

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.

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-253719

Subject to completion, dated August 9, 2021

Prospectus supplement
(To prospectus dated March 1, 2021)

\$200,000,000



Common stock

Pre-funded warrants to purchase shares of common stock

BioCryst Pharmaceuticals, Inc. is offering \$200,000,000 of shares of its common stock and, in lieu of common stock to certain investors that hold pre-funded warrants and so choose, pre-funded warrants to purchase shares of common stock. The purchase price of each pre-funded warrant will equal the price per share at which shares of our common stock are being sold to the public in this offering, minus the \$0.01 per share exercise price of each such pre-funded warrant. This prospectus supplement also relates to the offering of shares of our common stock issuable upon the exercise of such pre-funded warrants.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "BCRX." On August 6, 2021, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$17.61 per share. We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market or any other national securities exchange or any other nationally recognized trading system.

	Per share	Per pre-funded warrant	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 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 our securities.

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 , 2021. The pre-funded warrants are expected to be delivered on or about , 2021.

Joint book-running managers

J.P. Morgan

Evercore ISI

Piper Sandler

, 2021

Table of contents

Prospectus Supplement

	<u>Page</u>
About this prospectus supplement	S-ii
Forward-looking statements	S-iii
Prospectus supplement summary	S-1
Risk factors	S-8
Use of proceeds	S-38
Dilution	S-39
Description of pre-funded warrants	S-41
Listing of common stock and dividend policy	S-42
Underwriting	S-43
Legal matters	S-48
Experts	S-48
Where you can find more information	S-49
Incorporation of certain documents by reference	S-49

Prospectus

	<u>Page</u>
About this Prospectus	i
Prospectus Summary	1
Risk Factors	2
Information Regarding Forward-Looking Statements	3
Use of Proceeds	5
Description of Common Stock, Preferred Stock and Depositary Shares	6
Description of Purchase Contracts	10
Description of Warrants	11
Description of Debt Securities	12
Description of Units	17
Plan of Distribution	18
Legal Matters	21
Experts	21
Where You Can Find More Information	22
Incorporation of Certain Documents by Reference	22

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 pre-funded warrants 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 March 1, 2021, 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 or pre-funded warrants 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, 2020 and Quarterly Reports on Form 10-Q for the quarters ended March 31, 2021 and June 30, 2021, each of 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 those sections. In particular, statements about our expectations, beliefs, plans, objectives or assumptions of future events or performance are contained or incorporated by reference in this prospectus supplement. 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 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 preclinical development, clinical development, commercialization, or post-marketing studies of our products and product candidates, including ORLADEYO® (berotralstat), BCX9930, BCX9250, peramivir, galidesivir, and early-stage discovery programs;
- the timing and success of our commercialization of ORLADEYO in the U.S. and elsewhere;
- the potential for government stockpiling orders of our products and product candidates, including the timing or likelihood of entering into any U.S. government stockpile order and our ability to execute any such order;
- the potential funding from our contracts with the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services (“BARDA/HHS”) and the National Institute of Allergy and Infectious Diseases within the HHS (“NIAID/HHS”) for the development of galidesivir;
- additional regulatory approvals, or milestones, royalties or profit from sales of our products by us or our partners;
- 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 products and product candidates;
- plans, programs, progress and potential success of our collaborations, including with Torii Pharmaceutical Co., Ltd. (“Torii”) for ORLADEYO in Japan, Shionogi & Co., Ltd. (“Shionogi”) and Green Cross Corporation (“Green Cross”) for peramivir in their territories, and Mundipharma International Corporation Limited (“Mundipharma”) for mundesine;
- our and our subsidiary guarantors’ ability to satisfy obligations under our Credit Agreement, dated as of December 7, 2020 (the “Credit Agreement”), and to comply with the covenants as set forth in the agreements governing our debt obligations;
- the ability of our subsidiary, JPR Royalty Sub LLC (“Royalty Sub”), to satisfy its obligations in respect of its PhARMA Senior Secured 14.0% Notes due 2020 (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, annual cash utilization, and our needs for additional financing;
- the timing or likelihood of regulatory filings or regulatory agreements, deferrals, and approvals;
- our ability to manage our liquidity needs, including our ability to raise additional capital, to fund our operations or repay our recourse debt obligations;

TABLE OF CONTENTS

- our financial performance; and
- competitive companies, technologies, and our industry.

We have based any forward-looking statements on our current expectations about future events or performance. While we believe these expectations are reasonable, forward-looking statements are inherently subject to known and unknown risks and uncertainties, many of which are beyond our control. Actual results may differ materially from those suggested or implied by these forward-looking statements for various reasons, including, 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 is subject to these and other risks, uncertainties, and assumptions relating to our operations, results of operations, industry, and future growth. Given these risks and uncertainties, you are cautioned not to place undue reliance on our forward-looking statements. The forward-looking statements included in this prospectus supplement are made only as of the date hereof. We do not undertake, and specifically decline, any obligation to update any of these statements or to publicly announce the results of any revisions to any forward-looking statements to reflect future events or developments, except as may be required by U.S. federal securities laws.

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 Quarterly Reports on Form 10-Q for the quarters ended March 31, 2021 and June 30, 2021, and 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 or pre-funded warrants. 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 commercial-stage biotechnology company that discovers novel, small-molecule medicines. We focus on oral treatments for rare diseases in which significant unmet medical needs exist and an enzyme plays the key role in the biological pathway of the disease. We integrate the disciplines of biology, crystallography, medicinal chemistry and computer modeling to discover and develop small molecule pharmaceuticals through the process known as structure-guided drug design. Structure-guided drug design is a drug discovery approach by which we design synthetic compounds from detailed structural knowledge of the active sites of enzyme targets associated with particular diseases. We use X-ray crystallography, computer modeling of molecular structures and advanced chemistry techniques to focus on the three-dimensional molecular structure and active site characteristics of the enzymes that control cellular biology. Enzymes are proteins that act as catalysts for many vital biological reactions. Our goal generally is to design a compound that will fit in the active site of an enzyme and thereby prevent its catalytic activity. Molecules from our discovery efforts which are commercially available or that are in active development are summarized in the table below:

Drug/Drug Candidate	Drug Class	Therapeutic Area(s)	Phase	Rights*
ORLADEYO (berotralstat)	Oral Serine Protease Inhibitor Targeting Kallikrein (once-daily treatment)	Hereditary Angioedema (“HAE”)	Approved (U.S., European Union, Japan & United Kingdom)**	BioCryst (worldwide, except Japan and Israel); Torii Pharmaceutical Co., Ltd. (Japan); Neopharm Ltd. (Israel)
BCX9930	Oral Factor D Inhibitor	Complement-mediated diseases	Pivotal trials in PNH initiating in the second half of 2021	BioCryst (worldwide)
BCX9250	Oral Activin Receptor-Like Kinase-2 Inhibitors	Fibrodysplasia Ossificans Progressiva (“FOP”)	Phase 1	BioCryst (worldwide)
RAPIVAB® (peramivir injection)	Intravenous Neuraminidase Inhibitor	Acute uncomplicated Influenza	Approved (U.S., Australia & Canada)	BioCryst (worldwide, except Japan, Taiwan, Korea and Israel)
RAPIACTA® (peramivir injection)	Intravenous Neuraminidase Inhibitor	Uncomplicated seasonal influenza	Approved (Japan & Taiwan)	Shionogi & Co., Ltd. (Japan & Taiwan)

Drug/Drug Candidate	Drug Class	Therapeutic Area(s)	Phase	Rights*
PERAMIFLU® (peramivir injection)	Intravenous Neuraminidase Inhibitor	Uncomplicated seasonal influenza	Approved (Korea)	Green Cross Corporation (Korea)
Galidesivir (BCX4430)	RNA dependent- RNA Polymerase Inhibitor	Broad spectrum antiviral for 20 RNA viruses, including Marburg, Yellow Fever, and Ebola	Phase 1	BioCryst (worldwide)
Mundesine® (forodesine)	Oral Purine Nucleoside Phosphorylase Inhibitor	Oncology - PTCL	Approved (Japan)	Mundipharma International Corporation Limited (worldwide)

* See "Business—Collaborations and In-License Relationships" in our Annual Report on Form 10-K for the year ended December 31, 2020 incorporated by reference in this prospectus supplement and the accompanying prospectus for a description of our relationships with the third parties identified in this column.

** We recently announced our regulatory filing in Israel and we are continuing to file around the world.

Business Strategy

Our business strategy is to create stockholder value both by focusing our discovery and development efforts on oral drugs for rare diseases for which a significant unmet medical need exists and by efficiently commercializing these drugs in the United States and certain other regions upon regulatory approval. By focusing on rare disease markets, we believe that we can more effectively control the costs of, and our strategic allocation of financial resources toward, post-approval commercialization.

