BIOCRYST PHARMACEUTICALS INC
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March 10, 2017

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Registration No. 333-202466

Prospectus supplement
(To prospectus dated April 18, 2016)

5,294,118 shares

Common stock

BioCryst Pharmaceuticals, Inc. is offering 5,294,118 shares of its common stock.

Our common stock is listed on the NASDAQ Global Select Market under the symbol "BCRX." On March 9, 2017, the last reported sale price of our common stock on the NASDAQ Global Select Market was $8.74 per share.

	Per share	Total
Public offering price	$ 8.50	$ 45,000,003
Underwriting discounts and commissions[(1)]	$ 0.51	$ 2,700,000
Proceeds to BioCryst, before expenses	$ 7.99	$ 42,300,003

(1) We have agreed to reimburse the underwriters for certain FINRA-related expenses. See "Underwriting."

We have granted the underwriters an option for a period of 30 days to purchase up to 794,117 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-8 of this prospectus supplement and in the documents incorporated by reference into 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 of 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 March 15, 2017.

Sole book-running manager

J.P. Morgan

Sole lead manager

Piper Jaffray

Co-manager

JMP Securities

March 9, 2017

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About this prospectus supplement

This document is part of a registration statement that we filed with the Securities and Exchange Commission (the "SEC") using a "shelf" registration process and consists of two parts. The first part is the prospectus supplement, which describes the specific terms of this offering of shares of our common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part is the accompanying prospectus, or the base prospectus, dated April 18, 2016, including the documents incorporated by reference therein, which provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. 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.

Neither we nor the underwriters have authorized anyone to provide you with information different from that contained in or incorporated by reference into this prospectus supplement, the accompanying prospectus or any free writing prospectus prepared by us or on our behalf. We and the underwriters take no responsibility for, and can provide no assurances as to the reliability of, any information other than the information contained in or incorporated by reference into this prospectus supplement, the accompanying prospectus or any free writing prospectus prepared by us or on our behalf. Neither we nor the underwriters are offering to sell, nor seeking offers to buy, shares of our common stock in any jurisdiction where an offer or sale is prohibited. You should assume that the information appearing in or incorporated by reference into this prospectus supplement, the accompanying prospectus or any free writing prospectus prepared by us or on our behalf is accurate or complete only as of their respective dates or on the date or dates which are specified in such documents, and that any information in documents that we have incorporated by reference is accurate or complete only as of the date of such document incorporated by reference. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates. Management estimates are derived from publicly available information, our knowledge of our industry and assumptions based on such information and knowledge, which we believe to be reasonable. In addition, assumptions and estimates of our and our industry's future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in "Risk factors" in this prospectus supplement, the accompanying prospectus and in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, which is incorporated by reference into this prospectus supplement. These and other important factors could cause our future performance to differ materially from our assumptions and estimates. See "Forward-looking statements."

If the information set forth in this prospectus supplement, on the one hand, differs in any way from the information set forth in the accompanying prospectus or in a document which is incorporated by reference herein or therein that was filed with the SEC before the date of this prospectus supplement, on the other hand, you should rely on the information set forth in this prospectus supplement. If any statement in one of these documents conflicts with a statement in another document having a later date (for example, a document incorporated by reference in this prospectus supplement or in the accompanying prospectus), the statement in the document having the later date modifies or supersedes the earlier statement.

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.

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 27A of the Securities Act of 1933, as amended (the "Securities Act") and 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 herein and therein 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," "potential," the n 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 preclinical development, clinical development, commercialization, or post-marketing studies of our product candidates and products, including our hereditary angioedema ("HAE") program, peramivir, galidesivir, and early stage discovery programs;
- the potential funding from our contracts with the Biomedical Advanced Research and Development Authority (the "BARDA/HHS") and the National Institute of Allergy and Infectious Diseases ("NIAID/HHS") for the development of galidesivir;
- the potential for government stockpiling orders of peramivir, additional regulatory approvals of peramivir, or milestones, royalties or profit from sales of peramivir by us or our partners;
- the potential use of peramivir as a treatment for H1N1, H5N1, and H7N9 or other strains of influenza;
- the implementation of our business model, strategic plans for our business, products, product candidates and technology;
- our ability to establish and maintain collaborations or out-license rights to our product candidates;
- plans, programs, progress and potential success of our collaborations, including Seqirus UK Limited ("SUL") for peramivir, 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"), to service its payment obligations in respect of its PhaRMA Senior Secured 14.0% Notes due 2020 (the "PhaRMA Notes"), 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;

- 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, revenues, capital requirements, annual cash utilization, and our needs for additional financing;

- our ability to continue as a going concern;

- the timing or likelihood of regulatory filings or regulatory agreements, deferrals and approvals;

- our ability to raise additional capital to fund our operations or repay our recourse debt obligations;

- our ability to comply with the covenants as set forth in the agreements governing our debt obligations;

- 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 herein and therein. 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 included 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 Current Reports on Form 8-K, as well as any amendments we make to those filings with the SEC.

Prospectus supplement summary

This summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus prepared by us or on our behalf and does not contain all of the information that you should consider before investing in shares of 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-8 and the consolidated financial statements and related notes 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 small molecule drugs that block key enzymes involved in the pathogenesis of diseases. We focus on the treatment of rare diseases in which significant unmet medical needs exist and that align 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

Hereditary Angioedema ("HAE") Drug Candidates:

2nd generation HAE compounds

The goal of our second generation HAE discovery program is to discover and develop oral molecules for the prevention of HAE attacks which have a superior selectivity and bioavailability profile while maintaining similar potency as compared to avoralstat, our first oral drug candidate to treat HAE. HAE is a rare, severely debilitating and potentially fatal genetic condition that occurs in approximately 1 in 50,000 people. HAE symptoms include recurrent episodes of edema in various locations, including the hands, feet, face, genitalia 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 caused by swelling in the intestinal wall. By inhibiting plasma kallikrein, our HAE drug candidates suppress bradykinin production. Bradykinin is the mediator of acute swelling attacks in HAE patients.

In December 2013, we announced the selection of two optimized plasma kallikrein inhibitors to advance into preclinical development as potential once-daily, oral prophylactic treatments for HAE. Based on early preclinical development studies, these structurally different molecules have a similar mechanism of action as avoralstat and have achieved the principal goal of improved bioavailability. Both BCX7353 and the other compound had roughly five times better bioavailability than avoralstat. These compounds demonstrated sub-nanomolar potency on the isolated enzyme and single digit nanomolar potency in suppressing kallikrein activity in an ex-vivo activated normal human plasma kallikrein inhibition ("aPKI") assay. Plasma concentrations of each of the optimized compounds exceeded the aPKI assay EC80 concentration at 24 hours after a single oral dose of 10 mg/kg in rats, indicating potential for once-daily dosing. In January 2015, we selected BCX7353 to advance into Phase 1 development to

evaluate its potential as a once-daily, oral prophylactic HAE treatment. In addition to BCX7353, we continue to work on and advance other second generation compounds. These molecules are in preclinical development and are being assessed for safety and efficacy in prophylactic HAE treatment as well as for other potential indications. We will provide additional information on these molecules as we approach an Investigational New Drug filing or we obtain data suggesting efficacy and safety surrounding these molecules in HAE and other therapeutic indications.

BCX7353

BCX7353 is structurally different from and is expected to have superior efficacy as compared to avoralstat, but has a similar mechanism of action targeting plasma kallikrein. On May 13, 2015, we announced the initiation of a Phase 1 clinical trial to evaluate the safety, pharmacokinetics and pharmacodynamics of orally-administered BCX7353 in healthy volunteers.

In December 2015, we successfully completed a Phase 1 clinical trial of BCX7353 in Western and Japanese healthy volunteers. In the Western portion of this trial, we studied BCX7353 single doses of up to 1000mg, once-daily doses of up to 500mg for seven days, and once-daily doses of 350mg for 14 days in healthy Western volunteers. Plasma levels increased in approximate proportion to dose, and drug exposure was not affected by dosing with food. The half-life of BCX7353 was estimated at 67-79 hours. After daily dosing, blood levels met or exceeded a predicted target therapeutic range of 4 to 8 times the 50% effective concentration ("EC50") for plasma kallikrein inhibition throughout the 24 hour dosing interval. Inhibition of the target enzyme, plasma kallikrein, was measured in a sensitive and specific bioassay. Daily dosing with BCX7353 strongly inhibited plasma kallikrein at all four dose levels; the degree of inhibition was dose-related ($p < 0.0001$) and inhibition was sustained throughout the 24 hour dosing interval. This pharmacodynamic effect correlated strongly to the achieved drug concentration ($r = 0.91$, $p < 0.0001$).

In the Japanese portion of this trial, we enrolled cohorts of healthy Japanese volunteers and gave single oral doses of BCX7353 of 100mg and 500mg, and daily doses of 250mg of BCX7353 for seven days. Compared to Western subjects administered the same dose level, plasma drug levels in Japanese subjects were moderately higher. Kallikrein inhibition on day seven of daily dosing with 250mg in Japanese subjects was similar to that seen at the 350mg daily and 500mg daily dose levels in Western subjects.

The combined data from all Phase 1 clinical trials completed as of July 2016 indicates that oral BCX7353 has been generally safe and well tolerated in a total of 117 healthy volunteers, 46 receiving single doses of up to 1000 mg, and 71 receiving once-daily doses of up to 500 mg for 7 days and 350 mg for 14 days. In our Phase 1 trials, we have observed an approximate 5% rate of drug-related rash in healthy volunteers administered daily doses of BCX7353 for at least 7 days. This drug-related rash has appeared within the first 14 days of drug administration and has resolved within a few days after discontinuing the drug. No serious adverse events have been seen and no dose-limiting toxicity has been identified. There have been no clinically significant laboratory abnormalities, ECG changes, or vital sign changes observed.

