interest in Royalty Sub. Payments from Shionogi to us under the Shionogi Agreement will generally not be available to us for other purposes until Royalty Sub has repaid in full its obligations under the PhaRMA Notes. Accordingly, these funds will be required to be dedicated to Royalty Sub's debt service and not available to us for product development or other purposes.

If royalties from Shionogi are insufficient for Royalty Sub to make payments under the PhaRMA Notes or if an event of default occurs under the PhaRMA Notes, the holders of the PhaRMA Notes may be able to foreclose on the collateral securing the PhaRMA Notes and our equity interest in Royalty Sub, in which case we may not

Table of Contents

realize the benefit of future royalty payments that might otherwise accrue to us following repayment of the PhaRMA Notes.

Royalty Sub's ability to service its payment obligations in respect of the PhaRMA Notes, and our ability to benefit from our equity interest in Royalty Sub, is subject to numerous risks. Peramivir was first approved for marketing and manufacturing in Japan in October 2009 and has been offered for sale in Japan only since January 2010. As a result, there is very little sales history for peramivir in Japan, and there can be no assurance that peramivir will gain market acceptance in the Japanese market. In addition, Shionogi's sales of peramivir are expected to be highly seasonal and vary significantly from year to year, and the market for products to treat or prevent influenza is highly competitive. Under our license agreement with Shionogi, Shionogi has control over the commercial process for peramivir in Japan and Taiwan. Royalty Sub's ability to service the PhaRMA Notes may be adversely affected by, among other things, changes in or any termination of our relationship with Shionogi, reimbursement, regulatory, manufacturing and/or intellectual property issues, product returns, product recalls, product liability claims and allegations of safety issues, as well as other factors. In the event that for any reason Royalty Sub is unable to service its obligations under the PhaRMA Notes or an event of default were to occur under the PhaRMA Notes, the holders of the PhaRMA Notes may be able to foreclose on the collateral securing the PhaRMA Notes and our equity interest in Royalty Sub and exercise other remedies available to them under the indenture in respect of the PhaRMA Notes. In such event, we may not realize the benefit of future royalty payments that might otherwise accrue to us following repayment of the PhaRMA Notes and we might otherwise be adversely affected.

On September 3, 2013, we paid \$1.8 million of interest on the PhaRMA Notes from royalty payments received from RAPIACTA[®] sales from the preceding four calendar quarters. This payment resulted in an obligation shortfall of \$2.4 million associated with accrued interest due September 3, 2013. As stipulated under the PhaRMA Notes indenture, if the amount available for payment is insufficient to pay all of the interest due on a Payment Date, the shortfall in interest will accrue interest at the interest rate applicable to the PhaRMA Notes compounded annually. Accordingly, commencing on September 3, 2013, we began accruing interest at 14% per annum on the interest shortfall of \$2.4 million. In March 2014, we paid an additional \$0.4 million of interest, bringing the shortfall down to \$2.1 million as of March 31, 2014. Under the terms of the indenture relating to the PhaRMA Notes, the inability to pay the full amount of interest payable on September 3, 2013 will not constitute an event of default under the PhaRMA Notes unless we fail to pay such unpaid interest, plus interest thereon, on or prior to the next succeeding Payment Date for the PhaRMA Notes, which is September 1, 2014. Based on sales to date of RAPIACTA[®] provided to us by Shionogi, there can be no assurance that sufficient royalties will be available to fund the September 3, 2013 interest shortfall prior to September 1, 2014. Should these royalties be insufficient to cover the interest shortfall, the PhaRMA Notes will be in default at September 1, 2014.

Shionogi's failure to successfully market and commercialize peramivir in Japan would have a material adverse effect on Royalty Sub's ability to service its obligations on the PhaRMA Notes.