We select disease targets and product candidates in which a small molecule would offer a significant benefit over existing products or would be the first to market. We strive to advance our product candidate portfolio from discovery to commercial markets efficiently by utilizing a small group of talented and highly-skilled employees working in conjunction with strategic outsource partners. BioCryst is unique in its approach to treat orphan diseases with orally-administered, small molecules, identified by utilizing crystallography and structure-guided drug design. The principal elements of our strategy are:

- *Focusing on High Value-Added Structure-Guided Drug Design Technologies.* We utilize structure-guided drug design in order to most efficiently develop new therapeutic candidates. Structure-guided drug design is a process by which we design a product candidate through detailed analysis of the enzyme target, which the product candidate must inhibit in order to stop the progression of the disease or disorder. We believe that structure-guided drug design is a powerful tool for the efficient development of small-molecule product candidates that have the potential to be safe and effective. Our structure-guided drug design technologies typically allow us to design and synthesize multiple product candidates that inhibit the same enzyme target, with the goal of establishing broad intellectual property protection and formulating compounds with competitive advantages.
- *Selecting Inhibitors that are Promising Product Candidates.* We start by selecting disease targets with well-understood biology and characteristics that fit with our ability to utilize structure-guided drug design capabilities to build potent and specific enzyme inhibitors. Next, we narrow our selection of these product candidates based on product characteristics, such as initial indications of safety and biologic activity on the target.
- *Developing our Product Candidates Efficiently.* An important element of our business strategy is to efficiently progress our product candidates through the development process. In order to accomplish this, we typically strive for disease targets with a defined clinical and regulatory pathway for approval or diseases where high unmet needs allow for frequent interactions with regulators. In addition, as we

determine such relationships to be appropriate or desirable, we control certain fixed costs and overhead by outsourcing with strategic partners and contractors or entering into license agreements with third parties, including the U.S. Government. For example, our galidesivir research program is currently being developed under U.S. Government contracts. By contracting with the U.S. Government and outsourcing certain aspects of our operations, we are able to control overhead costs and focus financial resources directly where they provide the most benefit and reduce our business risk.

- *Commercializing our Product Candidates Globally.* A core part of our strategy is to commercialize our rare disease products globally. We have established commercial teams in the United States and Europe for the commercialization of ORLADEYO, and we are continuing to build the structure and expertise to commercialize our products in markets where we believe we can do this efficiently and effectively. We have also established relationships with licensing and distribution partners in certain markets, including Japan and Israel, and will continue to seek such relationships where we determine this to be an effective approach.

We are a Delaware corporation originally founded in 1986. Our corporate headquarters is located at 4505 Emperor Blvd., Suite 200, Durham, North Carolina 27703 and the corporate telephone number is (919) 859-1302. For more information about us, please visit our website at www.biocryst.com. The information on our website is not incorporated by reference into this prospectus supplement or the accompanying base prospectus and does not constitute a part of this prospectus supplement or the accompanying base prospectus.

	The offering
Securities offered	\$200,000,000 of shares of common stock and pre-funded warrants
Common stock offered	shares of common stock
Pre-funded warrants offered	We are also offering, in lieu of common stock to certain investors that hold pre-funded warrants and so choose, pre-funded warrants to purchase shares of common stock. The purchase price of each pre-funded warrant will equal the price per share at which shares of common stock are being sold to the public in this offering, minus the \$0.01 per share exercise price of each such pre-funded warrant. Each pre-funded warrant will be exercisable from the date of issuance. See “Description of pre-funded warrants.” This prospectus supplement also relates to the offering of the shares of common stock issuable upon the exercise of such pre-funded warrants.
Option to purchase additional shares	shares of common stock. The number of shares subject to the underwriters’ option to purchase additional shares will equal 15% of the total number of shares of common stock we are offering plus the shares underlying the pre-funded warrants.
Common stock to be outstanding after the offering	shares of common stock
Use of proceeds	We intend to use the net proceeds from this offering for general corporate purposes, including: <ul style="list-style-type: none"> • worldwide development, manufacturing, regulatory and commercial activities for ORLADEYO; • advancement of the worldwide development, manufacturing, regulatory and clinical activities for BCX9930 for complement-mediated diseases; • discovery, manufacturing, development and clinical activities for other pipeline molecules in rare diseases; and • capital expenditures and other general working capital needs. 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 or pre-funded warrants.

The number of shares of our common stock to be outstanding after this offering is based on 178,869,928 shares outstanding as of August 6, 2021 and excludes the shares of common stock issuable upon exercise of the pre-funded warrants being offered by us in this offering.

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

- 15,275,817 shares of common stock issuable upon the exercise of outstanding pre-funded warrants;
- 25,023,040 shares of common stock issuable upon the exercise of stock options outstanding under our Stock Incentive Plan and 4,387,793 shares of common stock issuable upon the exercise of stock options outstanding under our Inducement Equity Incentive Plan as of August 6, 2021, at a weighted average exercise price of \$7.04 per share and \$4.65 per share, respectively; and
- 10,198,379 additional shares of common stock reserved for issuance under our Stock Incentive Plan, 1,479,082 additional shares of common stock reserved for issuance under our Inducement Equity Incentive Plan, and 6,056,304 additional shares of common stock reserved for issuance under our Employee Stock Purchase Plan as of August 6, 2021.

Except as otherwise noted, all information in this prospectus supplement assumes no exercise of the outstanding stock options or pre-funded warrants, no vesting of the outstanding restricted stock units, no exercise of the underwriters' option to purchase additional shares of our common stock, and no exercise of the pre-funded warrants we are offering to certain investors.

Risk factor summary

An investment in us involves risks. You should carefully consider the uncertainties and risks discussed in the "Risk factors" section of this prospectus supplement, which may adversely affect our business, financial condition, or results of operations, along with the other information included in our other filings with the SEC, before deciding to invest in us. A summary of the principal factors that make an investment in us speculative or risky is set forth below.

- The ongoing novel coronavirus ("COVID-19") pandemic could create challenges in all aspects of our business, including, without limitation, delays, stoppages, difficulties, and increased expenses with respect to our and our partners' development, regulatory processes, and supply chains, negatively impact our ability to access the capital or credit markets to finance our operations, or have the effect of heightening many of the risks described under "Risk Factors" in this prospectus supplement.
- We have incurred losses since our inception, expect to continue to incur losses, and may never be profitable.
- We may need to raise additional capital in the future. If we are unable to raise capital when needed, we may need to adjust our operations.
- Our success depends upon our ability to advance our product candidates through the various stages of development, especially through the clinical trial process, to receive and maintain regulatory approval for the commercial sale of our product candidates, and to successfully commercialize any approved products. The development process and related regulatory processes are complex and uncertain, may be lengthy and expensive, and require, among other things, an indication that our products and product candidates are safe and effective. For example, applicable regulatory agencies could refuse to approve, or impose restrictions or warnings on, our product candidates, require us to conduct additional studies or adopt study designs that differ from our planned development strategies, suspend or terminate our clinical trials, or take other actions that could materially impact the cost, timing, and success of our planned development strategies.
- We rely heavily upon third parties, including development partners, contractors, contract research organizations, and third-party suppliers, manufacturers, and distributors, for many important stages of our product candidate development and in the commercialization of certain of our products and product candidates. Our failure to maintain these relationships, the failure of any such third party to perform its obligations under agreements with us, or the failure of such a relationship to meet our expectations could have a material adverse impact on our business, financial condition, and results of operations.

- If we fail to obtain additional financing or acceptable partnership arrangements, we may be unable to complete the development and commercialization of our products and product candidates or continue operations.
- The commercial viability of any approved product could be compromised if the product is less effective than expected, causes undesirable side effects that were not previously identified, or fails to achieve market acceptance by physicians, patients, third-party payors, health authorities, and others.
- There can be no assurance that our or our partners' commercialization efforts, methods, and strategies for our products or technologies will succeed, and our future revenue generation is uncertain.
- We expect to continue expanding our development and regulatory capabilities and implementing sales, marketing, and distribution capabilities, and as a result, we may encounter difficulties managing our growth, which could disrupt our operations.
- We face intense competition, and if we are unable to compete effectively, the demand for our products may be reduced. In addition, developments by others may render our products, product candidates, or technologies obsolete or noncompetitive.
- We are subject to various laws and regulations related to our products and product candidates, and if we or our employees, consultants, or partners do not comply with these laws and regulations, we could face substantial penalties and our reputation could be harmed. In addition, 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, obtain collaborators, and raise capital.
- 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. Legal proceedings to protect or enforce our patents, the patents of our partners, or our other intellectual property rights could be expensive, time consuming, and unsuccessful.
- We face an inherent risk of liability in the event that the use or misuse of our products or product candidates results in personal injury or death, and our product liability insurance coverage may be insufficient.
- We face risks related to our government-funded programs and are subject to various U.S. Government contract requirements, which 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.
- 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.
- Our Credit Agreement contains conditions and restrictions that limit our flexibility in drawing on the additional funds thereunder and in operating our business. We may be required to make a prepayment or repay our outstanding indebtedness under the Credit Agreement 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.
- International expansion of our business exposes us to business, regulatory, political, operational, financial, and economic risks. For example, our actual or perceived failure to comply with European governmental regulations and other obligations related to privacy, data protection, and information security could harm our business. In addition, the United Kingdom's withdrawal from the European Union could result in increased regulatory and legal complexity, which may make it more difficult for us to do business in Europe and impose additional challenges in securing regulatory approval of our product candidates in Europe.
- If our facilities incur damage or power is lost for a significant length of time, our business will suffer.
- A significant disruption in our information technology systems or a cybersecurity breach could adversely affect our business.

- 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 interests of other stockholders.
- 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.
- Natural disasters, epidemic or pandemic disease outbreaks, trade wars, political unrest, or other events could disrupt our business or operations or those of our development partners, manufacturers, regulators, or third parties with whom we conduct business now or in the future.
- We are subject to legal proceedings, which could harm our reputation or result in other losses or unexpected expenditure of time and resources.
- If we fail to retain our existing key personnel or fail to attract and retain additional key personnel, the development of our product candidates, the commercialization of our products, and the related expansion of our business will be delayed or stopped.

Risk factors

An investment in our securities 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 securities. 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 securities.

Risks relating to our business

Risks relating to COVID-19

Our business, operations, clinical development or commercialization plans and timelines, and access to capital could be adversely affected by the effects of the COVID-19 pandemic on us or on third parties with whom we conduct business, including without limitation our development partners, manufacturers, clinical research organizations (“CROs”), and others, as well as on the regulatory and government agencies with whom we work.