The safety, tolerability, drug exposure and on-target plasma kallikrein inhibition results strongly supported advancing the development program into a Phase 2 study in HAE patients. In August 2016, we commenced a Phase 2 trial ("APeX-1") to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of BCX7353 as a preventative treatment to reduce the frequency of attacks in HAE patients.

APeX-1 Trial

In August 2016, we announced that we had dosed the first subject in the APeX-1 clinical trial of BCX7353 for the oral treatment of HAE. APeX-1 is a multi-part, Phase 2, randomized, double-blind, placebo-controlled, dose ranging trial to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of BCX7353 as a preventative treatment to eliminate or reduce the frequency of angioedema attacks in HAE patients. APEX-1 is being conducted in several European countries, Australia and Canada. In part 1 of APeX-1, subjects with HAE were randomized in a 1:1 ratio to receive an oral dose of either 350 mg of BCX7353 once daily ("QD") or placebo QD for 28 days. The primary efficacy endpoints of APeX-1 are the number of angioedema attacks; attack rate per week, counts of attacks, proportion of subjects with no attacks, and number of attack-free days. Efficacy analyses will be conducted for HAE attacks reported over the entire dosing interval (Days 1 through 28) and during the dosing period in which plasma concentrations of BCX7353 should be at steady-state conditions (Days 8 through 28). Secondary efficacy endpoints include severity and duration of angioedema attacks and measures of health-related quality of

life. Safety will be characterized through evaluation of adverse events and laboratory testing. Pharmacokinetics and pharmacodynamic effects will be assessed through measurement of plasma drug levels and kallikrein inhibition. A total of approximately 36 subjects have been enrolled in part 1.

On February 27, 2017, we reported statistically significant and clinically meaningful reductions in attack frequency from an interim analysis of part 1 of our ongoing multi-part APeX-1 clinical trial in HAE patients. In the interim analysis, twenty-eight subjects were randomized equally to receive BCX7353 350 mg QD or placebo for 28 days. The baseline attack rate was approximately 1/week and average C1 inhibitor levels were less than 20% of the normal mean, indicating a severely affected patient population. Baseline characteristics of trial participants were generally well balanced between the two groups with the exception of prior androgen use, which was more common in the BCX7353 group (11 of 14 compared with 6 of 14 on placebo). Compliance with study drug dosing in the interim analysis of part 1 of the trial was greater than 98%.

The pre-specified per-protocol ("PP") interim analysis included data on 24 subjects with confirmed Type 1 or Type 2 HAE and completing 28 days of treatment (11 on BCX7353 and 13 on placebo). The mean rate of independently-adjudicated angioedema attacks for the pre-defined effective dosing period (weeks 2 through 4) in BCX7353-treated subjects was 0.34/week compared to 0.92/week for placebo, a reduction of 0.57/week (63%), p = 0.006. In the intent-to-treat ("ITT") population of 28 subjects, the rate of attack for the effective dosing period for BCX7353 and placebo groups was 0.44/week and 0.91/week, a reduction of 0.47/week (52%), p = 0.035.

A pre-planned analysis of peripheral and abdominal attacks showed reductions of 88% and 24%, respectively, for BCX7353 compared with placebo (PP analysis, weeks 2 through 4). To understand this difference, patient diaries were reviewed and abdominal attacks (n = 9, BCX7353 and n = 14, placebo) were subdivided into two groups: attacks with abdominal symptoms only and attacks with a combination of abdominal and peripheral symptoms (mixed attacks). This post-hoc analysis showed that there were 2, 2 and 7 peripheral, mixed and abdominal-only attacks on BCX7353 compared with 22, 12 and 2 attacks, respectively, for placebo. Based on this distribution, it is likely that subjects recorded abdominal adverse events as HAE attack symptoms in their diary. Accordingly, this post-hoc analysis indicated an 88% reduction in the number of attacks for subjects treated with BCX7353, as compared to the placebo arm, characterized by either peripheral symptoms-only or a combination of peripheral and abdominal symptoms.

Pharmacokinetic and pharmacodynamic analyses indicate steady state BCX7353 plasma levels in HAE subjects were similar to those in healthy subjects administered the same dose in a previously completed Phase 1 trial. Steady state trough drug levels (24 hours after dosing) were 11 – 32 times EC50 for plasma kallikrein inhibition. These observed steady state drug levels greatly exceeded our proposed therapeutic target range of 4 – 8 times the EC50. Daily oral dosing with BCX7353 strongly inhibited plasma kallikrein throughout the 24-hour dosing interval and the degree of inhibition was similar to that seen with this dose in the healthy subject Phase 1 trial.

Oral BCX7353 350 mg QD for 28 days was generally safe and well tolerated in subjects with HAE. There were no serious adverse events ("AEs") and no related severe AEs. Two subjects in the BCX7353 treatment group discontinued study drug before day 28, one due to an unrelated pre-existing liver disorder, and one due to an adverse event of gastroenteritis associated with elevated liver enzymes. Treatment-emergent adverse events occurring in at least two subjects overall, enumerated by treatment group (BCX7353 [n=14] and placebo [n=14]), respectfully, were: common cold (3, 4); diarrhea (4, 2); flatulence (2, 0); and fatigue (2, 0). No clinically significant changes in hematology parameters, renal function tests, electrolytes, or urinalysis were observed. One subject treated with BCX7353, with pre-existing colitis, hepatic steatosis (i.e., a fatty liver) and more than 20 years of prior androgen use, had an elevation of alanine aminotransferase > 3 times the upper limit of normal at the end of treatment, which resolved.

Based upon this interim analysis, the efficacy, safety and tolerability profile of BCX7353 observed strongly supports its continued development as a prophylactic treatment for HAE. Furthermore, the steady state drug levels observed greatly exceeded our proposed therapeutic target range of 4 – 8 times the EC50, thereby supporting and prompting us to evaluate doses of BCX7353 lower than the 350 QD tested in part 1 of the trial. Therefore, the APeX-1 trial has been amended to add a 62.5 mg QD dose level, and to increase the number of subjects at the 125 mg QD and 250 mg QD dose levels, in order to more fully characterize dose response. Specifically, part 2 of APeX-1 will enroll 14 additional subjects with HAE and they will be randomized to 250mg of BCX7353 QD (n=6), 125mg of BCX7353 QD (n=6) or placebo (n=2) and part 3 of APeX-1 will enroll 20 additional subjects with HAE and they will be randomized to 250mg of BCX7353QD (n=6), 125mg of BCX7353 QD (n=6), 62.5mg of BCX7353 QD (n=6) or placebo (n=2).

On October 27, 2015 The Japanese Ministry of Health Labor & Welfare ("MHLW") announced that BioCryst's BCX7353 was one of six products designated under MLHW's new Sakigake fast track review system. The Sakigake Designation System promotes R&D in Japan, aiming at early market availability for innovative pharmaceutical products. This designation provides for additional interactions with the regulatory agency in Japan from early development through filing, prioritized development and review, and introduction of the product as soon as possible to address a serious unmet medical need. We expect the results of APeX-1 to help us and the MHLW determine the regulatory pathway and timeline for BCX7353 in Japan.

Infectious disease programs

Peramivir injection (RAPIVAB®, *RAPIACTA®*, *PERAMIFLU®*, *ALPIVAB™)*

Peramivir is an intravenous neuraminidase inhibitor approved in multiple countries for the treatment of patients with influenza. Influenza is a seasonal virus with the highest infection rates generally observed in colder months. In countries for which peramivir is commercially available, influenza occurs primarily during the September to April timeframe. Peramivir is available commercially in the United States and has been approved for commercial use in Canada under the name RAPIVAB®, in Japan and Taiwan as RAPIACTA®, and in Korea as PERAMIFLU®.

Peramivir was most recently approved in Canada in January 2017, and was approved in the United States in December 2014, in each case for the treatment of acute uncomplicated influenza in patients 18 years and older who have been symptomatic for no more than two days. Data from over 2,700 subjects treated with peramivir in 27 clinical trials was utilized to support regulatory approval in these countries. We made RAPIVAB available for commercial sale in the U.S. through agreements with specialty distributorships during the 2014-2015 influenza season. On June 17, 2015, we announced that we licensed RAPIVAB (peramivir injection) for the treatment of influenza to CSL Limited ("CSL"), a global biopharmaceutical company. RAPIVAB is being commercialized by a subsidiary of CSL called Seqirus UK Limited ("SUL" or "Seqirus"), which specializes in influenza prevention through the supply of seasonal and pandemic influenza vaccine to global markets. Under the terms of the agreement, SUL obtained worldwide rights to commercialize RAPIVAB, with the exception of Japan, Korea, Taiwan and Israel. BioCryst retained all rights to pursue pandemic stockpiling orders for RAPIVAB from the U.S. Government, while SUL is responsible for government stockpiling outside the U.S. With the out-license of RAPIVAB to SUL, and our recent Canadian regulatory approval, our current goals for RAPIVAB are to: (1) obtain a stockpiling procurement contract with the U.S. Government; (2) fulfill our post-approval development requirements, including conducting a pediatric trial in the United States and submitting a supplemental New Drug Application ("sNDA") for a pediatric indication; and (3) receiving regulatory approval for our Marketing Authorization Application ("MAA") in the European Union.