The successful commercialization of peramivir in Japan depends on the efforts of Shionogi and is beyond the control of us or Royalty Sub. As discussed above, peramivir has only recently been introduced into the Japanese market, and there can be no assurance that peramivir will gain market acceptance in Japan. Future sales by Shionogi will depend on many factors, including the incidence and severity of seasonal influenza in Japan each year (both of which can vary very significantly from year to year), the perceived and actual efficacy and safety of peramivir, the experience of physicians and patients with peramivir, continued market acceptance, continued availability of supply, competition, sales and marketing efforts, governmental regulation, and pricing and reimbursement in Japan. Shionogi is responsible for the marketing and sale of peramivir in Japan, including with respect to the pricing of peramivir in that market. There are no minimum royalties, sales levels or other performance measures required of Shionogi under the Shionogi Agreement and Shionogi could in its sole

Table of Contents

discretion reduce or cease its sale efforts of peramivir in Japan, subject to its covenant in the Shionogi Agreement to use diligent efforts to commercialize peramivir in Japan. If Shionogi is unable to, or fails to, successfully market and commercialize peramivir, it would have a material adverse effect on Royalty Sub's ability to service its obligations under the PhaRMA Notes and our ability to benefit from our equity interest in Royalty Sub.

We may be required to pay significant premiums under the foreign currency hedge arrangement entered into by us in connection with the issuance of the PhaRMA Notes. In addition, because our potential obligations under the foreign currency hedge are marked to market, we may experience additional quarterly volatility in our operating results and cash flows attributable to the foreign currency hedge arrangement.

In connection with the issuance by Royalty Sub of the PhaRMA Notes, we entered into a foreign currency hedge arrangement to hedge certain risks associated with changes in the value of the Japanese yen relative to the U.S. dollar. Under the Currency Hedge Agreement, we may be required to pay a premium in the amount of \$2.0 million in each year beginning in May 2014 and, provided the foreign currency hedge arrangement remains in effect, continuing through May 2020. Such payment will be required if, in May of the relevant year, the spot rate of exchange for Japanese yen-U.S. dollars (determined in accordance with the foreign currency hedge arrangement) is such that the U.S. dollar is worth 100 yen or less. We will be required to mark-to-market our potential obligations under the currency hedge and post cash collateral, which may cause us to experience additional quarterly volatility in our operating results and cash flows as a result. Additionally, we may be required to pay significant premiums or a termination fee under the foreign currency hedge agreement entered into by us in connection with the issuance of the PhaRMA Notes. The Company is required to maintain a foreign currency hedge at 100 yen per dollar under the agreements governing the PhaRMA Notes.

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 and export laws of the United States. The FDA has not approved any of our 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, or if our vendor data systems fail, suffer damage or are destroyed. If we receive 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;

Table of Contents

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.

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. There are many companies seeking to develop products for the same indications that we are working on. Our competitors in the United States and elsewhere are numerous and include, among others, major multinational pharmaceutical and chemical companies and specialized biotechnology firms. Most of these competitors have greater resources than we do, including greater financial resources, larger research and development staffs and more experienced marketing and manufacturing organizations. In addition, most of our competitors have greater experience than we do in conducting clinical trials and obtaining FDA and other regulatory approvals. Accordingly, our competitors may succeed in obtaining FDA or other regulatory approvals of product candidates more rapidly than we do. Companies that complete clinical trials, obtain required regulatory approvals, and commence commercial sale of their drugs before we do may achieve a significant competitive advantage, including patent and FDA exclusivity rights that would delay our ability to market products. We face, and will continue to face, competition in the licensing of desirable disease targets, licensing of desirable 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 influenza, gout, HAE, and recurrent/refractory peripheral T-cell lymphoma, as well as broad spectrum antivirals which may be developed as medical countermeasures. We expect to encounter significant competition for any of the pharmaceutical products we plan to develop. Companies that complete clinical trials, obtain required funding or government support, obtain required regulatory approvals and commence commercial sales or stockpiling orders of their products before their competitors may achieve a significant competitive advantage. Such is the case with Eisai Co. Ltd.'s TARGRETIN[®] for cutaneous T-cell lymphoma and the current neuraminidase inhibitors marketed by GSK and Roche for influenza and CINRYZE[®] and FIRAZYR[®] for HAE marketed by Shire Pharmaceuticals, Inc. Both Roche and GSK may have i.v. formulations of neuraminidase inhibitors for influenza in clinical trial development. 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 Purine Nucleoside Phosphorylase, influenza, HAE, 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.