The global COVID-19 pandemic continues to affect the United States and global economies, and may cause significant disruptions to our business, operations, and clinical development or commercialization plans and timelines, as well as the business and operations of third parties with whom we conduct business. For example, quarantines, shelter-in-place, similar government orders and evolving business policies and procedures have impacted and may continue to impact, among other things: (1) our personnel and those of third parties on whom we rely, including our development partners (such as Torii), manufacturers, CROs, and others; (2) the conduct of our current and future clinical trials and commercial interactions; and (3) the operations of the U.S. Food and Drug Administration (“FDA”), European Medicines Agency (“EMA”), Japanese Pharmaceuticals and Medical Devices Agency (“PMDA”), and other health and governmental authorities, which could result in delays of reviews and approvals.

If our operations or those of third parties with whom we conduct business are impaired or curtailed as a result of these events, the development and commercialization of our products and product candidates could be stopped or delayed, or the costs of such development and commercialization activities could increase, any of which could have a material adverse impact on our business. For example, our suppliers or other vendors may be unable to meet their obligations to us or perform their services as expected as a result of the COVID-19 pandemic or other health epidemics. In such circumstances, we may not be able to enter into arrangements with alternative suppliers or vendors or do so on commercially reasonable terms or in a timely manner. Such delays could adversely impact our ability to meet our desired clinical development and any commercialization timelines. Although we carefully manage our relationships with our suppliers and vendors, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have an adverse impact on our business, financial condition and prospects.

In addition, our clinical trials have been and may continue to be affected by the COVID-19 pandemic. For example, the acceleration of COVID-19 slowed startup of the inadequate C5 responder cohorts in our complement oral Factor D inhibitor program and, as a result, delayed the reporting of related data in 2020. Clinical site initiation and patient enrollment may be delayed due to prioritization of hospital resources toward the COVID-19 pandemic or concerns among patients about participating in clinical trials during a pandemic. Some patients may have difficulty following certain aspects of clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Similarly, our inability to successfully recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 or experience additional restrictions by their institutions, city, or state could adversely impact our clinical trial operations.

If global health concerns prevent the FDA, EMA, PMDA or other regulatory authorities from conducting their inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA, EMA, PMDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business and clinical development and commercialization plans and timelines.

TABLE OF CONTENTS

We continue to utilize work-from-home policies for our employees, which may negatively impact productivity, disrupt our business and delay our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. These and similar, and perhaps more severe, disruptions in our operations could negatively impact our business, operating results and financial condition.

The spread of COVID-19, which has caused a broad impact globally, may also materially affect our access to capital. While the future economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, the pandemic could result in significant disruption of global financial markets, reducing our ability to access the equity or debt capital markets or obtain other sources of capital, which could negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

The global pandemic of COVID-19 continues to evolve, with the ultimate impact of the COVID-19 pandemic or a similar health epidemic being uncertain and subject to change. These effects could be material, and we will continue to monitor the COVID-19 situation closely. We do not yet know the full extent and magnitude of the impacts that COVID-19 has had or will have on our business, on the healthcare system, or on the global economy. In addition, the COVID-19 pandemic could have the effect of heightening many of the other risks described below.

Financial and liquidity risks

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 and commercial activities progress. We expect that such losses will fluctuate from quarter to quarter and that losses and fluctuations may be substantial. To become profitable, we, or our collaborative partners, must successfully manufacture and develop products and product candidates, receive regulatory approval, and successfully commercialize our products and/or enter into profitable commercialization arrangements with other parties. It could take longer than expected before we receive, or we may never receive, significant revenue from any current or future license agreements or significant revenues directly from product sales. Even if we are able to successfully commercialize our existing products, or to develop new commercially viable products, certain obligations we have to third parties, including, without limitation, our obligation to pay to RPI 2019 Intermediate Finance Trust (“RPI”) royalties on certain ORLADEYO and BCX9930 revenues pursuant to the Purchase and Sale Agreement (the “Royalty Purchase Agreement”) between RPI and us, may reduce the profitability of such products.

Because of the numerous risks and uncertainties associated with developing our product candidates, launching new products, 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.

We may need to raise additional capital in the future. If we are unable to raise capital when needed, we may need to adjust our operations.

We have sustained operating losses for the majority of our corporate history and expect that our 2021 expenses will exceed our 2021 revenues. We expect to continue to incur operating losses and negative cash flows unless and until revenues reach a level sufficient to support ongoing operations.

Our liquidity needs will be largely determined by the success of operations in regard to the commercialization of our products and the progression of our product candidates in the future. Our plans for managing our liquidity needs primarily include controlling the timing and spending on our research and development programs, raising additional funds through equity and/or debt financings, and commercializing our approved products. We also may consider other plans to fund operations including: (1) securing or increasing U.S. Government funding of our programs, including obtaining additional and delivering on procurement contracts; (2) out-licensing rights to certain of our products or product candidates, pursuant to which we would

TABLE OF CONTENTS

receive cash milestone payments and/or royalties; (3) raising additional capital through equity or debt financings or from other sources, including royalty or other monetization transactions; (4) obtaining additional product candidate regulatory approvals, which would generate revenue, milestone payments and cash flow; (5) reducing spending on research and development programs, including by discontinuing and suspending 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 adjust or curtail our operations; delay, reduce, or stop ongoing clinical trials or commercialization efforts; cease operations altogether; or file for bankruptcy.

Risks relating to drug development and commercialization

Our success depends upon our ability to advance our product candidates through the various stages of development, especially through the clinical trial process, and to receive regulatory approval for the commercial sale of our product candidates.

To receive the regulatory approvals necessary for the commercial 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. The preclinical and clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of drug development, including failure to demonstrate efficacy and safety, the occurrence of adverse events that are severe or medically or commercially unacceptable, our or our partners' failure to comply with trial protocols, applicable regulatory requirements, and industry standards, or a determination by the FDA or any comparable foreign regulatory authority that a product candidate may not continue development or be approved in accordance with our development plans or at all. We cannot guarantee that any preclinical studies and clinical trials will be conducted as planned or completed on schedule, if at all, or that the results of such trials will be sufficient to support regulatory approval for our product candidates.

Progression of our product candidates through the clinical development process is dependent upon our trials indicating that 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 BCX9930, BCX9250, galidesivir, and our other rare disease product candidates, could result in delays in or modifications to our trials or require the performance of additional unplanned trials. If any of our product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Product candidates that initially show promise in clinical or preclinical testing could later be found to cause undesirable or unexpected side effects that could result in delays in the development of our product candidates, significant unexpected costs, or the termination of programs. The development plans for our product candidates, including our clinical trials, may not be adequately designed or executed, which could negatively affect the outcome and analysis of study results. Because of the cost and duration of clinical trials, we may decide to discontinue development of product candidates that are unlikely to show favorable results in clinical trials, unlikely to help advance a product to the point of a meaningful collaboration, or unlikely to have reasonable commercial potential.

Undesirable or inconclusive data in our pre-clinical studies and clinical trials or side effects in humans could result in the FDA or foreign regulatory authorities (including, e.g., the EMA, the Japanese Ministry of Health, Labor & Welfare ("MHLW") or the U.K. Medicines and Healthcare products Regulatory Agency ("MHRA")) refusing to approve a product candidate for any targeted indications or imposing restrictions or warnings that could impact development or the ultimate commercial viability of a product candidate. In addition, the FDA or foreign regulatory authorities may determine that study data from our product candidates necessitates additional studies or study designs which differ from our planned development strategy, and such regulatory authorities 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.

TABLE OF CONTENTS

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

- our or our partners' ability to secure suitable clinical sites and investigators and to enroll and maintain an adequate number of patients on a timely basis or at all;
- patients that enroll in a clinical trial may not comply with the clinical trial protocol or maintain contact with investigators to provide complete data during and after treatment;
- our product candidates may not prove to be either safe or effective or may produce unfavorable or inconclusive results;
- we or our partners may decide, or be required by regulatory authorities, to suspend or terminate clinical research for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate, noncompliance with regulatory requirements or their standards of conduct, or findings of undesirable effects caused by a chemically or mechanistically similar product or product candidate;
- regulatory authorities may disagree with our or our partners' clinical trial protocols or our or their interpretation of data from preclinical studies and clinical trials;
- 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;
- regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we or our partners enter into agreements for clinical and commercial supplies;
- the supply or quantity of raw materials or manufactured product candidates or other materials necessary to conduct development activities may be insufficient, inadequate, or unavailable at an acceptable cost, and we or our partners may experience interruptions in supply;
- our or our partners' development plans may be delayed or changed as a result of changes in development strategy, the impact of new or different regulations, requirements, and guidelines, or other unexpected events or conditions;
- the cost of pre-clinical studies and clinical trials may be greater than we anticipate;
- we or our third-party contractors, including those manufacturing our product candidates or components or ingredients thereof, or conducting clinical trials or laboratory testing on our or our partners' behalf, may fail to comply with regulatory requirements and industry standards or meet contractual obligations in a timely manner or at all; and
- the impact of the COVID-19 pandemic on one or more of the foregoing factors.

Clinical trials are lengthy and expensive. Many of the factors listed above could result in increased clinical development costs or longer clinical development times for any of our programs. 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. 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, may not receive regulatory approval for the product candidates, in which case we would be unable to generate any revenues from product sales or licensing arrangements, or any product candidate, if approved, may be subject to restrictions on labeling, marketing, distribution, prescribing, and use, which could adversely impact the sales of such product.

