BIOCRYST PHARMACEUTICALS INC
Form 424B5
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The information in this preliminary prospectus supplement and the accompanying prospectus is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated March 8, 2017

Preliminary prospectus supplement
(To prospectus dated April 18, 2016)

$45,000,000

Common stock

BioCryst Pharmaceuticals, Inc. is offering $45,000,000 of shares of its common stock.

Our common stock is listed on the NASDAQ Global Select Market under the symbol “BCRX.” On March 7, 2017, the last reported sale price of our common stock on the NASDAQ Global Select Market was $7.76 per share.

	Per share	Total
Public offering price	$	$
Underwriting discounts and commissions[(1)]	$	$
Proceeds to BioCryst, before expenses	$	$

(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 $6,750,000 of additional shares of our common stock at the public offering price less the underwriting discounts and commissions.

Investing in our common stock involves risks. See "Risk Factors" on page S-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 , 2017.

Sole book-running manager

J.P. Morgan

March , 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.

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The offering	
Common stock offered	$45,000,000 of shares of common stock
Option to purchase additional shares	Up to $6,750,000 of shares of common stock
Common stock to be outstanding after the offering	79,818,249 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 assumes the sale of $45,000,000 of shares of common stock at $7.76 per share, the last reported sale price of our common stock on the NASDAQ Global Select Market on March 7, 2017. A five percent increase or decrease in the assumed public offering price of $7.76 per share would increase or decrease the number of shares of our common stock issued in this offering by approximately five percent.

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