In January 2017, we announced that the European Medicines Agency ("EMA") has accepted the filing of our peramivir injection MAA for treatment of symptoms typical of influenza in adults 18 years and older. If the MAA is approved, Seqirus will commercialize peramivir as ALPIVAB™ in the European Union. The acceptance of the MAA begins the review process by the EMA under the centralized licensing procedure for all 28 member states of the European Union, Norway and Iceland.

RAPIVAB was developed under a $234.8 million contract from the Biomedical Advanced Research and Development Authority within the United States Department of Health and Human Services ("BARDA/HHS"), which expired on June 30, 2014.

In January 2010, our partner Shionogi & Co., Ltd. ("Shionogi") received the first approval for peramivir injection and launched it in Japan under the commercial name RAPIACTA. It is approved for the treatment of adults, children and infants with uncomplicated seasonal influenza and those patients at high-risk for complications associated with influenza. In August 2010, Green Cross Corporation ("Green Cross") received marketing and manufacturing approval from the Korean Food & Drug Administration under the commercial name PERAMIFLU to treat patients with influenza A & B viruses, including pandemic H1N1 and avian influenza. In addition, we have a regional collaboration for the development and commercialization of peramivir in Israel.

Galidesivir (formerly BCX4430) broad spectrum anti-viral

Galidesivir is a broad-spectrum antiviral ("BSAV") research program and is currently being developed under contracts with the National Institute of Allergy and Infectious Diseases ("NIAID/HHS") and BARDA/HHS. The objective of our BSAV program is to develop galidesivir as a broad-spectrum therapeutic for viruses that pose a threat to national health and security. The primary focus of the program is treatment of hemorrhagic fever viruses. NIAID/HHS funding has supported galidesivir's development as a treatment for Marburg virus and Ebola virus. In March 2014, galidesivir was featured in an online *Nature* publication depicting successful efficacy results in animal models of infection with Marburg virus and Ebola virus. Galidesivir completely protected cynomolgus macaques from Marburg virus infection when administered by intramuscular ("i.m.") injection 48 hours post-infection. Post-exposure i.m. administration of galidesivir also protected rodents against Marburg virus and Ebola virus infections. In addition, galidesivir was shown to be active in vitro against a broad range of other RNA viruses, including the emerging viral pathogen Middle East Respiratory Syndrome Coronavirus. The publication, which reported the protection of non-human primates from filovirus disease by galidesivir, describes efficacy results generated from an ongoing collaboration between scientists in the U.S. Army Medical Research Institute of Infection Diseases ("USAMRIID") and us. Galidesivir has been shown to be active against more than 20 RNA viruses in nine different families, including filoviruses, togaviruses, bunyaviruses, arenaviruses, paramyxoviruses, coronaviruses and flaviviruses. In tests conducted at USAMRIID, galidesivir protected animals against parenteral exposures to Marburg, Ebola and Rift Valley Fever viruses and from exposures to aerosolized Marburg virus, an experimental condition designed to mimic an exposure scenario that could result during a bioterrorist attack.

On December 15, 2014, we announced the dosing of the first subject in a randomized, placebo-controlled Phase 1 clinical trial to evaluate i.m. administration of galidesivir in healthy volunteers. The main goals of this first-in-human study are to evaluate the safety, tolerability and pharmacokinetics of escalating doses of galidesivir administered via i.m. injection in healthy subjects. In one part of the study, subjects received a single dose of galidesivir; in another part of the study, subjects received galidesivir for seven days. There were six single-dose cohorts and four multiple-dose cohorts evaluated, and 94 healthy volunteers participated. In August 2016, we reported the results of this study. Galidesivir administered by i.m. injection was generally safe and well tolerated over the range of doses up to 10 mg/kg, and durations tested (up to 7 days.) Seventy-six subjects received doses of study drug and there were no serious or severe adverse events. The most frequently reported adverse event across all cohorts was injection site pain and there were no clinically significant laboratory abnormalities which occurred at any doses. In addition, co-administration of lidocaine with galidesivir was determined to ameliorate injection site pain without altering the plasma pharmacokinetics profile of galidesivir. From this clinical trial, we determined galidesivir was safe and well tolerated, and that exposure was dose-proportional and supported the continued development of this BSAV drug candidate for serious emerging viral infections.

On December 23, 2014, we announced results from a successful proof-of-concept study of galidesivir for the treatment of experimental Ebola virus infection in Rhesus macaques, conducted at USAMRIID. The primary goal of the study was to assess the effect of galidesivir treatment on survival through Day 41 in animals infected with Ebola virus. Dosing of placebo or galidesivir by i.m. injection was initiated 30-120 minutes after virus challenge and continued twice a day (“BID”) for 14 days. Animals were dosed with either placebo, 16 mg/kg of galidesivir BID or 25 mg/kg of galidesivir BID. Survival at day 41 in the 16 mg/kg BID group of galidesivir treated animals was 4 of 6 (66.7%, $p < 0.001$ compared to 0% survival in controls) and 6 of 6 in the 25 mg/kg BID group (100%, $p < 0.001$ compared to controls). The overall survival rate for galidesivir treated animals at day 41 was 10 of 12 (83%, $p < 0.001$ compared to controls). Preliminary evaluation of the quantity of virus in the blood showed an approximate 3-log reduction in Ebola virus RNA copies/mL of plasma, compared with control animals. This Rhesus macaque study was conducted following the completion, in November 2014, of a dose-ranging study of galidesivir for the experimental treatment of cynomolgus macaques infected with Ebola virus. The cynomolgus macaque study was designed to evaluate whether galidesivir showed a meaningful benefit for survival in Ebola virus non-human primate disease models and explore a dose range. In this study galidesivir demonstrated a statistically significant prolongation of survival for the animals at the highest dose regimen tested, but no animals survived beyond 21 days.

On March 7, 2016, results from a preclinical study of our antiviral galidesivir in interferon-receptor-deficient mice infected with Zika virus were presented at a World Health Organization conference in Geneva, Switzerland. The primary goal of the study was to assess the effect of galidesivir treatment on survival through Day 28 in interferon-receptor-deficient mice infected with the Zika virus. Galidesivir was administered by i.m. injection twice a day beginning four hours prior to virus challenge and continuing for eight days; two dose levels were tested. In the standard dose galidesivir group, 7 of 8 mice survived through Day 28. In the low dose galidesivir group (n=8), and in control groups administered vehicle placebo (n=8) or ribavirin at two dose levels (n=16); no animals survived to Day 28. Overall survival for the standard dose level of galidesivir was superior to both the placebo and the ribavirin treatment control groups ($p < 0.0001$). For both dose levels of galidesivir, median survival was superior to both control groups (>28 days for galidesivir standard dose and 23 days for low dose) compared to 14 to 17 days for controls.

Additional studies of galidesivir in the same mouse model were conducted at Utah State University. In one study, surviving mice that were previously treated with the standard dose of galidesivir after initial Zika virus challenge

were re-challenged with the Zika virus on Day 28, without additional galidesivir treatment. All the re-challenged mice survived through day 56 with no disease signs observed, indicating the development of effective immune responses. A further experiment using the same AG129 mouse model tested the delayed treatment with galidesivir after viral challenge. Groups of mice received galidesivir 150 mg/kg twice-daily by i.m. injection starting on days 1, 3, 5, or 7 post infection, or vehicle (control group). All galidesivir treated groups showed a statistically significant survival benefit compared to vehicle controls.

On October 29, 2016, galidesivir nonclinical results from a Zika virus infection model were presented in a late-breaker scientific session at IDWeek by Dr. James B. Whitney, PhD, Assistant Professor of Medicine, Harvard Medical School, and Principal Investigator in the Center for Virology and Vaccine Research at Beth Israel Deaconess Medical Center in Boston. Three groups of five healthy animals were inoculated with a Puerto Rico strain of Zika virus and administered either galidesivir by i.m. injection 200 mg/kg loading dose followed by 25 mg/kg BID for nine days, galidesivir single dose of 200 mg/kg, or vehicle control. Both galidesivir groups showed reduction in the proportion of animals viremic and in the amount of virus shed of into cerebrospinal fluid, saliva and urine. Galidesivir dosing in rhesus macaques was well-tolerated and offered significant protection against Zika virus infection. In a follow-on experiment, the same animals were rechallenged with a Thai strain of Zika virus, 72 days after initial inoculation. All animals demonstrated immune responses, and the initial treatments with galidesivir did not impair the generation of immunity.

Financial outlook for 2017

Based upon our development plans, expected operations and our awarded government contracts, we expect 2017 operating cash usage to be in the range of $30 to $50 million, and expect our total 2017 operating expenses to be in the range of $53 to $73 million. Our operating expense range excludes equity-based compensation expense due to the difficulty in accurately projecting this expense as it is significantly impacted by the volatility and price of our stock, as well as vesting of our outstanding performance-based stock options. Our operating cash forecast excludes any impact of our royalty monetization, hedge collateral posted or returned, and any other non-routine cash outflows or inflows. Our ability to remain within our operating expense and operating cash 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, the accompanying prospectus and in the documents incorporated herein by reference.

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.