TABLE OF CONTENTS

If our development collaborations with third parties, such as our development partners, contractors 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 natural proteins that cause or enable biological reactions necessary for the progression of the disease or disorder, called enzyme targets;
- execution of certain pharmacology preclinical studies and late-stage development for our compounds and product candidates;
- management of our phase 1, 2 and 3 clinical trials, including medical monitoring, laboratory testing, and data management;
- execution of toxicology studies that may be required to obtain approval for our product candidates;
- formulation improvement strategies and methods;
- 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; and
- management of certain regulatory interactions outside of the United States.

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 or third-party contractors that conduct our initial or late-stage clinical trials, conduct our toxicology or other studies, manufacture our starting materials, drug substance and product candidates, provide laboratory testing or other services in connection with our clinical trials, or assist with our regulatory function breach their obligations to us, perform their services inconsistent with industry standards, or fail to comply with regulatory requirements, 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.

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

As our programs advance, our costs are likely to increase. Our current and planned discovery, development, approval, and commercialization efforts will require significant capital. Our expenses, revenues and cash utilization rate could vary significantly depending on many factors, including: our ability to obtain regulatory approval for our product candidates, including BCX9930, BCX9250, and galidesivir; our ability to maintain regulatory approval for, successfully commercialize, and achieve market acceptance of our products, including ORLADEYO; our ability to raise additional capital; the amount of funding we receive from partnerships with third parties for the development and commercialization of our products and product candidates (including our collaborations with Torii, BARDA/HHS, and NIAID/HHS); the commercial success of our products 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 product candidates; and the progress made in the manufacture of our lead products and the progression of our other programs.

TABLE OF CONTENTS

In order to continue future operations, progress our drug development programs, and commercialize our current products and product candidates, we will be required to raise additional capital. In addition to seeking strategic partnerships, transactions and government funding, we may access the equity or debt markets, incur additional borrowings, or seek other sources of funding to meet liquidity needs at any time, including to take advantage of attractive opportunities in the capital markets. Additional funding, whether through additional sales of securities, additional borrowings, royalty or other monetization transactions, collaborative arrangements with partners, including corporate partners such as Torii and governmental agencies such as BARDA/HHS or NIAID/HHS, or from other sources, 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 our 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 Credit Agreement. 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.

Our ability to raise additional capital when needed or at all may be limited and may greatly depend upon our success in commercializing and achieving market acceptance of ORLADEYO and the success of our current drug development programs, including the progress, timeline and ultimate outcome of the development programs (including but not limited to formulation progress, long-term human safety studies, and carcinogenicity, drug-drug interaction, toxicity, or other required studies) for BCX9250 for the treatment of FOP, BCX9930 for diseases of the complement system, our broad-spectrum antiviral program, including galidesivir, and other rare disease product candidates, as well as any post-approval studies for our products. In addition, constriction and volatility in the equity and debt markets, including as a result of the impacts of COVID-19, 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, including as a result of the impacts of COVID-19. Any such instability may impact these parties' ability to fulfill contractual obligations to us, or it 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 and commercialization of our products and product candidates.

If we or our partners do not obtain governmental approval for our product candidates or maintain governmental approval for our products, we or our partners will not be able to commercialize and sell these products and 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 products. If the FDA or a comparable foreign regulatory authority delays or denies regulatory approval of one of our product candidates, or revokes approval of a previously approved product, we would be unable to market or sell the product in the applicable jurisdiction and would not receive revenue from sales or licensing arrangements related thereto, which could have a material and adverse impact on our business.

The process of preparing for and obtaining regulatory approval in any jurisdiction may be lengthy and expensive, and approval is never certain. Because of the risks and uncertainties inherent to the development process, including risks and uncertainties related to the impact of COVID-19, our product candidates could take a significantly longer time to gain regulatory approval than we expect or may never gain approval. As discussed under "Risk factors—Risks relating to our business—Risks relating to drug development and commercialization—Our success depends upon our ability to advance our product candidates through the various stages of development, especially through the clinical trial process, and to receive regulatory approval for the

TABLE OF CONTENTS

commercial sale of our product candidates,” we or our partners may experience any number of unfavorable outcomes during or as a result of pre-clinical studies and clinical trials that could delay or prevent regulatory approval of our product candidates, or negatively impact our management’s credibility, our value and our operating results.

Even if the FDA or foreign regulatory authorities approve a product candidate, the approval may limit the indicated uses for a product candidate, impose other restrictions on the product candidate, and/or may require post-approval studies that could impair the commercial viability of a product candidate. Even upon any 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 for regulatory approval, or our loss of, or changes to, previously obtained approvals, could impair our ability to generate any revenues from product sales or licensing arrangements, which could have a material adverse effect on our business, financial condition, and results of operations.

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 authorities have broad discretion in determining whether or not to grant such designations. We cannot guarantee that our product candidates will receive orphan drug status from the FDA or equivalent designations from other regulatory authorities. We also cannot guarantee that we will receive breakthrough therapy, fast track, or equivalent designations, which provide certain potential benefits such as more frequent meetings with the applicable regulatory authorities to discuss development plans, intensive guidance on efficient drug development programs, and potential eligibility for rolling review or priority review. Even if we are successful in obtaining any such designations for our product candidates, such designations may not lead to faster development or regulatory review or approval and do not increase the likelihood that our product candidates will receive marketing approval. For instance, although BCX9930 for paroxysmal nocturnal hemoglobinuria (“PNH”) has received Fast Track and Orphan Drug designations from the FDA, we may not experience a faster development, review or approval process compared to the conventional process in the relevant jurisdictions. We may not be able to obtain or maintain these designations for BCX9930 or other product candidates that receive them, and our competitors may obtain these designations for their product candidates, which could impact our ability to develop and commercialize our products and product candidates or compete with such competitors, which may adversely impact our business, financial condition or results of operations.

The commercial viability of any approved product could be compromised if the product is less effective than expected, causes undesirable side effects that were not previously identified, or fails to achieve market acceptance within the medical community.

If, after obtaining regulatory approval of a product, we or others discover that it is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of, or impose marketing or manufacturing restrictions on, the product, or require us or our partners to create a medication guide outlining the risks of unidentified side effects for distribution to patients;
- we or our partners may be required to recall the product, change the way the product is administered, conduct additional clinical trials, or be subject to civil or criminal penalties; and
- the product may become less competitive and our reputation may suffer.

TABLE OF CONTENTS

Even after receiving regulatory approval, any product could fail to gain sufficient, or even any, market acceptance by physicians, patients, third-party payors, health authorities and others in the medical community. For example, physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies. If an approved product does not achieve an adequate level of market acceptance, it may not generate significant revenues. The occurrence of any of the foregoing could have a material and adverse impact on our business.

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

Our business strategy is to increase the asset value of our product and 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 products and product candidates.

Currently, we have established collaborative relationships with Torii for the commercialization of ORLADEYO in Japan, with each of Shionogi and Green Cross for the development and commercialization of peramivir, and with Mundipharma for the development and commercialization of Mundesine (forodesine). 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 commercial, regulatory or 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;
- the possibility that expiration or termination of collaborative relationships, such as those with certain of our distribution partners, may trigger repurchase obligations of the Company for unsold product held by our partner;
- 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, such as the recent arbitration proceeding between us and Seqirus UK Limited, which could result in substantial costs and divert the attention of our management;
- 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 toward our products and 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 development and 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 or commercialization of one or more of our products or product candidates, undertake commercialization activities at our own expense or find alternative sources of funding. Any delay in the development or commercialization of our products and 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, or if our products do not achieve market success, we may not receive any revenues from product sales or licensing arrangements.

The results of our partnership with Torii may not meet our current expectations.

We have an agreement with Torii for the development and commercialization of ORLADEYO in Japan (the “Torii Agreement”). We do not have a history of working with Torii and cannot predict the success of this collaboration. Our ability to realize the expected benefits of this collaboration, including with respect to the receipt or amounts of royalty payments, is subject to a number of risks, including that the commercial potential of ORLADEYO may not meet our current expectations, we or Torii may fail to comply with our respective obligations under the Torii Agreement, and third parties may fail to perform their obligations to us on a timely basis or at all.

The Torii Agreement provides that we will be entitled to receive tiered royalty payments, the amounts of which will depend upon the amount of annual net sales of ORLADEYO in Japan during each calendar year and other factors. We remain responsible for regulatory activities with respect to ORLADEYO in Japan for one year after the first commercial sale. We continue to use third parties to satisfy many of our obligations under the Torii Agreement, including but not limited to our regulatory and other responsibilities in Japan. If our interactions, or those of our third-party agents, are unsuccessful, we could fail to meet our obligations under the Torii Agreement, which could negatively impact the commercial success and the partnership, impact the economic benefit expected or require additional development of ORLADEYO.

Torii may terminate the Torii Agreement under certain limited circumstances, including upon one year’s written notice after the sixth anniversary of the first commercial sale of ORLADEYO in Japan. If the Torii Agreement is terminated in connection with these provisions, we will no longer be entitled to receive any milestone or royalty payments thereunder, which could have a material adverse impact on our business and results of operations.

Torii will have sole control over, and decision-making authority with respect to, commercialization activities for ORLADEYO for the prevention of HAE attacks in Japan, subject to oversight from a joint steering committee. Therefore, our receipt, and the amounts, of any royalty payments under the Torii Agreement are dependent upon Torii’s successful performance of such commercialization activities. In addition, competitive products and variations in patient demand, prescription levels, reimbursement determinations or other factors may limit the commercial potential of ORLADEYO in Japan, which could materially reduce the amount of any royalties we would be entitled to receive under the Torii Agreement.