Table of Contents

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 impede our funding efforts, render technology and product candidates noncompetitive or eliminate or reduce demand for our product candidates.

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, trademark 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. Further, we may not have worldwide patent protection for all of our product candidates and our intellectual property rights may not be legally protected or enforceable in all countries throughout the world. In some jurisdictions, some of our product candidates in certain programs, including our HAE program, may have short or no composition of matter patent life and we may therefore rely on orphan drug exclusivity or data exclusivity. There can be no assurance that we will obtain orphan drug exclusivity or data exclusivity in every jurisdiction. Further, in some jurisdictions, we may rely on formulation patents or method of use patents. Both the ability to achieve issuance and the enforcement of formulation and method of use patents can be highly uncertain and can vary from jurisdiction to jurisdiction, and such patents may therefore not adequately prevent competitors and potential infringers in some jurisdictions. The validity, scope, enforceability and commercial value of the rights protected by such patents, therefore, is highly uncertain.

We also rely on trade secrets to protect technology in cases when we believe patent protection is not appropriate or obtainable. However, trade secrets are difficult to protect. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborators and advisors, our ability to receive patent protection or protect our proprietary information may be imperiled.

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 United States, 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

Table of Contents

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 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 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 cannot 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

Table of Contents

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. 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.

Insurance coverage is increasingly more costly and difficult to obtain or maintain.

While we currently have insurance for our business, property, directors and officers, and our products, insurance is increasingly more costly and narrower in scope, and we may be required to assume more risk in the future. If we are subject to claims or suffer a loss or damage in excess of our insurance coverage, we will be required to bear any loss in excess of our insurance limits. If we are subject to claims or suffer a loss or damage that is outside of our insurance coverage, we may incur significant uninsured costs associated with loss or damage that could have an adverse effect on our operations and financial position. Furthermore, any claims made on our insurance policies may impact our ability to obtain or maintain insurance coverage at reasonable costs or at all.

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

We store clinical and stability samples at our facility that could be damaged if our facility incurs 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 store most of our preclinical and clinical data at our facilities. Duplicate copies of most critical data are secured off-site. 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.

Table of Contents

If we fail to retain our existing key personnel or fail to attract and retain additional key personnel, the development of our 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 or a violation of such 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 existing principal stockholders hold a substantial amount of our common stock and may be able to influence significant corporate decisions, which may conflict with the interest of other stockholders.

Several of our stockholders own greater than 5% of our outstanding common stock. These stockholders, if they act together, may be able to influence the outcome of matters requiring approval of the stockholders, including the election of our directors and other corporate actions.

Our stock price has been, and is likely to continue to be, highly volatile, which could result in the value of your investment in our common stock to 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 March 31, 2014, the 52-week range of the market price of our stock was from \$1.26 to \$13.33 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;

developments and announcements regarding new and virulent strains of influenza;

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;

S-20

Table of Contents

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.

Future sales and issuances of securities may dilute your ownership interest and cause our stock price to decline.

Future sales of our common stock by current stockholders into the public market could cause the market price of our stock to fall. As of May 19, 2014, there were 60,074,837 shares of our common stock outstanding (prior to the consummation of this offering). We may from time to time issue securities in relation to a license arrangement, collaboration, merger or acquisition. We may also sell, for our own account, shares of common stock or other equity securities, from time to time at prices and on terms to be determined at the time of sale.

As of May 19, 2014, there were 9,397,640 stock options and restricted stock units outstanding, 3,832,645 shares available for issuance under our Amended and Restated Stock Incentive Plan and 559,176 shares available for issuance under our Employee Stock Purchase Plan, and we could also make equity compensation grants outside of our Stock Incentive Plan. The shares underlying existing stock options and restricted stock and possible future stock options, stock appreciation rights and stock awards have been registered pursuant to registration statements on Form S-8.