The offering	
Common stock offered	5,294,118 shares of common stock
Option to purchase additional shares	Up to 794,117 shares of common stock
Common stock to be outstanding after the offering	79,313,398 shares of common stock
Use of proceeds	We intend to use the net proceeds of this offering for general corporate purposes, including future clinical development of BCX7353, continued development of our second generation HAE compounds, including for other indications, and the advancement of our other preclinical rare disease programs. See “Use of Proceeds.”
NASDAQ global select market symbol	BCRX
Dividend policy	We have never paid cash dividends and do not anticipate paying cash dividends in the foreseeable future.
Risk factors	See “Risk factors” beginning on page S-8 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 74,019,280 shares outstanding as of March 7, 2017 and excludes:

- 13,906,904 shares of common stock issuable upon the exercise of stock options outstanding under our Stock Incentive Plan as of February 28, 2017, at a weighted average exercise price of $6.21 per share;

- 220,373 shares of common stock issuable upon the vesting of restricted stock units outstanding as of February 28, 2017; and

- 458,478 additional shares of common stock reserved for issuance under our Stock Incentive Plan and 363,646 additional shares of common stock reserved for issuance under our Employee Stock Purchase Plan as of February 28, 2017.

Except as otherwise noted, all information in this prospectus supplement assumes no exercise of the outstanding stock options, no vesting of the outstanding restricted stock units and no exercise of the underwriters' option to purchase additional shares of our common stock.

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, liquidity, results of operations, or prospects, along with all of the other information included in our other filings with the SEC, before deciding to buy our common stock.

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 sustained 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 revenue 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 development process and related regulatory process are 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 reasonable commercial potential. We may suffer significant setbacks in pivotal pre-clinical studies and clinical trials (e.g. galidesivir, BCX7353, other kallikrein inhibitors and our other rare disease product candidates), even after earlier clinical trials show promising results. The development of our product candidates, including our 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. The pre-clinical and clinical data from our product candidates could cause us or regulatory authorities to interrupt, delay, modify or halt preclinical or clinical trials of a product candidate. Undesirable or inconclusive data or side effects in humans could also result in the FDA or foreign regulatory authorities refusing to approve the product candidate for any targeted indications. In addition, the FDA or other regulatory agencies may determine that study data from our product candidates necessitates additional studies or study designs which differ from our planned development strategy, and regulatory agencies may also require patient monitoring and testing or may implement restrictions or other conditions on our development activities, any of which could materially impact the cost and timing of our planned development strategy. 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 ability to maintain contact with patients to provide complete data after treatment;
- our product candidates may not prove to be either safe or effective;
- clinical protocols or study procedures may not be adequately designed or followed by the investigators;
- formulation improvements may not work as expected, which could negatively impact commercial demand for our product candidates;
- manufacturing or quality control problems could affect the supply of product candidates for our trials; and
- delays or changes in our planned development strategy, the regulations or guidelines, or other unexpected conditions or requirements of government 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 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 candidates.

We focus on rare diseases, which may create additional risks and challenges.

Because we focus on developing drugs as treatments for rare diseases, we may seek orphan drug, breakthrough therapy or fast track designations for our product candidates in the United States or the equivalent designations elsewhere in the world. Often, regulatory agencies have broad discretion in determining whether or not to grant such designations. We cannot guarantee that we will be able to receive orphan drug status from the FDA or equivalent regulatory designations elsewhere. We also cannot guarantee that we will obtain breakthrough therapy or fast track designation, which may provide certain potential benefits such as more frequent meetings with the FDA to discuss the development plan, intensive guidance on an efficient drug development program, and potential eligibility for rolling review or priority review. Even if we are successful in obtaining any such designation by the FDA or other regulatory agency for our product candidates, such designations may not lead to faster development or regulatory review or approval, and it does not increase the likelihood that our product candidates will receive marketing approval. We may not be able to obtain or maintain such designations for our product candidates, and our competitors may obtain these designations for their product candidates, which could impact our ability to develop and commercialize our product candidates or compete with such competitors, which may adversely impact our business, financial condition or results of operations.

Although we have received Sakigake designation for BCX7353 in Japan, we may not experience a faster development, review or approval process compared to the conventional process.

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

Progression of our product candidates through the clinical development process is dependent upon our trials indicating our product candidates have adequate safety and efficacy in the patients being treated by achieving pre-determined safety and efficacy endpoints according to the clinical trial protocols. Failure to achieve any of these endpoints in any of our programs, including BCX7353 and our other rare disease product candidates, 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 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 third 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 designing of enzyme inhibitors for development as product candidates;
- execution of certain 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;
- formulation improvement strategies and methods; and
- manufacturing the starting materials and drug substance required to formulate our products and the product candidates to be used in our clinical trials, toxicology studies and any potential commercial product.

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 product candidates 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, current Good Manufacturing Practices (“cGMP”) and current Good Clinical Practices, 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. If any of the foregoing risks are realized, our business, financial condition and results of operations could be materially adversely affected.

Because we have limited manufacturing experience, we depend on third-party manufacturers to manufacture our product, product candidates and the materials for our product candidates. Often, especially early in the development and commercialization process, we have only one source for manufacturing. If we cannot rely on existing 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 a very limited number of third-party manufacturers to manufacture the materials required for our product, 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, which may be the only manufacturer we have engaged for a particular product, may encounter difficulties with meeting our requirements, including but not limited to problems involving:

- inconsistent production yields;
- product liability claims or recalls of commercial product;
- 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;
- potential impurities in our drug substance or products that could affect availability of product for our clinical trials or future commercialization;
- poor quality control and assurance or inadequate process controls; and
- lack of compliance or cooperation with regulations and specifications or requests set forth by the FDA or other foreign regulatory agencies, particularly associated with peramivir, BCX7353, galidesivir and our early stage compounds.

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, 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 may at any time 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 any of which could be costly to the Company and could result in a delay or shortage of product.

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 product candidates are manufactured by a limited group of suppliers, including 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.

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 currently target. 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 potential product candidates for 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 are performing research on or developing products for the treatment of several rare disorders, including HAE, as well as developing broad spectrum antivirals for use 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 the current neuraminidase inhibitors marketed by GSK and Roche for influenza; CINRYZE®, KALBITOR® and FIRAZYR®, marketed by Shire Pharmaceuticals, Inc. for HAE; and BERINERT®, marketed by CSL for HAE. Therapeutic products with potentially promising data to treat Ebola include Mapp Biopharmaceutical, Inc.'s ZMapp (antibody-based) and Gilead Sciences, Inc.'s product currently under development (small molecule), both of which have been used in Ebola infected patients. 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 molecules in development in the fields of HAE and in other therapeutic areas where we have discovery and development efforts ongoing. If one or more of our competitors' products or programs are successful, the market for our products may be reduced or eliminated.

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

- capital resources;

- research and development resources, including personnel and technology;

- regulatory experience;

- preclinical study and clinical testing experience;

- manufacturing and marketing experience; and

- production facilities.

Any of these competitive factors could impede our funding efforts, render technology and product candidates noncompetitive or eliminate or reduce demand for our product candidates.

We face risks related to our government-funded programs; if BARDA/HHS or NIAID/HHS were to eliminate, reduce or delay funding from our contracts, this would have a significant negative impact on the programs associated with such funding and could 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 galidesivir program. 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.

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. 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 completed work under a contract with BARDA/HHS for the development of our neuraminidase inhibitor, RAPIVAB. We also have entered into contracts with BARDA/HHS and NIAID/HHS for the development of galidesivir as a treatment for diseases caused by RNA pathogens, including Marburg virus disease and Ebola 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 a number of extraordinary provisions that would not typically be found in commercial contracts and which may create a disadvantage and additional risks to us as compared to competitors that do not rely on U.S. Government contracts.

These risks include the ability of the U.S. Government to unilaterally:

- terminate or reduce the scope of our contract with or without cause;
- interpret relevant regulations (federal acquisition regulation clauses);
- require performance under circumstances which may not be favorable to us;
- require an in process review where the U.S. Government will review the project and its options under the contract;
- control the timing and amount of funding, which impacts the development progress of our programs; and
- audit and object to our contract-related costs and fees, including allocated indirect costs.

Our government contracts with BARDA/HHS and NIAID/HHS have termination and audit provisions which create additional risks to us.

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 does not permit these recoveries under default provisions. 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 completed BARDA/HHS peramivir contract have been performed and concluded through fiscal 2009; all subsequent fiscal years are still open and auditable. Audits under the active BARDA/HHS and NIAID/HHS galidesivir contracts may occur at the election of the U.S. Government and have been concluded through fiscal 2013. 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 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 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, product supply obligations, post approval commitments for RAPIVAB, 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 discovery activities, pre-clinical and clinical trials, the related development, manufacturing, regulatory approval process requirements, and the 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 NIAID/HHS and BARDA/HHS for galidesivir or from other new partnerships with third parties for the development of our product candidates, including BCX7353 and our other rare disease product candidates; the commercial success of peramivir achieved by our partners; the amount or profitability of any orders for peramivir or galidesivir by any government agency or other party; the progress and results of our current and proposed clinical trials for our most advanced product candidates, including BCX7353 and our other rare disease product candidates; the progress made in the manufacture of our lead products and the progression of our other programs.

We expect that we will be required to raise additional capital to complete the development and commercialization of our current product candidates and we may seek to raise capital at any time. Additional funding, whether through additional sales of securities, additional borrowings, or collaborative arrangements with partners, 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. Additional borrowings may subject us to more restrictive covenants than are currently applicable to us under our September 23, 2016, Senior Credit Facility with an affiliate of MidCap Financial Services, LLC, as administrative agent (the “Senior Credit Facility”). 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, incur additional borrowings, 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 post approval studies for RAPIVAB, the progress, timeline and ultimate outcome of our kallikrein inhibitors, including the BCX7353 program (including, but not limited to, formulation progress, phase 3 trials, long-term human safety studies, and the timing of carcinogenicity or other required studies), the progress of our other rare disease product candidates, funding for and continued successful development of galidesivir, and the progress of our early discovery programs. 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 price of our common stock and may decrease opportunities to raise capital in the capital or credit markets, and further 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.