Under the Torii Agreement, we will be responsible for supplying Torii with its required amounts of ORLADEYO for commercial sale. If, due to the failure of our third-party contract manufacturers to produce sufficient drug product, we fail to supply to Torii the required amounts of ORLADEYO, then Torii’s ability to successfully commercialize ORLADEYO in Japan could be materially impaired, and we may receive less royalty income under the Torii Agreement, or none at all.

Any of the foregoing risks could materially adversely impact our ability to perform our obligations under the Torii Agreement, which could materially reduce the economic benefits of the Torii Agreement to us and impair or result in the termination of our collaboration with Torii.

TABLE OF CONTENTS

There can be no assurance that our commercialization efforts, methods, and strategies for our products or technologies will succeed, and our future revenue generation is uncertain.

There can be no assurance that our and our partners' commercialization efforts, methods and strategies will succeed. Although we have expanded and added experienced professionals to our internal commercial team, as a company we do not have a great deal of experience in commercializing our products or technologies. In addition, we may be unable to establish or sufficiently increase our sales, marketing and distribution capabilities for products we currently, or plan to, commercialize. Our ability to receive revenue from products we or our partners commercialize is subject to several risks, including:

- we or our partners may fail to successfully complete clinical trials, or satisfy post-marketing commitments, sufficient to obtain and keep regulatory agency 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 products and product candidates;
- we may fail to employ a comprehensive and effective intellectual property strategy, which could result in decreased commercial value of our Company, our products and product candidates, or royalties associated with such products (e.g., the loss of the peramivir patent in Korea, which may result in a reduced royalty from Green Cross);
- 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 and our partners' ability to successfully commercialize our products is affected by the competitive landscape, which cannot be fully known at this time;
- revenue from product sales would depend on our ability to obtain and maintain favorable pricing;
- reimbursement is constantly changing, which could greatly affect usage of our products;
- future revenue from product sales would depend on our ability to successfully complete clinical studies, obtain regulatory approvals, and manufacture, market, distribute and commercialize our approved drugs; and
- the impact of the COVID-19 pandemic on us or our partners.

In addition, future revenue from sales of ORLADEYO is subject to uncertainties and will depend on several factors, including the success of our and our partners' commercialization efforts in the U.S. and elsewhere, the number of new patients switching to ORLADEYO, patient retention and demand, the number of physicians prescribing ORLADEYO, the rate of monthly prescriptions, reimbursement from third-party payors, the conversion of patients from our clinical trials and early access programs to commercial customers, and market trends.

Even if we are able to successfully commercialize our existing products, or to develop new commercially viable products, certain obligations we have to third parties, including, without limitation, our obligations to pay royalties on certain ORLADEYO and BCX9930 revenues under the Royalty Purchase Agreement may reduce the profitability of such products.

We expect to continue expanding our development and regulatory capabilities and implementing sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to continue experiencing significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs, sales, marketing, and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. For example, we expanded our internal commercial team in 2020 in preparation for the commercial launch of ORLADEYO. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit, train, and retain additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. In addition, if a

TABLE OF CONTENTS

commercial launch for any product or product candidate for which we recruit a commercial team and establish marketing capabilities in any region is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

We depend on third-party vendors in the manufacture and distribution of our products, product candidates and the materials for our products and product candidates. If we cannot rely on existing third-party vendors, we will be required to incur significant costs and potential delays in finding new third-party vendors, which could adversely impact the development and commercialization timeframes for our products and product candidates.

We depend on third-party vendors, including third-party manufacturers, distributors, and specialty pharmacies, in the manufacture and distribution of our products, product candidates, and the materials for our product candidates. Often, especially in the early development and commercialization process, we have only one or limited sources for a particular product or service, such as manufacturing and/or distribution. We depend on these third-party vendors to perform their obligations in a timely manner and in accordance with applicable governmental regulations. Our third-party vendors, particularly our third-party manufacturers and distributors, which may be the only vendor we have engaged for a particular product or service or in a particular region, may encounter difficulties with meeting our requirements, including but not limited to problems involving, as applicable:

- insufficient resources being devoted in the manner necessary to satisfy our requirements within expected timeframes;
- 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;
- failure to distribute commercial supplies of our products to commercial vendors or end users in a timely manner;
- 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;
- failure to provide us with accurate or timely information regarding inventories, the number of patients who are using our products, or serious adverse events and/or product complaints regarding our products;
- inability of third parties to satisfy their financial obligations to us or to others;
- potential breach of the manufacturing or distribution agreement by the third party;
- possible termination or nonrenewal of a critical agreement by the third party at a time that is costly or inconvenient to us; and
- lack of compliance or cooperation with regulations and specifications or requests set forth by the FDA or other foreign regulatory agencies or local customs, particularly associated with ORLADEYO, BCX9930, BCX9250, galidesivir, peramivir and our early-stage compounds.

Many additional factors could cause production or distribution interruptions with the manufacture and distribution of any of our products and product candidates, including human error, natural disasters, pandemics, labor disputes, acts of terrorism or war, equipment malfunctions, or raw material shortages. If our commercial distribution partners are not able to satisfy our requirements within the expected timeframe, or are unable to provide us with accurate or timely information and data, including inventories and sales, serious adverse events, and/or product complaints, our business, including our commercial launch and sales of ORLADEYO may be at

risk. In addition, if specialty pharmacy services, including our third-party call center services, which provide patient support and financial services, prescription intake and distribution, reimbursement adjudication, and ongoing compliance support is not effectively managed, the continuance of our commercial launch and sales of ORLADEYO may be delayed or compromised.

In addition, our contract manufacturers may not be able to manufacture the materials required for our products or product candidates at a cost or in quantities necessary to make them commercially viable. Our raw materials, drug substances, products, 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 products and product candidate material for further preclinical testing and clinical trials. 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 foreign regulatory authorities 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 us and could result in a delay or shortage of product.

If we are unable to maintain current third-party relationships, or enter into new agreements with additional third parties on commercially reasonable terms, or if there is poor manufacturing or distribution performance or failure to comply with any regulatory agency on the part of any of our third-party vendors, we may not be able to complete development of, obtain timely approval of, or commercialize, our products and product candidates.

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

Commercialization success of our products 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 our products is subject to further risks and may be negatively impacted by a number of factors, including, but not limited to, the following:

- our products may not prove to be adequately safe and effective for market approval in markets other than the markets in which they are currently approved;
- necessary funding for post-marketing commitments and further development of our products may not be available timely, at all, or in sufficient amounts;
- advances in competing products could substantially replace potential demand for our products;
- government and third-party payors may not provide sufficient coverage or reimbursement, which would negatively impact the demand for our products;
- 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 our products by healthcare providers and by patients may not be sufficient to result in substantial product revenues to us or to our partners and may result in little to no revenue, milestone payments, or royalties to us;
- effectiveness of marketing and commercialization efforts for our products by us or 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;

TABLE OF CONTENTS

- 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.

Risks relating to competing in our industry.

We face intense competition, and if we are unable to compete effectively, the demand for our products 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 manufacturing, marketing, and sales 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 or for products that compete with our products. 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 commercialization of our products, 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 products, product candidates, or technologies obsolete or noncompetitive.

We received FDA approval of ORLADEYO, an oral, once-daily therapy for the prevention of HAE attacks in adults and pediatric patients 12 years and older, in December 2020. We subsequently received regulatory approvals for ORLADEYO in Japan, the European Union, and the United Kingdom in January 2021, April 2021, and May 2021, respectively. In addition, we are performing research on or developing products for the treatment of several other rare diseases, including diseases of the complement system and FOP, as well as developing broad spectrum antivirals for use as medical countermeasures. We expect to encounter significant competition for our pharmaceutical products and product candidates. 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. There are licensed therapies for HAE (including Berinert®, Haegarda®, Cinryze®, Kalbitor®, Takhzyro®, Firazyr® (icatibant), generic icatibant, and Ruconest®), therapies for certain complement-mediated diseases such as PNH, aHUS, myasthenia gravis, and neuromyelitis optica spectrum disorder (Soliris®, Ultomiris™ and Empaveli™), products for the prevention or treatment of influenza (seasonal flu vaccines, Tamiflu® (oseltamivir), generic oseltamivir, Relenza®, and Inavir®, favipiravir, and Xofluza™), and a number of additional products in clinical development in these therapeutic areas and for the treatment of FOP. In addition, various government entities throughout the world may offer incentives, grants and contracts to encourage additional investment into preventative and therapeutic agents against viruses such as influenza, coronavirus, Ebola, and others, which may have the effect of further increasing the number of our competitors and/or providing advantages to certain competitors. See “Business—Competition” in Part I, Item 1 of our Annual Report on Form 10-K for the year ended December 31, 2020 for further discussion of our competitors, competitive products or programs, and the competitive conditions in these and other therapeutic areas.

If one or more of our competitors’ products or programs, including potential competitors not currently identified, are successful, the market for our products may be reduced or eliminated.

TABLE OF CONTENTS

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

- capital resources;
- research and development resources, including personnel and technology;
- regulatory experience;
- preclinical study and clinical testing experience;
- manufacturing, marketing and sales experience; and
- production facilities.

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

Legal and regulatory risks

We are subject to various laws and regulations related to our products and product candidates and, if we or our partners do not comply with these laws and regulations, we could face substantial penalties.

Our or our partners' activities related to approved products or, following their regulatory approval, any of our product candidates under development, such as BCX9930, BCX9250, and galidesivir, are subject to regulatory and law enforcement authorities in the United States (including the FDA, the Federal Trade Commission, the Department of Justice, and state and local governments) and their foreign equivalents (including the EMA, MHLW, MHRA, and others).