If some or all of such shares are sold or otherwise issued into the public market over a short period of time, our current stockholders' ownership interests may be diluted and the value of all publicly traded shares is likely to decline, as the market may not be able to absorb those shares at then-current market prices. Additionally, such sales and issuances may make it more difficult for us to sell equity securities or equity-related securities in the future at a time and price that our management deems acceptable, or at all.

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 4,800,000 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.

S-21

Table of Contents

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.

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

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.

Table of Contents

Use of proceeds

We estimate that we will receive net proceeds of approximately \$92.5 million from the sale of common stock offered by us in this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that the net proceeds to us will be approximately \$106.6 million. We intend to use the net proceeds from this offering for general corporate purposes, including funding clinical development of BCX4161, the continued development of both second generation HAE compounds, commercialization activities relating to peramivir and the advancement of other preclinical rare disease programs.

The amount and timing of these expenditures will depend on a number of factors, including the progress of our research and development efforts and amounts received under our existing and any future government contracts and collaboration arrangements, as well as the amount of cash used in our operations. Accordingly, our management will have broad discretion in the application of these proceeds, and investors will be relying on the judgment of our management with regard to the use of these proceeds. Pending application of the net proceeds as described above, we intend to invest the proceeds in investment grade interest bearing instruments.

S-23

Table of Contents**Dilution**

As of March 31, 2014, our net tangible book value was approximately \$(0.1) million, or approximately \$0.00 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 60,064,634 shares of our common stock outstanding as of March 31, 2014.

Investors participating in this offering will incur immediate, substantial dilution. After giving effect to our receipt of approximately \$92.5 million of estimated net proceeds (after deducting underwriting discounts and commissions and estimated offering expenses payable by us) from our sale of common stock in this offering, assuming a public offering price of \$9.01 per share, the last reported sale price of our common stock on the NASDAQ Global Select Market on May 23, 2014, our as adjusted net tangible book value as of March 31, 2014 would have been \$92.4 million, or \$1.30 per share. This amount represents an immediate increase in net tangible book value of \$1.30 per share of our common stock to existing stockholders and an immediate dilution in net tangible book value of \$7.71 per share of our common stock to new investors purchasing shares of common stock in this offering.

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

Public offering price per share	\$ 9.01
Net tangible book value per share as of March 31, 2014	\$ 0.00
Increase in net tangible book value per share attributable to new investors	\$ 1.30
Net tangible book value per share as of March 31, 2014 after giving effect to this offering	\$ 1.30
Dilution in net tangible book value per share to new investors	\$ 7.71

Each \$1.00 increase or decrease in the assumed public offering price of \$9.01 per share, the last reported sale price of our common stock on the NASDAQ Global Select Market on May 23, 2014, would increase or decrease, respectively, the as adjusted net tangible book value per share by approximately \$0.02 per share and the dilution to investors purchasing shares in this offering by approximately \$0.02 per share, assuming the dollar amount of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters' option to purchase additional shares is exercised in full, the as adjusted net tangible book value per share after giving effect to this offering would be \$1.46 per share, which amount represents an immediate increase in as adjusted net tangible book value of \$1.46 per share of our common stock to existing stockholders and an immediate dilution in net tangible book value of \$7.55 per share of our common stock to new investors purchasing shares of common stock in this offering.

The above discussion and table are based on 60,064,634 shares of common stock outstanding as of March 31, 2014 and exclude:

8,543,202 shares of common stock issuable upon the exercise of stock options outstanding under our stock incentive plan as of March 31, 2014, at a weighted average exercise price of \$5.24 per share;

977,500 additional shares of common stock reserved for issuance under our stock incentive plan and 59,176 additional shares of common stock reserved for issuance under our employee stock purchase plan as of March 31, 2014; and

3,750,000 additional shares of common stock reserved for issuance under our stock incentive plan and 500,000 additional shares of common stock reserved for issuance under our employee stock purchase plan, each under the increases approved by stockholders at our annual meeting on May 2, 2014.