We may not be able to continue as a going concern if we do not obtain additional capital.

We have sustained operating losses for the majority of our corporate history and expect that our 2017 expenses will exceed our 2017 revenues. We expect to continue to incur operating losses and negative cash flows until revenues reach a level sufficient to support ongoing operations.

Our liquidity needs will be largely determined by the success of operations in regards to the progression of our product candidates in the future. Our plans to alleviate the doubt regarding our ability to continue as a going concern primarily include our ability to control the timing and spending on our research and development programs and raising additional funds through equity financings. We also may consider other plans to fund operations including: (1) securing or increasing U.S. Government funding of our programs, including obtaining procurement contracts; (2) out-licensing rights to certain of our products or product candidates, pursuant to which the we would receive cash milestones; (3) raising additional capital through debt financings or from other sources; (4) obtaining additional product candidate regulatory approvals, which would generate revenue, milestones and cash flow; (5) reducing spending on one or more research and development programs by discontinuing development; and/or (6) restructuring operations to change our overhead structure.

There can be no assurance that any of our plans will be successful or that additional capital will be available to us on reasonable terms, or at all, when needed. If we are unable to obtain sufficient additional capital, we may be forced to curtail operations, delay or stop ongoing clinical trials, cease operations altogether or file for bankruptcy.

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 relationships 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 in Japan, Taiwan and South Korea. Most recently we have established a collaborative relationship with Seqirus UK Limited for RAPIVAB on a worldwide basis other than Israel, Japan, Korea and Taiwan. 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, including post approval clinical commitments, 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;

- we or our partners may not devote sufficient capital or resources towards our product candidates; and

- we or 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 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 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 do not have a great deal of experience in commercializing our products or technologies, and our future revenue generation is uncertain.

We do not have a great deal of experience in commercializing our product candidates or technologies. We currently have limited marketing and commercial capability, no direct or third-party sales force and limited distribution capabilities. We may be unable to establish or sufficiently increase these capabilities for products we currently, or plan to, commercialize. In addition, our revenue from collaborative agreements may be dependent upon the status of our preclinical and clinical programs.

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

- we or our collaborators may fail to successfully complete clinical trials, or satisfy post-marketing commitments, sufficient to obtain and keep 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

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

Commercialization of peramivir by our partners is subject to the potential commercialization risks described herein and numerous additional risks. Any potential revenue benefits to us in the form of milestone payments, royalties or other consideration are highly speculative.

Commercialization success of peramivir is uncertain and is subject to all the risks and uncertainties disclosed in our other risk factors relating to drug development and commercialization. In addition, commercialization of peramivir products is subject to further risks and may be negatively impacted by a number of factors, including, but not limited to, the following:

- peramivir may not prove to be adequately safe and effective for market approval in markets other than the United States, Japan, Korea and Taiwan;

- necessary funding for post-marketing commitments and 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 ;

- a limited number of governmental entities are expected to be the primary potential stockpiling 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;

- government and third party payors may not provide sufficient coverage or reimbursement which would negatively impact the demand for peramivir ;

- we may not be able to supply commercial material to our partners and our partners may not be able to maintain or establish sufficient and acceptable commercial manufacturing, either directly or through third-party manufacturers;

- the commercial demand and acceptance for peramivir by healthcare providers and by patients may not be sufficient to result in substantial revenues of peramivir to our partners and may result in little to no milestones or royalties to us;

- effectiveness of marketing and commercialization efforts for peramivir by our partners;
- market satisfaction with existing alternative therapies;
- perceived efficacy relative to other available therapies;
- disease prevalence;
- cost of treatment;
- pricing and availability of alternative products;
- marketing and sales activities of competitors;
- shifts in the medical community to new treatment paradigms or standards of care; and
- relative convenience and ease of administration.

We are subject to various federal and state laws related to RAPIVAB and other products under development and, if we or our partners do not comply with these regulations, we could face substantial penalties.

Our or our partners' activities related to RAPIVAB, or any of our other products under development and following their regulatory approval, are subject to regulatory and law enforcement authorities in addition to the FDA, including the Federal Trade Commission, the Department of Justice, and state and local governments. In the case of our collaboration with SUL, although SUL is responsible for RAPIVAB marketing and commercialization efforts, we continue to carry certain risks associated with RAPIVAB because we hold the RAPIVAB NDA. For example, we are responsible for reporting adverse drug experiences, we have responsibility for certain post-approval studies, we may have responsibilities and costs related to a recall or withdrawal of RAPIVAB from sale, we may incur liability associated with RAPIVAB manufacturing contracted by us or in support of any of our partners, we are required to maintain records and provide data and reports to regulatory agencies related to RAPIVAB (e.g. risk evaluation and mitigation strategies, track and trace requirements, adverse events), and we may incur certain promotional regulatory and government pricing risks, all of which could have a material adverse impact on our operations and financial condition.

In addition, we are subject to the federal physician sunshine act and certain similar physician payment and drug pricing transparency legislation in various states. We are also subject to various federal and state laws pertaining to health care "fraud and abuse," including both federal and state anti-kickback and false claims laws. These laws regulate our or our partners' operations, sales and marketing practices, price reporting, and relationships with physicians and other customers and third-party payors. Anti-kickback laws generally prohibit a manufacturer from soliciting, offering, receiving, or paying any remuneration to generate business, including the purchase or prescription of a particular drug. Although the specific provisions of these laws vary, their scope is generally broad and there may be no regulations, guidance or court decisions that clarify how the laws apply to particular industry practices. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented for payment to third party payors (including Medicare and Medicaid) claims for reimbursement or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. The sunshine provisions apply to manufacturers with products reimbursed under certain government programs and require those manufacturers to disclose annually to the federal government certain payments made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as, ownership and investment interests held by physicians (as defined above) and their immediate family members. State laws may also require disclosure of pharmaceutical pricing information and marketing expenditures. Although we seek to comply with these statutes, it is possible that our practices, or those of our partners, might be challenged under health care fraud and abuse, anti-kickback, false claims or similar laws. Violations of the physician sunshine act and similar state legislation or the fraud and abuse laws may be punishable by civil or criminal sanctions, including fines and civil monetary penalties, and future exclusion from participation in government healthcare programs.

We have a number of outstanding post-marketing commitments to the FDA that we retain, despite our partnership with SUL, which we may not complete successfully or on time for any number of reasons, including but not limited to lack of funds to complete the studies and insufficient interest by appropriate sites, investigators or study subjects. For example, as a condition of the approval of RAPIVAB, we are required to complete a pediatric patient study of RAPIVAB and to submit the final results of this clinical trial to the FDA. Depending on the outcome of this clinical trial, we may be unable to expand the indication for RAPIVAB or we may be required to include specific warnings or limitations on dosing this product, which could negatively impact sales of RAPIVAB and negatively impact our

relationship with our partner. We may be subject to penalties if we fail to comply with post-approval legal and regulatory requirements and our products could be subject to continual recordkeeping and reporting requirements, review and periodic inspections by the FDA and other regulatory bodies. Regulatory approval of a product may be subject to limitations on the indicated uses for which the product may be marketed or to the other restrictive conditions of approval that limit our ability to promote, sell or distribute a product. Furthermore, the approval of RAPIVAB and any other future product candidates may be subject to requirements for costly post-marketing testing and surveillance to monitor its safety or efficacy.

Advertising and promotion are subject to stringent FDA rules and oversight and as the holder of the NDA we may be held responsible for any advertising and promotion conducted by our partner that is not in compliance with the rules and regulations. In particular, the claims in all promotional materials and activities must be consistent with the FDA approvals for approved products, and must be appropriately substantiated and fairly balanced with information on the safety risks and limitations of the products. Adverse event information concerning approved products must be reviewed and as the NDA holder of RAPIVAB we are required to make expedited and periodic adverse event reports to the FDA and other regulatory authorities.

In addition, the research, manufacturing, distribution, sale and promotion of products are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services, other divisions of the U.S. Department of Health and Human Services, the U.S. Department of Justice and individual U.S. Attorney offices within the Department of Justice, and state and local governments. Until we can successfully transfer the pricing responsibilities to our partner, we remain responsible for pricing and rebate programs. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Veterans Health Care Act of 1992, as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to federal and state healthcare false claims and fraud and abuse laws, as well as consumer protection and unfair competition laws.

If our operations with respect to RAPIVAB or our other products that are subject to healthcare laws and regulations are found to be in violation of any of the healthcare fraud and abuse laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with all applicable federal and state fraud and abuse laws may be costly.

We and our partners may be subject to new legislation, regulatory proposals and healthcare payor initiatives that may increase our costs of compliance and adversely affect our or our partners' ability to market our products, including RAPIVAB, obtain collaborators and raise capital.