We are responsible for reporting adverse drug experiences, have responsibility for certain post-approval studies, and may have responsibilities and costs related to a recall or withdrawal of our products from sale in the jurisdictions in which they are approved. We may also incur liability associated with product 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 our products (e.g. risk evaluation and mitigation strategies, track and trace requirements, and 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. Similar responsibilities would apply upon regulatory approval of any of our other product candidates currently under development.

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. Outside of the United States, we may be subject to analogous foreign laws and regulations in the various jurisdictions in which we operate. These laws and regulations apply to 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 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.

TABLE OF CONTENTS

The principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to certain regulatory authorities, including the FDA and comparable foreign regulatory authorities. Consequently, the FDA or other regulatory authority may conclude that a financial relationship between us and a principal investigator creates a conflict of interest or otherwise affects interpretation of the study. In the event of a conflict of interest with respect to a study, the integrity of the data generated at the applicable clinical trial site may be questioned or the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or other regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

The FDA and foreign regulatory authorities may also impose post-approval commitments on us for approved products, 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. We are currently subject to certain post-approval commitments. If we fail to comply with post-approval legal and regulatory requirements, we could be subject to penalties, 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 our products and any other future product candidates may be subject to requirements for costly post-approval testing and surveillance to monitor its safety or efficacy.

Advertising and promotion are subject to stringent FDA rules and oversight, and as an NDA-holder, we may be held responsible for any advertising and promotion 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. We are also required to engage in appropriate truthful, non-misleading, and non-promotional scientific exchange concerning our products, and applicable regulatory authorities, competitors, and other third parties may take the position that we are not in compliance with such regulations. In addition to medical education efforts, we may offer patient support services to assist patients receiving treatment with our commercially approved products which have increasingly become the focus of government investigation.

Adverse event information concerning approved products must be reviewed, and as an NDA-holder, 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, state and local governments, and foreign equivalents of the foregoing. All of these activities are also potentially subject to healthcare false claims and fraud and abuse laws, as well as consumer protection and unfair competition laws.

If our operations with respect to our 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 fraud and abuse laws may be costly.

Our employees and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are subject to the risk of fraud or other misconduct by our employees and consultants, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory

TABLE OF CONTENTS

authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee and consultant misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee and consultant misconduct, whether intentional, reckless, negligent, or unintentional, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

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, 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.

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. For example, 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 in the U.S. and other markets is critical to the commercial success of our approved products. Recently in the U.S. 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.

TABLE OF CONTENTS

Individual states in the United States have been increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. 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 our products 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.

We are subject to data security and privacy risks, and our actual or perceived failure to comply with regulations and other legal obligations related to privacy and data protection could harm our business.

We are subject to legal obligations related to privacy and data protection. Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use, and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. For example, we are subject to the California Consumer Privacy Act, which gives California residents expanded rights to access and require deletion of their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. We are also subject to the General Data Protection Regulation in the EU. See "Risks relating to our business—Risks relating to international operations—Our actual or perceived failure to comply with European governmental regulations and other legal obligations related to privacy, data protection and information security could harm our business" in this section for additional discussion of international privacy laws and regulations. Failure to comply with these laws and regulations could result in government enforcement actions, private litigation, or harm to our reputation and 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.

Intellectual property risks

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 legal proceedings 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 legal 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 our products and 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.

TABLE OF CONTENTS

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 litigation or administrative 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 products and product candidates and any such events would significantly impair the value of such products and product candidates.

Product liability risks

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

If the use or misuse of any products we sell, or a partner sells, 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 have 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 products or product candidates. We have product liability insurance covering our clinical trials. Clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance or increase our existing coverage at a reasonable cost to protect us against losses that could have a material adverse effect on our business. An individual may bring a product liability claim against us if one of our products or product candidates causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any product liability claim brought against us, with or without merit, could result in:

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

- the diversion of management’s attention from managing our business.

Risks relating to contractual arrangements

We face risks related to our government-funded programs and are subject to various U.S. Government contract requirements, which may create a disadvantage and additional risks to us.

We have 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, Yellow Fever 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. 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, this could have an adverse impact on the programs associated with such funding and could also adversely impact our cash flows and operations.

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.

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, this could have an adverse impact on our cash flows and operations.

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 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 2015; all subsequent fiscal years are still open and auditable. Based on the results of its audits, the U.S. Government may adjust our contract-related costs and fees, including allocated indirect costs. This adjustment could impact the amount of revenues reported on a historic basis and could impact our cash flows under the contracts prospectively. In addition, in the event BARDA/HHS or NIAID/HHS determines that certain costs and fees were unallowable or determines that the allocated indirect cost rate was higher than the actual indirect cost rate, BARDA/HHS or NIAID/HHS would be entitled to recoup any overpayment from us as a result. In addition, if an audit or review uncovers any improper or illegal activity, we 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

[TABLE OF CONTENTS](#)

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.

There are risks related to the potential government use or sale of our antivirals.

Government use or sale, in emergency situations or otherwise, of our antivirals—including peramivir for the treatment of influenza—may result in risks to us or our collaborative partners. There can be no assurance that government use of our antivirals (whether as indicated or outside of their current indications) will prove to be generally safe, well-tolerated and effective. Any government sale or use (on an emergency basis or otherwise) of our antivirals in any country may create liabilities for us or our partners.

In September 2018, we entered into a contract with the U.S. Government for the procurement of up to 50,000 doses of RAPIVAB (peramivir injection) over a five-year period. In addition, we are working with NIAID/HHS to further develop galidesivir. There can be no assurance that we or our manufacturers will be able to fully meet the demand for such antivirals with respect to these or future arrangements. Further, we may not receive a favorable purchase price for future orders, if any, of our antivirals by governmental entities. Our competitors may develop products that could compete with or replace any antivirals selected for government sale or use. 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 can be 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 or that peramivir will be approved for any use or will achieve market approval in additional countries. There can be no assurance that galidesivir will be approved for use in any countries. In the event that any emergency use or market approval is granted in any country, there can be no assurance that any government order or commercialization of the applicable product or product candidate in such countries will be substantial or will be profitable to us.

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, 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 any of our in-licenses relating to our products or product candidates, 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.

Royalties and milestone payments from Shionogi under our agreement with Shionogi (the “Shionogi Agreement”) are required to be used by Royalty Sub to satisfy its obligations under its PhaRMA Notes, and generally will not be available to us for other purposes unless and 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 and (ii) the pledge by us of our equity interest in Royalty Sub. Payments from Shionogi to us on non-governmental sales under the Shionogi Agreement will generally not be available to us for other purposes unless and until Royalty Sub has repaid in full its obligations under the PhaRMA Notes. Accordingly, these funds have been and will continue to be required to be dedicated to Royalty Sub’s debt service and not available to us for product development or other purposes. Since September 1, 2014, payments from Shionogi have been insufficient for Royalty Sub to service its obligations under the PhaRMA Notes, resulting in a continuing event of default with respect to the PhaRMA Notes since that time. As a result of the continuing event of default, the holders of the PhaRMA Notes may be able to foreclose on the collateral securing the PhaRMA Notes and our equity interest in Royalty Sub and may exercise other remedies available to them

TABLE OF CONTENTS

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.

The PhaRMA Notes had a final legal maturity date of December 1, 2020, at which time the outstanding principal amount of the PhaRMA Notes of \$30.0 million, together with accrued and unpaid interest of \$20.6 million, was due in full. The failure by Royalty Sub to repay in full the outstanding principal amount of the PhaRMA Notes, together with any accrued and unpaid interest, at the December 1, 2020 final maturity date constituted an additional event of default under the PhaRMA Notes. We cannot predict whether holders of PhaRMA Notes will seek to pursue any remedies as a result of the continuing events of default with respect to the PhaRMA Notes. The PhaRMA Notes are the obligation of Royalty Sub. As a result, we do not currently expect the continuing events of default on the PhaRMA Notes to have a significant impact on our future results of operations or cash flows. However, we cannot assure you that this will be the case or that we will not otherwise be adversely affected as a result the continuing events of default under the PhaRMA Notes or the failure by Royalty Sub to repay the PhaRMA Notes at maturity.

Because continuing events of default exist under the PhaRMA Notes, the holders of the PhaRMA Notes may be able to foreclose on the collateral securing the PhaRMA Notes and our equity interest in Royalty Sub. As a result, 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.

As Royalty Sub has been unable to service its obligations under the PhaRMA Notes and continuing events of default exist under the PhaRMA Notes, the holders of the PhaRMA Notes may be able to foreclose on the collateral securing the PhaRMA Notes and our equity interest in Royalty Sub and 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. In addition, the PhaRMA Notes have a final legal maturity date of December 1, 2020, at which time the outstanding principal amount of the PhaRMA Notes, together with accrued and unpaid interest, was due in full. The failure by Royalty Sub to repay in full the outstanding principal amount of the PhaRMA Notes, together with any accrued and unpaid interest, at the December 1, 2020 final maturity date constituted an additional event of default under the PhaRMA Notes. We cannot predict whether holders of PhaRMA Notes will seek to pursue any remedies as a result of the continuing events of default with respect to the PhaRMA Notes. The PhaRMA Notes are the obligation of Royalty Sub. As a result, we do not currently expect the continuing events of default on the PhaRMA Notes to have a significant impact on our future results of operations or cash flows. However, we cannot assure you that this will be the case or that we will not otherwise be adversely affected as a result the continuing events of default under the PhaRMA Notes or the failure by Royalty Sub to repay the PhaRMA Notes at maturity.