Table of Contents

To the extent that outstanding options have been or may be exercised or other shares issued, there may be further dilution to investors. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital by issuing equity securities or convertible debt, your ownership may be further diluted.

S-25

Table of Contents**Price range of common stock and dividend policy**

Our common stock is listed on the Nasdaq Global Select 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 Select Market.

	High	Low
Year ended December 31, 2012		
1 st Quarter	\$ 5.95	\$ 2.37
2 nd Quarter	5.00	2.90
3 rd Quarter	4.74	3.47
4 th Quarter	4.95	1.08
Year ended December 31, 2013		
1 st Quarter	\$ 2.04	\$ 1.12
2 nd Quarter	2.21	1.26
3 rd Quarter	7.59	1.51
4 th Quarter	7.84	4.55
Year ending December 31, 2014		
1 st Quarter	\$ 13.33	\$ 7.46
2 nd Quarter (through May 23, 2014)	11.20	7.29

The last reported sale price of our common stock on the Nasdaq Global Select Market on May 23, 2014 was \$9.01 per share. As of May 19, 2014 there were approximately 210 holders of record of our common stock.

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

Table of Contents

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, and by-laws, 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 200,000,000 shares of common stock, par value \$0.01 per share, and 5,000,000 shares of preferred stock, par value \$0.01 per share. On May 19, 2014, there were 60,074,837 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.

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.

Table of Contents

Underwriting

We are offering the shares of common stock described in this prospectus supplement through a number of underwriters. J.P. Morgan Securities LLC is acting as sole book-running manager of the offering and as representative of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares
J.P. Morgan Securities LLC	
Piper Jaffray & Co.	
Total	

The underwriters are committed to purchase all the common shares offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common shares directly to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of \$ _____ per share. After the public offering of the shares, the offering price and other selling terms may be changed by the underwriters. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to _____ additional shares of common stock from us. The underwriters have 30 days from the date of this prospectus supplement to exercise this option. If any shares are purchased with this option, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is \$ _____ per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without option exercise	With option exercise
Per share	\$	\$
Total	\$	\$

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately \$1.5 million.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

Table of Contents

We have agreed, subject to limited exceptions, that we will not (i) offer, pledge, announce the intention to sell, 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 or otherwise dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act of 1933 relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities LLC for a period of 90 days after the date of this prospectus supplement, other than (A) the shares of our common stock to be sold hereunder (B) shares and options to purchase shares of Common Stock issued pursuant to our existing equity compensation plans and (C) any shares of our common stock issued upon the exercise of options granted under our existing management incentive plans. Notwithstanding the foregoing, if (1) during the last 17 days of the 90-day restricted period, we issue an earnings release or material news or a material event relating to our company occurs; or (2) prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day period, the restrictions described above shall 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.

Our directors and executive officers have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons, with limited exceptions, for a period of 90 days after the date of this prospectus supplement, may not, without the prior written consent of J.P. Morgan Securities LLC, (1) offer, pledge, announce the intention to sell, 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, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors and executive officers in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant), (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of any shares of our common stock or such other securities, whether any such transaction described in clause (1) above or this clause (2) is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock. Notwithstanding the foregoing, if (1) during the last 17 days of the 90-day restricted period, we issue an earnings release or material news or a material event relating to our company occurs; or (2) prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day period, the restrictions described above shall 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. Each of the lock-up agreements contain certain exceptions, including transfers of shares of common stock pursuant to a contract or plan meeting the requirements of Rule 10b5-1 under the Exchange Act that has been entered into by certain of our executive officers or the disposition of shares of common stock to the Company for the purpose of covering tax liabilities and and/or the exercise price in connection with the exercise of options to purchase shares of common stock awarded pursuant to our existing equity compensation plans.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