The Patient Protection and Affordable Care Act, or PPACA, made extensive changes to the delivery of health care in the U.S. The PPACA included numerous provisions that affect pharmaceutical companies, some of which became effective immediately and others of which have taken effect over the past several years. For example, the PPACA expanded health care coverage to the uninsured through private health insurance reforms and an expansion of Medicaid. The PPACA also imposed substantial costs on pharmaceutical manufacturers, such as an increase in liability for rebates paid to Medicaid, new drug discounts that must be offered to certain enrollees in the Medicare prescription drug benefit, an annual fee imposed on all manufacturers of brand prescription drugs in the U.S., and an expansion of an existing program requiring pharmaceutical discounts to certain types of hospitals and federally subsidized clinics. The PPACA also contains cost containment measures that could reduce reimbursement levels for health care items and services generally, including pharmaceuticals. It also required reporting and public disclosure of payments and other transfers of value provided by pharmaceutical companies to physicians and teaching hospitals.

We expect that the current presidential administration and U.S. Congress will seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the PPACA. There is still significant uncertainty with respect to the impact that the current presidential administration and the U.S. Congress may have on the PPACA, if any, and any changes will likely take time to unfold. As such, we cannot predict what effect the PPACA or other healthcare reform initiatives

that may be adopted in the future will have on our business.

The continuing efforts of the government, insurance companies, managed care organizations and other payors of health care services to contain or reduce costs of health care could result in decreased net revenues from our pharmaceutical products and decrease potential returns from our development efforts. In addition, pharmaceutical and device manufacturers are also required to report and disclose certain payments and transfers of value to, and investment interests held by, physicians and their immediate family members during the preceding calendar year. Failure to submit required information may result in civil monetary penalties for payments, transfers of value or ownership or investment interests not reported in an annual submission. Compliance with the PPACA and state laws with similar provisions is difficult and time consuming, and companies that do not comply with these state laws face civil penalties. Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Such a challenge could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In addition, there have been a number of other legislative and regulatory proposals aimed at changing the pharmaceutical industry. In particular, legislation has been enacted in certain states and at a federal level that requires development of an electronic pedigree to track and trace each prescription drug at the saleable unit level through the distribution system. Compliance with these electronic pedigree requirements may increase our operational expenses and impose significant administrative burdens. In addition, our compliance may be deemed insufficient and we could face a material adverse effect on our business, financial condition, results of operations and growth prospects. As a result of these and other new proposals, we may determine to change our current manner of operation, provide additional benefits or change our contract arrangements, any of which could have a material adverse effect on our business, financial condition and results of operations.

Adequate coverage and reimbursement is critical to the commercial success of RAPIVAB or any other product that we might bring to market. Recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, reform government program reimbursement methodologies. Third-party payors are increasingly challenging the prices charged for medical products and services and, in some cases, imposing restrictions on the coverage of particular drugs. Many third-party payors negotiate the price of medical services and products and develop formularies which establish pricing and reimbursement levels. Exclusion of a product from a formulary can lead to its sharply reduced usage in the third-party payor's patient population. The process for obtaining coverage can be lengthy and costly, and we expect that it could take several months before a particular payor initially reviews our product and makes a decision with respect to coverage. For example, third-party payors may require cost-benefit analysis data from us in order to demonstrate the cost-effectiveness of RAPIVAB or any other product we might bring to market. For any individual third-party payor, we may not be able to provide data sufficient to gain reimbursement on a similar or preferred basis to competitive products, or at all which may have a material adverse effect on our business, financial condition and results of operations.

There are risks related to the potential government use or sale of peramivir (RAPIVAB).

United States Government use or sale of RAPIVAB in emergency situations, or otherwise, may result in the use of RAPIVAB outside of its approved use. To the extent that RAPIVAB is used as a treatment for influenza by the U.S. Government or peramivir by any other government entity, there can be no assurance that it will prove to be generally safe, well-tolerated and effective. Such government use of RAPIVAB/peramivir may create certain liabilities for us or our partners in the case of government use outside of the U.S. 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 RAPIVAB in the U.S. or peramivir 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 any use or will achieve market approval in additional countries. In the event that any emergency use or market approval is granted, there is no assurance that any government order or commercialization of peramivir in any countries will be substantial or will be profitable to us. In addition, the sale of peramivir , emergency use or other use of peramivir in any country may create

certain liabilities for us and our partners.

If we or our partners do not obtain and maintain governmental approvals for our product candidates 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 product candidates. If we or our partners are unable to receive regulatory approval and do not market or sell our future product candidates, we will never receive any revenue from such product sales. In the United States, we or our partners must obtain FDA approval for product candidates 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. 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 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-approval 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;
- 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.

Royalties and milestone payments from Shionogi under our 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 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. As of September 1, 2014, the payments from Shionogi were insufficient for Royalty Sub to service its obligations under the PhaRMA Notes, resulting in an event of default with respect to the PhaRMA Notes. As a result of this event of default, the holders of the PhaRMA Notes may be able to pursue acceleration of the PhaRMA Notes and foreclose on the collateral securing the PhaRMA Notes and our equity interest in Royalty Sub and may exercise other remedies available to them under the indenture or other documents related to 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, we may incur legal costs and we might otherwise be adversely affected.

Because an event of default has occurred under the PhaRMA Notes, the holders of the PhaRMA Notes may be able to pursue acceleration of the PhaRMA Notes and foreclose on the collateral securing the PhaRMA Notes and our equity interest in Royalty Sub, in which case we may not realize the benefit of future royalty payments that might otherwise accrue to us following repayment of the PhaRMA Notes and we could otherwise be adversely affected.

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. 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. As Royalty Sub has been unable to service its obligations under the PhaRMA Notes and an event of default has occurred under the PhaRMA Notes, the holders of the PhaRMA Notes may be able to pursue acceleration of the PhaRMA Notes and foreclose on the collateral securing the PhaRMA Notes and our equity interest in Royalty Sub and may exercise other remedies available to them under the indenture or other documents related to 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, we may incur legal costs and we might otherwise be adversely affected.

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 foreign currency hedge agreement, we may be required to pay an annual premium in the amount of $2.0 million in each May 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. We are required to maintain a foreign currency hedge at 100 yen per dollar under the agreements governing the PhaRMA Notes.

Our Senior Credit Facility contains restrictions that limit our flexibility in operating our business. We may be required to make a prepayment or repay the outstanding indebtedness earlier than we expect if a prepayment event or an event of default occurs, including a material adverse change with respect to us, which could have a material adverse effect on our business.

The Senior Credit Facility contains various covenants that limit our ability to engage in specified types of transactions. These covenants limit our ability to, among other things:

- convey, sell, lease, license, transfer or otherwise dispose of certain parts of our business or property;
- change the nature of our business;
- liquidate or dissolve;
- enter into certain change in control or acquisition transactions;
- incur or assume certain debt;
- grant certain types of liens on our assets;

- modify, liquidate or transfer assets in certain collateral accounts;
- pay dividends or make certain distributions to our stockholders;
- make certain investments;
- enter into material transactions with affiliates; and
- modify existing debt or collaboration arrangements.

The restrictive covenants contained in the Senior Credit Facility could cause us to be unable to pursue business opportunities that we or our stockholders may consider beneficial without the lender's permission or without repaying all Senior Credit Facility obligations.

A breach of any of these covenants could result in an event of default under the Senior Credit Facility. An event of default will also occur if, among other things, a material adverse change in our business, operations or condition occurs, which could potentially include negative results in clinical trials, or a material impairment of the prospect of our repayment of any portion of the amounts we owe under the Senior Credit Facility occurs. In the case of a continuing event of default under the agreement, the lender could elect to declare all amounts outstanding to be immediately due and payable, proceed against the collateral in which we granted to the lender a security interest under the Senior Credit Facility, or otherwise exercise the rights of a secured creditor. Amounts outstanding under the Senior Credit Facility are secured by substantially all of our assets and those of our subsidiaries, excluding certain specified assets but including proceeds from those assets.

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.

We may be involved in lawsuits to protect or enforce our patents, the patents of our partners or our other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive and time-consuming and unsuccessful. An adverse result in any litigation or defense proceeding could put one or more of our patents at risk. 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 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 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.

Our failure to comply with data protection laws and regulations could lead to government enforcement actions and significant penalties against us and adversely impact our operating results.

European Union ("EU") Member States, Switzerland and other countries have adopted data protection laws and regulation, which impose significant compliance obligations. For example, the EU Data Protection Directive, as implemented into national laws by the EU Member States, imposes strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. Data protection authorities from the different EU Member States may interpret the EU Data Protection Directive and national laws differently, which adds to the complexity of processing personal data in the European Union, and guidance on implementation and compliance practices is often updated or otherwise revised. Our failure to comply with these laws and regulations could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

We are subject to periodic litigation, which could result in losses or unexpected expenditure of time and resources.

From time to time, we may be called upon to defend ourselves against lawsuits relating to our business. Due to the inherent uncertainties in litigation, we cannot accurately predict the ultimate outcome of any such proceedings. An unfavorable outcome in any such proceedings could have an adverse impact on our business, financial condition and results of operations. If our stock price is volatile, we may become involved in securities class action lawsuits in the future. Any litigation in the future, regardless of its merits, could result in substantial costs and a diversion of management's attention and resources that are needed to successfully run our business.

We face an inherent risk of liability in the event that the use or misuse of our products results in personal injury or death and our product liability insurance coverage may be insufficient.

If the use or misuse of peramivir or any other regulatory body-approved products we or a partner may sell in the future harms people, we may be subject to costly and damaging product liability claims brought against us by consumers, healthcare providers, pharmaceutical companies, third-party payors or others. The use of our product candidates in clinical trials, including post marketing clinical studies, could also expose us to product liability claims. We cannot predict all of the possible harms or side effects that may result from the use of our products or the testing of product candidates and, therefore, the amount of insurance coverage we currently may not be adequate to cover all liabilities or defense costs we might incur. A product liability claim or series of claims brought against us could give rise to a substantial liability that could exceed our resources. Even if claims are not successful, the costs of defending such claims and potential adverse publicity could be harmful to 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 commercial sale of peramivir and 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.