We have incurred significant indebtedness, which could adversely affect our business. Additionally, our Credit Agreement contains conditions and restrictions that limit our flexibility in drawing on the additional funds thereunder and in operating our business. We may be required to make a prepayment or repay our 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.

As of June 30, 2021, we had an outstanding principal balance under our \$200,000 Credit Agreement (the "Credit Agreement") with Athyrium Opportunities III Co-Invest 1 LP of \$132.4 million, net of deferred financing costs and inclusive of our option to, for each of the first eight full fiscal quarters following December 7, 2020, make the applicable interest payment in-kind by capitalizing the entire amount of interest accrued during the applicable interest period with the unpaid original principal amount outstanding on the last day of such period. We may also draw up to another \$75.0 million in aggregate principal amount under the Term B Loan and the Term C Loan (each as defined in the Credit Agreement) under the Credit Agreement if, among other conditions, the Company reaches defined revenue milestones and, with respect to a draw on the Term C Loan, the Term B Loan has been funded prior to or contemporaneously with the Term C Loan. Our indebtedness could have important consequences to our stockholders. For example, it:

- increases our vulnerability to adverse general economic or industry conditions;
- limits our flexibility in planning for, or reacting to, changes in our business or the industry in which we operate;

TABLE OF CONTENTS

- makes us more vulnerable to increases in interest rates, as borrowings under our Credit Agreement are at variable rates;
- requires us to dedicate a portion of our cash flow from operations to interest payments, limiting the availability of cash for other purposes;
- limits our ability to obtain additional financing or refinancing in the future for working capital or other purposes; and
- places us at a competitive disadvantage compared to our competitors that have less indebtedness.

Furthermore, our Credit Agreement contains various covenants that limit our ability to engage in specified types of transactions. Subject to certain exceptions, these covenants limit our ability to, among other things, grant certain types of liens on our assets; make certain investments; incur or assume certain debt, including accessing additional tranches of debt under the Credit Agreement; engage in certain mergers, acquisitions, and similar transactions; dispose of assets; license certain property; distribute dividends; make certain restricted payments; change the nature of our business; engage in transactions with affiliates and insiders; prepay other indebtedness; or engage in sale and leaseback transactions.

The Credit Agreement also contains certain financial covenants, including a minimum liquidity covenant that requires us to maintain at all times, as applicable, at least \$15.0 million of unrestricted cash and cash equivalents if only the Term A Loan (as defined in the Credit Agreement) has been drawn; at least \$20.0 million of unrestricted cash and cash equivalents if the Term B Loan has been drawn but the Term C Loan has not been drawn; and at least \$15.0 million (or, in certain circumstances, \$20.0 million) of unrestricted cash and cash equivalents if the Term C Loan has been drawn, subject to certain exceptions. In addition, if we draw upon the Term C Loan, we will be required to achieve certain minimum targets for consolidated net revenues from ORLADEYO sales in the U.S.

The covenants contained in the Credit Agreement could cause us to be unable to pursue business opportunities that we or our stockholders may consider beneficial without the lenders' permission or without repaying all outstanding obligations under the Credit Agreement.

A breach of any of these covenants could result in an event of default under the Credit Agreement. An event of default will also occur if, among other things, we fail to pay amounts due under the Credit Agreement, we fail to repay certain other indebtedness having an aggregate principal amount in excess of one percent of our borrowings under the Credit Agreement, a material adverse change in our business, assets, properties, liabilities, or condition occurs, or a material impairment of our ability to perform our obligations under the Credit Agreement occurs, we experience a change of control, certain negative regulatory events occur, including without limitation the loss of a required permit or a recall of a product, or we fail to make required payments under our Royalty Purchase Agreement with RPI. In the case of a continuing event of default under the Credit Agreement, the lenders under the Credit Agreement could elect to declare all amounts outstanding to be immediately due and payable, proceed against the collateral in which we granted to the lenders a security interest, or otherwise exercise the rights of a secured creditor. Amounts outstanding under the Credit Agreement are secured by a security interest in, subject to certain exceptions, substantially all of our assets. Because substantially all of our assets are pledged to secure the Credit Agreement obligations, our ability to incur additional secured indebtedness or to sell or dispose of assets to raise capital may be impaired, which could have an adverse effect on our financial flexibility.

Risk relating to international operations

International expansion of our business exposes us to business, regulatory, political, operational, financial, and economic risks.

Our business strategy includes international expansion, including the commercialization of products outside of the United States. We currently conduct clinical studies and regulatory activities and have hired, and expect to continue hiring, employees outside of the United States. Doing business internationally involves a number of risks, including but not limited to:

- multiple, conflicting, and changing laws and regulations such as privacy and data regulations, transparency regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses;

TABLE OF CONTENTS

- introduction of new health authority requirements and/or changes in health authority expectations;
- failure by us or our partners to obtain and maintain regulatory approvals for the use of our products in various countries;
- complexities and difficulties in obtaining and maintaining protection for, and enforcing, our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits on our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations;
- natural disasters and political and economic instability, including wars, terrorism, political unrest, results of certain elections and votes, actual or threatened public health emergencies and outbreak of disease (including for example, the recent coronavirus outbreak), boycotts, adoption or expansion of government trade restrictions, and other business restrictions;
- certain expenses including, among others, expenses for travel, translation, and insurance;
- regulatory and compliance risks that relate to maintaining accurate information and control over commercial operations and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, or FCPA, including its books and records provisions or anti-bribery provisions, or the U.K. Bribery Act and similar foreign laws and regulations; and
- regulatory and compliance risks relating to doing business with any entity that is subject to sanctions administered by the Office of Foreign Assets Control of the U.S. Department of the Treasury.

Any of these factors could significantly harm our future international expansion of operations and, consequently, our business and results of operations.

Additionally, in some countries, such as Japan and the countries of the EU, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our partners may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

Our actual or perceived failure to comply with European governmental regulations and other legal obligations related to privacy, data protection and information security could harm our business.

EU member states, Switzerland and other countries have adopted data protection laws and regulations, which impose significant compliance obligations. For example, the General Data Protection Regulation (“GDPR”) imposes strict requirements on controllers and processors of personal data, including special protections for “special category data,” which includes health, biometric and genetic information of data subjects located in the EU. Further, GDPR provides a broad right for EU member states to create supplemental national laws, for example relating to the processing of health, genetic and biometric data, which could further limit our ability to use and share such data or could cause our costs to increase and harm our business and financial condition. GDPR grants individuals the opportunity to object to the processing of their personal information, allows them to request deletion of personal information in certain circumstances, and provides the individual with an express right to seek legal remedies in the event the individual believes his or her rights have been violated. Further, the GDPR imposes strict rules on the transfer of personal data out of the EU to the United States or other regions that have not been deemed to offer “adequate” privacy protections.

Failure to comply with the requirements of the GDPR and the related national data protection laws of the EU member states, which may deviate slightly from the GDPR, may result in significant fines of up to 4% of

global revenues, or €20.0 million, whichever is greater, and in addition to such fines, our failure to comply with the requirements of GDPR may subject us to litigation and/or adverse publicity, which could have material adverse effects on our reputation and business. As a result of the implementation of the GDPR, we are required to put in place additional mechanisms to ensure compliance with the new data protection rules. For example, the GDPR requires us to make more detailed disclosures to data subjects, requires disclosure of the legal basis on which we can process personal data, makes it harder for us to obtain valid consent for processing, will require the appointment of a data protection officer where sensitive personal data (i.e., health data) is processed on a large scale, introduces mandatory data breach notification throughout the EU, imposes additional obligations on us when we are contracting with service providers and requires us to adopt appropriate privacy governance including policies, procedures, training and data audit.

We are subject to the supervision of local data protection authorities in those jurisdictions where we undertake clinical trials. We depend on a number of third parties in relation to the provision of our services, a number of which process personal data of EU individuals on our behalf. With each such provider we are required to enter into contractual arrangements under which they are contractually obligated to only process personal data according to our instructions, and conduct diligence to ensure that they have sufficient technical and organizational security measures in place.

We are also subject to evolving European privacy laws on electronic marketing and cookies. The EU is in the process of replacing the e-Privacy Directive (2002/58/EC) with a new set of rules taking the form of a regulation that will be directly implemented in the laws of each EU member state. While this e-Privacy Regulation was originally intended to be adopted on May 25, 2018, it is still going through the European legislative process and the timing of its adoption remains unclear.

The United Kingdom's decision to withdraw from the EU could result in increased regulatory and legal complexity, which may make it more difficult for us to do business in Europe and impose additional challenges in securing regulatory approval of our product candidates in Europe.

The United Kingdom's exit from the EU, or Brexit, has caused political and economic uncertainty, including in the regulatory framework applicable to our operations and product candidates, and this uncertainty may persist for years. Brexit could, among other outcomes, disrupt the free movement of goods, services and people between the United Kingdom and the EU, and result in increased legal and regulatory complexities, as well as potential higher costs of conducting business in Europe. The long-term effects of Brexit will depend in part on how the current and future trade agreements between the United Kingdom and the EU take effect in practice. Changes in United Kingdom or EU regulations may cause disruption or delays in granting clinical trial authorization or opinions for marketing authorization, disruption of importation and export of active substance and other components of new drug formulations, and disruption of the supply chain for clinical trial product and final authorized formulations.

The cumulative effects of the disruption to the regulatory framework may add considerably to the development lead time to marketing authorization and commercialization of products in the EU and/or the United Kingdom. It is possible that there will be increased regulatory complexities, which can disrupt the timing of our clinical trials and regulatory approvals. In addition, changes in, and legal uncertainty with regard to, national and international laws and regulations may present difficulties for our clinical and regulatory strategy. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the EU and restrict our ability to generate revenues and achieve and sustain profitability.