Table of Contents

Our common stock is listed on the Nasdaq Global Select Market under the symbol BCRX.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be covered shorts, which are short positions in an amount not greater than the underwriters' option referred to above, or may be naked shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through their option to purchase additional shares. 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 that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act of 1933, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

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

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus supplement in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and

Table of Contents

to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

This document is only being distributed to and is only directed at (i) persons who are outside the United Kingdom or (ii) to investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order) or (iii) high net worth entities, and other persons to whom it may lawfully be communicated, falling with Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons). The securities are only available to, and any invitation, offer or agreement to subscribe, purchase or otherwise acquire such securities will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), from and including the date on which the European Union Prospectus Directive (the EU Prospectus Directive) was implemented in that Relevant Member State (the Relevant Implementation Date) an offer of securities described in this prospectus supplement may not be made to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the EU Prospectus Directive, except that, with effect from and including the Relevant Implementation Date, an offer of securities described in this prospectus supplement may be made to the public in that Relevant Member State at any time:

to any legal entity which is a qualified investor as defined under the EU Prospectus Directive;

to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the EU Prospectus Directive); or

in any other circumstances falling within Article 3(2) of the EU Prospectus Directive, provided that no such offer of securities described in this prospectus supplement shall result in a requirement for the publication by us of a prospectus pursuant to Article 3 of the EU Prospectus Directive.

For the purposes of this provision, the expression an offer of securities to the public in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the same may be varied in that Member State by any measure implementing the EU Prospectus Directive in that Member State. The expression EU Prospectus Directive means Directive 2003/71/EC (and any amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in each Relevant Member State, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

Table of Contents

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 Latham & Watkins LLP, San Diego, California.

Experts

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2013, and the effectiveness of our internal control over financial reporting as of December 31, 2013, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements and our management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2013 are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

S-32

Table of Contents

Where you can find more information

We file electronically with the SEC our annual reports on Form 10-K, quarterly 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 4505 Emperor Blvd., Suite 200, Durham, North Carolina 27703 or sending an email to investorelations@biocryst.com. You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street NE, 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 a website 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 supplement.

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 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, 2013, filed with the SEC on March 10, 2014 (including the sections of our proxy statement relating to our May 2, 2014 annual meeting of stockholders that are incorporated by reference therein);

Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2014, filed with the SEC on May 9, 2014;

Our Current Reports on Form 8-K filed with the SEC on February 26, 2014 (excluding the information furnished under Items 2.02, 7.01 and 9.01 thereof), April 3, 2014, May 2, 2014, May 5, 2014, May 7, 2014 and May 27, 2014 (two filed on this date; excluding any information furnished under Items 7.01 and 9.01 thereof); and

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. 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

Table of Contents

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.

4505 Emperor Blvd., Suite 200

Durham, North Carolina 27703

(919) 859-7910

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 supplement 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.

S-34

Table of Contents

PROSPECTUS

\$125,000,000

Common Stock

Preferred Stock

Depository 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 Select 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 on page 2 of this prospectus, in the applicable prospectus supplement we will deliver with this prospectus and in the documents incorporated herein and therein by reference.

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.

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 November 15, 2013.

Table of Contents

TABLE OF CONTENTS

	Page
<u>ABOUT THIS PROSPECTUS</u>	i
<u>PROSPECTUS SUMMARY</u>	1
<u>RISK FACTORS</u>	2
<u>INFORMATION REGARDING FORWARD-LOOKING STATEMENTS</u>	3
<u>USE OF PROCEEDS</u>	5
<u>DESCRIPTION OF COMMON STOCK, PREFERRED STOCK AND DEPOSITARY SHARES</u>	6
<u>DESCRIPTION OF STOCK PURCHASE CONTRACTS</u>	9
<u>DESCRIPTION OF WARRANTS</u>	10
<u>DESCRIPTION OF UNITS</u>	11
<u>PLAN OF DISTRIBUTION</u>	12
<u>LEGAL MATTERS</u>	15
<u>EXPERTS</u>	15
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	16
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	16

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 \$125.0 million.