A significant disruption in our information technology systems or a cyber-security breach could adversely affect our business.

We are increasingly dependent on information technology systems to operate our business. Like other companies in our industry, our networks and infrastructure may be vulnerable to cyber-attacks or intrusions, including by computer hackers, foreign governments, foreign companies or competitors, or may be breached by employee error, malfeasance or other disruption. A breakdown, invasion, corruption, destruction or interruption of critical information technology systems could negatively impact operations. If our systems are damaged, fail to function properly or otherwise become unavailable, we may incur substantial costs to repair or replace them, and we may experience loss of critical data and interruptions or delays in our ability to perform critical functions, which could adversely affect our business, financial condition or results of operations. Any compromise of our data security could also result in a violation of applicable privacy and other laws, significant legal and financial exposure, damage to our reputation, loss or misuse of the information and a loss of confidence in our data security measures, which could harm our business. There can be no assurance that our efforts to protect our data and information technology systems will prevent breakdowns or breaches in our systems, or those of third parties with which we do business, and any such events could adversely affect our business.

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 commercialization of our products and the related 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, commercial, 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. Our top ten stockholders own more than 50% of BioCryst and can individually, and as a group, influence our operations based upon their concentrated ownership. 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 cause the value of an 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 December 31, 2016, the 52-week range of the market price of our stock was from $1.63 to $10.24 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;
- 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 March 7, 2017, there were 74,019,280 shares of our common stock outstanding. 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 February 28, 2017, there were 14,127,277 stock options and restricted stock units outstanding, 458,478 shares available for issuance under our Amended and Restated Stock Incentive Plan, and 363,646 shares available for issuance under our Employee Stock Purchase Plan. In addition, we could also make equity compensation grants outside of our Stock Incentive Plan. The shares underlying existing stock options, restricted stock units 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 anticipate entering into a Registration Rights Agreement with entities affiliated with Baker Bros. Advisors LP (the "Baker Entities") to provide that, if requested, we will register the shares of our common stock beneficially owned by the Baker Entities for resale under the Securities Act. Our registration obligations, as proposed, are expected to cover all shares now held or hereafter acquired by the Baker Entities, to be in effect for up to ten years, and to include our obligation to facilitate certain underwritten public offerings of our common stock by the Baker Entities in the future. If the Baker Entities, by exercising these registration and/or underwriting rights or otherwise, sell a large number of our shares, or the market perceives that the Baker Entities intend to sell a large number of our shares, this could adversely affect the market price of our common stock.

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.

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.

Use of proceeds

We estimate that we will receive net proceeds of approximately $41.9 million from the sale of shares of our 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 $48.1 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering for general corporate purposes, including future clinical development of BCX7353, continued development of our second generation HAE compounds, including for other indications, and the advancement of our 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.

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Dilution

As of December 31, 2016, our net tangible book value was approximately $11.5 million, or approximately $0.16 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 73,781,854 shares of our common stock outstanding as of December 31, 2016.

Investors participating in this offering will incur immediate, substantial dilution. After giving effect to our receipt of approximately $41.9 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, our as adjusted net tangible book value as of December 31, 2016 would have been $53.3 million, or $0.67 per share. This amount represents an immediate increase in net tangible book value of $0.51 per share of our common stock to existing stockholders and an immediate dilution in net tangible book value of $7.83 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		$ 8.50
Net tangible book value per share as of December 31, 2016	$ 0.16	
Increase in net tangible book value per share attributable to new investors	$ 0.51	
Net tangible book value per share as of December 31, 2016 after giving effect to this offering		$ 0.67
Dilution in net tangible book value per share to new investors		$ 7.83

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 $0.75 per share, which amount represents an immediate increase in as adjusted net tangible book value of $0.59 per share of our common stock to existing stockholders and an immediate dilution in net tangible book value of $7.75 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 73,781,854 shares of our common stock outstanding as of December 31, 2016 and exclude:

- 12,094,470 shares of common stock issuable upon the exercise of stock options outstanding under our Stock Incentive Plan as of December 31, 2016, at a weighted average exercise price of $6.55 per share;
-

434,573 shares of common stock issuable upon the vesting of restricted stock units outstanding under our Stock Incentive Plan as of December 31, 2016; and

- 2,274,512 additional shares of common stock reserved for issuance under our Stock Incentive Plan and 421,748 additional shares of common stock reserved for issuance under our Employee Stock Purchase Plan as of December 31, 2016.

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.

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, 2015		
1st Quarter	$12.71	$7.85
2nd Quarter	$16.43	$8.50
3rd Quarter	$16.83	$10.26
4th Quarter	$12.88	$8.01
Year ended December 31, 2016		
1st Quarter	$10.24	$1.63
2nd Quarter	$4.03	$2.49
3rd Quarter	$5.80	$2.82
4th Quarter	$7.56	$3.75
Year ending December 31, 2017		
1st Quarter (through March 9, 2017)	$8.86	$4.20

The last reported sale price of our common stock on the NASDAQ Global Select Market on March 9, 2017 was $8.86 per share. As of March 7, 2017 there were approximately 182 holders of record of our common stock.

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

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	3,705,882
Piper Jaffray & Co.	1,058,824
JMP Securities LLC	529,412
Total	5,294,118

The underwriters are committed to purchase all the shares of common stock 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 shares of common stock 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 $0.306 per share. After the offering of the shares to the public, 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 794,117 additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus supplement to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, 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 $0.51 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 exercise of option to purchase additional shares	**With full exercise of option to purchase additional shares**
Per Share	$ 0.51	$ 0.51
Total	$ 2,700,000	$ 3,105,000

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 $500,000. We have agreed to reimburse the underwriters for all expenses related to qualification of our common stock under states securities laws and the clearing of this offering with the Financial Industry Regulatory Authority. In addition, we have granted to J.P. Morgan Securities LLC the right to participate in any public offering of our common stock until March 21, 2018, subject to certain limitations.

A prospectus supplement 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 representative to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

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 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 60 days after the date of this prospectus supplement (the “Restricted Period”), 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 or the vesting of restricted stock units granted under our existing management incentive plans.

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 60 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) or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above 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. Each of the lock-up agreements contain certain exceptions, including the establishment of a contract or plan meeting the requirements of Rule 10b5-1 under the Exchange Act for the transfer or sale of shares of common stock after the expiration of a period of 60 days after the date of this

prospectus supplement, provided that such plan does not provide for the sale of common stock during the Restricted Period and, provided further, that no filing by any party under the Exchange Act, or other public announcement regarding the establishment of such plan, shall be required or shall be voluntarily made during the Restricted Period; the transfer or sale of shares of common stock pursuant to a 10b5-1 plan that has been entered into by certain of our executive officers prior to the date hereof and provided any filing required or voluntarily made under the Exchange Act shall note that such transaction was conducted pursuant to a pre-established 10b5-1 plan; or the disposition of shares of common stock to the Company for the purpose of covering tax liabilities and/or the exercise price in connection with the exercise of options to purchase shares of common stock or the vesting of restricted stock units or shares of restricted stock, in each case awarded pursuant to our existing equity compensation plans, provided that any required filing under the Exchange Act shall clearly indicate the circumstances of such disposition.

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

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 to purchase additional shares 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 the 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, 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 representative of the underwriters purchases common stock in the open market in stabilizing transactions or to cover short sales, the representative 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 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.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant Member State"), no offer of shares may be made to the public in that Relevant Member State other than:

A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;

B. 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 Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representative; or

C. in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require the Company or the representative to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representative has been obtained to each such proposed offer or resale.

The Company, the representative and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus supplement has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly, any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus supplement may only do so in circumstances in which no obligation arises for the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation

arises for the Company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression “an offer to the public” in relation to any shares 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 shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression “Prospectus Directive” means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression “2010 PD Amending Directive” means Directive 2010/73/EU.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this prospectus supplement is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the “Order”) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”).

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this prospectus supplement or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this prospectus supplement relates to may be made or taken exclusively by relevant persons. Any person in the United Kingdom that is not a relevant person should not act or rely on this prospectus supplement or any of its contents.

Notice to Prospective Investors in Canada

The shares of common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the shares of common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (**NI 33-105**), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

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.

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, 2016, and the effectiveness of our internal control over financial reporting as of December 31, 2016, 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, 2016 are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

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 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 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, 2016, filed with the SEC on February 27, 2017;

- The information in our Definitive Proxy Statement, filed with the SEC on April 11, 2016, set forth under the captions "Items to be Voted on — 1. Election of Directors," "Executive Officers," "Section 16(a) Beneficial Ownership Reporting Compliance," "Corporate Governance," "Compensation Discussion and Analysis," "Summary Compensation Table," "Grants of Plan-Based Awards in 2015," "Outstanding Equity Awards at December 31, 2015," "2015 Option Exercises and Stock Vested," "Potential Payments Upon Termination or Change in Control," "2015 Director Compensation," "Compensation Committee Interlocks and Insider Participation," "Compensation Committee Report," "Equity Compensation Plan Information," "Security Ownership of Certain Beneficial Owners and Management," "Certain Relationships and Related Transactions," and "Items to be Voted on — 2. Ratification of Appointment of Independent Registered Public Accountants";

- Our Current Report on Form 8-K filed with the SEC on February 27, 2017; and

- The description of our common stock 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 reference herein and to be a part of this prospectus supplement from the date of filing of such documents. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed above or filed in the future, that are not deemed “filed” with the SEC, including 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

Neither we nor the underwriters have authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus prepared by us or on our behalf. We and the underwriters take no responsibility for, or can provide no assurances as to the reliability of, any information other than the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus prepared by us or on our behalf. If you are in a jurisdiction where offers to sell, or solicitations of offers to purchase, the securities offered by this document are unlawful, or if you are a person to whom it is unlawful to direct these types of activities, then the offer presented in this document does not extend to you.

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PROSPECTUS

$150,000,000

Common Stock
Preferred Stock
Depositary Shares
Stock Purchase Contracts
Warrants
Units

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

We have not authorized anyone else to make additional representations or to provide you with information other than information provided or incorporated by reference in this prospectus or any prospectus supplement. We take no responsibility for, and can provide no assurances as to the reliability of, any other information that others may give you or representations that others may make. 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.

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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.

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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 April 18, 2016.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, using a "shelf" registration or continuous offering process. Under this registration statement, we may sell any combination of the securities described in this prospectus from time to time, either separately or in units, in one or more offerings. Together, these offerings may total up to $150.0 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 may add, update or change information contained in this prospectus and will also include the following information:

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

If there is any inconsistency between the information in this prospectus and any prospectus supplement, you should rely on the information in the prospectus supplement. You should read both this prospectus and any prospectus supplement together with the additional information described under the heading "Where You Can Find More Information." The registration statement containing this prospectus, including the exhibits to the registration statement, provides additional information about us and the securities offered under this prospectus. The registration statement, including the exhibits, can be read at the SEC's website or at the SEC's offices referenced under the heading "Where You Can Find More Information."

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

trademarks or trademarks of their respective holders.

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PROSPECTUS SUMMARY

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

Business of BioCryst Pharmaceuticals, Inc.

We are a biotechnology company that designs, optimizes and develops novel small molecule drugs that block key enzymes involved in the pathogenesis of diseases. We focus on the treatment of rare diseases in which significant unmet medical needs exist and that align 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.

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. For more information about us, please visit our website at http://www.biocryst.com. The information on our web site is not incorporated by reference into this prospectus.

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 business, 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. Any subsequent prospectus supplement may contain a discussion of additional risks applicable to an investment in us and the particular type of securities we are offering under such prospectus supplement. 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.

INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any subsequent prospectus supplement, 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, any subsequent prospectus supplement 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," "pre "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 to the extent applicable, post-marketing commitments, for our HAE product candidates, RAPIVAB, BCX4430, and our other research and development efforts;
- the further preclinical development, clinical development, commercialization, or post-marketing studies by either us or partners of our product candidates and products, including our HAE program, RAPIVAB, BCX4430, and early stage discovery programs;
- 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") and the National Institute of Allergy and Infectious Diseases within the United States Department of Health and Human Services ("NIAID/HHS") for the development of BCX4430;
- the potential for government stockpiling orders of RAPIVAB, additional regulatory approvals of RAPIVAB or milestones royalties or profit from commercial sales of RAPIVAB by us or our partners;
- the potential use of RAPIVAB as a treatment for H1N1, H5N1, and H7N9 or other strains of influenza;
- the implementation of our business model, strategic plans for our business, products, 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 Sequirus UK Limited ("SUL") for RAPIVAB, Mundipharma International Holdings Limited ("Mundipharma") for forodesine and Shionogi & Co., Ltd. ("Shionogi") and Green Cross Corporation ("Green Cross") for peramivir in their territories;
- JPR Royalty Sub LLC's ("Royalty Sub") ability to service its payment obligations in respect of the PhaRMA Notes, 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;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our products, product candidates and technology;
- 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;
- the timing or likelihood of regulatory filings or regulatory agreements, deferrals 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, any subsequent prospectus supplement 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 future amendments we make to those filings or future filings with the SEC.

USE OF PROCEEDS

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

- funding development, manufacturing and regulatory activities for avoralstat;
- funding development, manufacturing and regulatory activities for BCX7353;
- funding development, manufacturing and regulatory activities for other second generation HAE compounds;
- post-approval commitments such as the pediatric study for RAPIVAB™;
- pre-launch commercial activities for the HAE market;
- the advancement of development activities on other rare disease targets;
- funding our research and development efforts;
- capital expenditures and enhancing our laboratory facilities; and
- general working capital needs.

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 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 net proceeds in investment grade interest bearing instruments.

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 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, of which 200,000 shares are designated Series B Junior Participating Preferred Stock with a par value of $0.001 per share. On February 24, 2016, there were 73,629,816 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 office in the United States and a combined capital and surplus of at least $50,000,000. Subject to the terms of the deposit agreement, each owner of a depositary share will be entitled, in proportion to the applicable fraction of a share of preferred stock underlying the depositary share, to all the rights and preferences of the preferred stock underlying that depositary share. Those rights may include dividend, voting, redemption, conversion and liquidation rights.

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

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

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

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

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

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

Voting. Upon receipt of notice of any meeting at which the holders of the underlying stock are entitled to vote, the depositary will mail the information contained in the notice to the record holders of the depositary shares underlying the preferred stock. Each record holder of the depositary shares on the record date, which will be the same date as the record date for the underlying stock, will be entitled to instruct the depositary as to the exercise of the voting rights pertaining to the amount of the underlying stock represented by that holder's depositary shares. The depositary will then try, as far as practicable, to vote the number of shares of preferred stock underlying those depositary shares in accordance with those instructions, and we will agree to take all actions which may be deemed necessary by the depositary to enable the depositary to do so. The depositary will not vote the underlying shares to the extent it does not receive specific instructions from the holders of depositary shares underlying the preferred stock.

Conversion of Preferred Stock. If the prospectus supplement relating to the depositary shares provides that the deposited preferred stock is convertible into or exchangeable for common stock or preferred stock of another series of

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

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

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

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

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

Resignation and Removal of Depositary. The depositary may resign at any time by delivering notice to us of its election to resign. We may remove the depositary at any time. Any resignation or removal will take effect upon the appointment of a successor depositary and its acceptance of the appointment. The successor depositary must be appointed within 60 days after delivery of the notice of resignation or removal and must be a bank or trust company having its principal office in the United States and having a combined capital and surplus of at least $50,000,000.

DESCRIPTION OF STOCK PURCHASE CONTRACTS

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

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

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

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

DESCRIPTION OF WARRANTS

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

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

- the title and the aggregate number of warrants;
- the price or prices at which the warrants will be issued;
- the currency or currencies in which the price of the warrants will be payable;
- the securities or other rights, including rights to receive payment in cash or securities based on the value, rate or price of one or more specified commodities, currencies, securities or indices, or any combination of the foregoing, purchasable upon exercise of the warrants;
- the price at which, and the currency or currencies in which, the securities or other rights purchasable upon exercise of such warrants may be purchased;
- the periods during which, and places at which, the warrants are exercisable;
- the date or dates on which the warrants shall commence and the date or dates on which the warrants will expire;
- the terms of any mandatory or optional call provisions;
- the price or prices, if any, at which the warrants may be redeemed at the option of the holder or will be redeemed upon expiration;
- whether the warrants will be sold separately or with other securities as part of a unit;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- any provisions for the adjustment of the number or amount of securities receivable upon exercise of warrants;
- the identity of the warrant agent;
- the exchanges, if any, on which the warrants may be listed;
- the maximum or minimum number of warrants which may be exercised at any time;
- if applicable, a discussion of any material United States federal income tax considerations;
- whether the warrants shall be issued in book-entry form; and

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

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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.

PLAN OF DISTRIBUTION

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

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

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

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

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

We may designate agents who agree to use their reasonable efforts to solicit purchases for the period of their appointment or to sell securities on a continuing basis. Agents may receive compensation in the form of commissions, discounts or concessions from us. Agents may also receive compensation from the purchasers of the securities for whom they sell as principals. Each particular agent will receive compensation in amounts negotiated in connection with the sale, which might be in excess of customary commissions. Agents and any other participating broker-dealers may be deemed to be "underwriters" within the meaning of Section 2(11) of the Securities Act of 1933 (the "Securities Act") in connection with sales of the securities. Accordingly, any commission, discount or concession received by them and any profit on the resale of the securities purchased by them may be deemed to be underwriting discounts or commissions under the Securities Act. We have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of their securities. As of the date of this prospectus, there are no special selling arrangements between any broker-dealer or other person and us. No period of time has been fixed within which the securities will be offered or sold.

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

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

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

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

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

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

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

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

Unless otherwise specified in the related prospectus supplement, all securities we offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We may apply to list any series of securities on an exchange, but we are not obligated to do so. Therefore, no assurance can be given as to the liquidity of, or the trading market for, any series of securities.

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

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, 2015, and the effectiveness of our internal control over financial reporting as of December 31, 2015, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file electronically with the SEC 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 site that contains reports, proxy and information 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, 2015, filed with the SEC on February 26, 2016;
- Our Current Reports on Form 8-K filed with the SEC on January 8, 2016 and February 8, 2016; 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 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.

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 this Amendment No. 1 and prior to its effectiveness and on or after the 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 else to make additional representations or to provide you with information other than information provided or incorporated by reference in this prospectus or any prospectus supplement. We take no responsibility for, and can provide no assurances as to the reliability of, any other information that others may give you or representations that others may make. 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.

5,294,118 shares

Common stock

Prospectus supplement

J.P. Morgan

Piper Jaffray

JMP Securities

March 9, 2017