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

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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.

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.

We are a biotechnology company that designs, optimizes and develops novel drugs that block key enzymes involved in the pathogenesis of diseases. We focus on therapeutic areas with unmet medical needs that are of interest to us and aligned with our capabilities and expertise. 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-guided drug design.

Structure-guided drug design is a drug discovery approach by which we design synthetic compounds from detailed structural knowledge of the active sites of enzyme targets associated with particular diseases. We use X-ray crystallography, computer modeling of molecular structures and advanced chemistry techniques to focus on the three-dimensional molecular structure and active site characteristics of the enzymes that control cellular biology. Enzymes are proteins that act as catalysts for many vital biological reactions. Our goal generally is to design a compound that will fit in the active site of an enzyme and thereby prevent its catalytic activity. Molecules in development by us and our partners are summarized in the table below:

Drug/Drug Candidate	Drug Class	Therapeutic Area(s)	Phase	Rights
		Influenza	Phase 3/NDA filing expected in 2013	BioCryst (worldwide, except Japan, Taiwan, Korea and Israel)
Peramivir	Intravenous Neuraminidase Inhibitor	Influenza	Approved	Shionogi (Japan & Taiwan)
			(Japan)	
			Approved (Korea)	Green Cross (Korea)
Ulodesine	Oral Purine Nucleoside Phosphorylase Inhibitor	Gout	Phase 3 ready	BioCryst (worldwide)
BCX4161	Oral Serine Protease Inhibitor Targeting Kallikrein	Hereditary angioedema (HAE)	Phase 2	BioCryst (worldwide)
BCX4430	RNA dependent-RNA Polymerase Inhibitor	Filoviruses, including Marburg virus and other hemorrhagic fever viruses	Preclinical	BioCryst (worldwide)
Forodesine	Oral Purine Nucleoside Phosphorylase Inhibitor	Oncology	Phase 2	Mundipharma (worldwide)

In addition, we are developing a series of molecules with the objective of selecting a second generation kallikrein inhibitor for the treatment of HAE and advancing it into preclinical development in 2013.

BioCryst is a Delaware corporation originally founded in 1986. Our principal offices are located at 4505 Emperor Blvd. Suite 200, Durham, North Carolina 27703, and our telephone number is (919) 859-1302. 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

RISK FACTORS

Investing in our securities involves risks. Our business is influenced by many factors that are difficult to predict and beyond our control and that involve uncertainties that may materially affect our results of operations, financial condition or cash flows, or the value of these securities. These risks and uncertainties are described in the risk factors section of the documents that are incorporated by reference in this prospectus. Subsequent prospectus supplements may contain a discussion of additional risks applicable to an investment in us and the particular type of securities we are offering under the prospectus supplements. You should carefully consider all of the information contained in or incorporated by reference in this prospectus and in the applicable prospectus supplement before you invest in our securities.

Table of Contents

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 (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. These forward-looking statements can generally be identified by the use of words such as may, will, intends, plans, believes, anticipates, expects, estimates, potential, the negative of these words or similar expressions. Statements that describe our future plans, strategies, intentions, expectations, objectives, goals or prospects are also forward-looking statements. 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 the Biomedical Advanced Research and Development Authority within the United States Department of Health and Human Services (BARDA/HHS) for the development and support of the New Drug Application (NDA) for peramivir and the potential funding from our contract with the National Institute of Allergy and Infectious Diseases (NIAID) within the National Institutes of Health for the development of BCX4430;

the NDA filing or U.S. Food and Drug Administration (FDA) approval 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, H5N1 and H7N9 or other strains of influenza;

the further preclinical or clinical development and commercialization of our product candidates, including our HAE program, peramivir, BCX4430, forodesine, ulodesine and other purine nucleoside phosphorylase (PNP) inhibitor development programs;

the implementation of our business model, strategic plans for our business, product candidates and technology;

our ability to establish and maintain collaborations or out-license rights to our drug candidates;

plans, programs, progress and potential success of our collaborations, including Mundipharma International Holdings Limited (Mundipharma) for forodesine and Shionogi & Co., Ltd. (Shionogi) and Green Cross Corporation (Green Cross) for peramivir in their territories;

the ability of our wholly-owned subsidiary, JPR Royalty Sub LLC (Royalty Sub), which was formed in connection with our \$30.0 million financing transaction completed on March 9, 2011, to service its payment obligations in respect of its Pharma Senior Secured 14.0% Notes due 2020 (the Pharma Notes) issued in that financing transaction, and our ability to benefit from our equity interest in Royalty Sub;

the foreign currency hedge agreement entered into by us in connection with the issuance by Royalty Sub of the Pharma Notes;

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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 including our financial outlook for the remainder of 2013;

the timing or likelihood of regulatory filings and approvals;

our ability to raise additional capital to fund our operations;

our financial performance; and

competitive companies, technologies and our industry.

Table of Contents

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. Any forward-looking statement in this prospectus 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 Securities and Exchange Commission (the **SEC**).

Table of Contents

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:

clinical development of BCX4161 and the second generation HAE compounds as well as other preclinical product candidates;

pre-commercialization activities relating to intravenous peramivir;

funding our research and development efforts;

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 or investments.

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.

Table of Contents

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 October 28, 2013, there were 59,091,393 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.

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 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

Table of Contents

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

Table of Contents

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.

Table of Contents

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.

Table of Contents

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;

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;

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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.

Table of Contents

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.

Table of Contents

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.

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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.

In compliance with the guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum compensation or discount to be received by any FINRA member or independent broker dealer may not exceed eight percent of the offering proceeds from the securities offered pursuant to this prospectus and any applicable prospectus supplement.

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

Table of Contents

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.

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

Table of Contents

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.

Any underwriter may engage in over-allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment 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 Select Market or otherwise.

Any underwriters who are qualified market makers on The NASDAQ Global Select Market may engage in passive market making transactions in the common stock on The NASDAQ Global Select 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.

Table of Contents

LEGAL MATTERS

Gibson, Dunn & Crutcher LLP has rendered an opinion with respect to the validity of the securities being offered by this prospectus. We have filed this opinion as an exhibit to the registration statement of which this prospectus is a part. If counsel for any underwriters passes on legal matters in connection with an offering made by this prospectus, we will name that counsel in the prospectus supplement relating to that offering.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2012, and the effectiveness of our internal control over financial reporting as of December 31, 2012, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements and our management's assessment of the effectiveness of internal control over financial reporting at December 31, 2012 are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

Table of Contents

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 4505 Emperor Blvd., Suite 200, Durham, North Carolina 27703 or sending an email to investorrelations@biocryst.com. You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street NE, 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 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, 2012, filed with the SEC on March 11, 2013 (including the sections of our proxy statement relating to our May 31, 2013 annual meeting of stockholders that are incorporated by reference therein);

Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2013 and June 30, 2013, filed with the SEC on May 7, 2013 and August 8, 2013, respectively;

Our Current Reports on Form 8-K filed with the SEC on January 4, 2013, January 8, 2013, January 28, 2013, February 7, 2013, April 1, 2013, April 16, 2013, June 4, 2013, June 5, 2013, July 11, 2013, July 22, 2013, July 23, 2013, July 30, 2013, August 1, 2013, August 5, 2013 and September 18, 2013;

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 7, 1994, together with the amendment thereto filed with the SEC on March 14, 1994, including any other amendment or reports filed for the purpose of updating such description; and

All documents filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of the initial registration statement and prior to effectiveness of the registration statement and on or after the

Table of Contents

date of this prospectus and prior to the termination of our offering of securities 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.

4505 Emperor Blvd., Suite 200

Durham, North Carolina 27703

(919) 859-1302

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.

Table of Contents

\$100,000,000

Common stock

Prospectus supplement

J.P. Morgan

Piper Jaffray

, 2014