In addition, as a result of Brexit, other European countries may seek to conduct referenda with respect to their continuing membership with the EU. Given these possibilities and others we may not anticipate, as well as the absence of comparable precedent, it is unclear what financial, regulatory and legal implications the withdrawal of the United Kingdom from the EU will have and how such withdrawal will affect us, and the full extent to which our business could be adversely affected.

Risks relating to technology.

If our facilities, or the facilities of our third-party vendors, incur damage or power is lost for a significant length of time, our business will suffer.

We and our third-party vendors store commercial product, clinical and stability samples at our facilities that could be damaged if the facilities incur 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 products or samples could result in significant delays in our commercialization or 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 cybersecurity breach could adversely affect our business.

We are increasingly dependent on information technology systems to operate our business. In addition, the FDA and comparable foreign regulatory authorities regulate, 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.

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.

Risks relating to investing in our common stock and the pre-funded warrants

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 close to 50% of BioCryst and can individually, and as a group, influence our operations based upon their concentrated ownership and may also 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 June 30, 2021, the 52-week range of the market price of our stock was from \$3.30 to \$17.74 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:

TABLE OF CONTENTS

- 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 the ownership interests of our current stockholders and cause our stock price to decline.

Future sales of our common stock by us or our current stockholders into the public market could cause the market price of our stock to fall. As of July 30, 2021, there were 178,869,928 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 July 30, 2021, there were 25,039,041 stock options outstanding and 10,198,379 shares available for issuance under our Amended and Restated Stock Incentive Plan, 4,390,793 stock options outstanding and 1,479,082 shares available for issuance under our Amended and Restated Inducement Equity Incentive Plan and 6,056,304 shares available for issuance under our Amended and Restated Employee Stock Purchase Plan. In addition, we could also make equity grants outside of our Amended and Restated Stock Incentive Plan or Amended and Restated Inducement Equity 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.

TABLE OF CONTENTS

In March 2017, we entered 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 pursuant to the Registration Rights Agreement cover all shares then held or thereafter acquired by the Baker Entities, for up to ten years, and include our obligation to facilitate certain underwritten public offerings of our common stock by the Baker Entities in the future. On May 10, 2017, we filed a registration statement on Form S-3 with respect to 11,710,951 shares of common stock held by the Baker Entities. Subsequently, on November 21, 2019, certain of the Baker Entities acquired pre-funded warrants to purchase 11,764,706 shares of our common stock at a price of \$1.69 per warrant. In addition, on June 1, 2020, we issued the Baker Entities pre-funded warrants to purchase 3,511,111 shares of our common stock at a price of \$4.49 per warrant. Each warrant has an exercise price of \$0.01 per share. If the Baker Entities, by exercising their 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 5,000,000 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 of Incorporation also requires supermajority approval of any amendment of these provisions. These provisions and other provisions of our bylaws and of Delaware law applicable to us could delay or make more difficult a merger, tender offer or proxy contest involving us.

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.

Our Amended and Restated Bylaws provide that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for certain litigation that may be initiated by our stockholders, which may limit a stockholder’s ability to obtain a favorable judicial forum for such disputes with us or our directors, officers or employees.

Our Amended and Restated Bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, stockholders, employees or agents to us or our stockholders, (iii) any action asserting a claim against us or any of our directors, officers, stockholders, employees or agents arising out of or relating to any provision of the General Corporation Law of Delaware or our Certificate of Incorporation or Amended and Restated Bylaws or (iv) any action against us or any of our directors, officers, stockholders, employees or agents governed by the internal affairs doctrine of the State of Delaware. This exclusive forum provision does not apply to establish the Delaware Court of Chancery as the forum for actions or proceedings brought to enforce a duty or liability created by the Securities Act of 1933, as amended, or the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction.

This exclusive forum provision may limit a stockholder’s ability to choose its preferred judicial forum for disputes with us or our directors, officers, employees or agents, which may discourage the filing of lawsuits with respect to such claims. If a court were to find this exclusive forum provision to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in another jurisdiction, which could adversely affect our business and financial condition.

There is no public market for the pre-funded warrants being offered in this offering.

There is no established public trading market for the pre-funded warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list these warrants on any securities exchange or nationally recognized trading system, including The Nasdaq Global Select Market. Without an active market, the liquidity of these warrants will be limited.

Holders of pre-funded warrants purchased in this offering will have no rights as common stockholders until such holders exercise their warrants and acquire our common stock.

Until holders of the pre-funded warrants acquire shares of our common stock upon exercise of such warrants, the holders will have no rights with respect to the shares of our common stock underlying such warrants. Upon exercise of the pre-funded warrants, the holders will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise.

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.

General risk factors

Natural disasters, epidemic or pandemic disease outbreaks, trade wars, political unrest or other events could disrupt our business or operations or those of our development partners, manufacturers, regulators or other third parties with whom we conduct business now or in the future.

A wide variety of events beyond our control, including natural disasters, epidemic or pandemic disease outbreaks (such as the ongoing COVID-19 pandemic), trade wars, political unrest or other events could disrupt our business or operations or those of our development partners (such as Torii), manufacturers, regulatory authorities, or other third parties with whom we conduct business. These events may cause businesses and government agencies to be shut down, supply chains to be interrupted, slowed, or rendered inoperable, and individuals to become ill, quarantined, or otherwise unable to work and/or travel due to health reasons or governmental restrictions. If our operations or those of third parties with whom we have business are impaired or curtailed as a result of these events, the development and commercialization of our products and product candidates could be impaired or halted, which could have a material adverse impact on our business. See “Risk Factors—Risks relating to our business—Risks relating to COVID-19—Our business, operations, clinical development or commercialization plans and timelines, and access to capital could be adversely affected by the effects of the COVID-19 pandemic on us or on third parties with whom we conduct business, including without limitation our development partners, manufacturers, clinical research organizations (“CROs”), and others, as well as on the regulatory and government agencies with whom we work.”

We are subject to legal proceedings, which could harm our reputation or result in other losses or unexpected expenditure of time and resources.

From time to time, we may be involved in disputes, including, without limitation, disputes with our employees, collaborative partners, and third-party vendors. We may be called upon to initiate legal proceedings or to defend ourselves in such legal proceedings relating to our relationships with these parties, our decisions and actions or omissions with respect thereto, and our business. In addition, if our stock price is volatile, we may become involved in securities class action lawsuits in the future. Due to the inherent uncertainties in legal proceedings, 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. Any current or future dispute resolution or legal proceeding, regardless of the merits of any such proceeding, could harm our reputation and result in substantial costs and a diversion of management’s attention and resources that are needed to successfully run 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

[TABLE OF CONTENTS](#)

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 we fail to retain our existing key personnel or fail to attract and retain additional key personnel, the development of our product candidates, the 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. This risk has been heightened in the current environment as a result of the ongoing COVID-19 pandemic. 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.

Use of proceeds

We estimate that we will receive net proceeds of approximately \$187.5 million from this offering, after deducting estimated 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 \$215.7 million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We will receive nominal proceeds, if any, from the exercise of the pre-funded warrants.

We intend to use the net proceeds from this offering for general corporate purposes, including:

- worldwide development, manufacturing, regulatory and commercial activities for ORLADEYO;
- advancement of the worldwide development, manufacturing, regulatory and clinical activities for BCX9930 for complement-mediated diseases;
- discovery, manufacturing, development and clinical activities for other pipeline molecules in rare diseases; and
- capital expenditures and other general working capital needs.

Dilution

As of June 30, 2021, our net tangible book value was approximately \$(105.5) million, or approximately \$(0.59) 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 178,725,163 shares of our common stock outstanding as of June 30, 2021.

Investors participating in this offering will incur immediate, substantial dilution. After giving effect to the sale of _____ shares of our common stock and pre-funded warrants to purchase up to _____ shares of our common stock at the public offering price of \$ _____ per share of common stock and \$ _____ per pre-funded warrant (which equals the public offering price per share of the common stock less the \$0.01 per share exercise price of each such pre-funded warrant) (and excluding shares of common stock issued and any proceeds received upon exercise of the pre-funded warrants or any resulting accounting associated with the pre-funded warrants) and after deducting estimated underwriting discounts and commissions and estimated offering expenses, our as adjusted net tangible book value as of June 30, 2021 would have been \$ _____ million, or \$ _____ per share. This amount represents an immediate increase in net tangible book value of \$ _____ per share of our common stock to existing stockholders and an immediate dilution in net tangible book value of \$ _____ per share to investors purchasing shares of common stock and pre-funded warrants in this offering.

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

Public offering price per share	\$
Net tangible book value per share as of June 30, 2021	\$(0.59)
Increase in net tangible book value per share attributable to investors purchasing our common stock and pre-funded warrants in this offering	\$
Net tangible book value per share as of June 30, 2021 after giving effect to this offering	\$
Dilution in net tangible book value per share to investors purchasing our common stock in this offering	\$

If holders of pre-funded warrants purchased in this offering exercise such pre-funded warrants, the as adjusted net tangible book value per share of our common stock after giving effect to this offering would be \$ _____ per share, and the dilution in net tangible book value per share to investors purchasing common stock in this offering would be \$ _____ per share.

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 \$ _____ per share, and the dilution in net tangible book value per share to investors purchasing common stock in this offering would be of \$ _____ per share.

The above discussion and table are based on 178,725,163 shares of our common stock outstanding as of June 30, 2021 and excludes the shares of common stock issuable upon the exercise of the pre-funded warrants being offered by us in this offering as well as:

- 15,275,817 shares of common stock issuable upon the exercise of outstanding pre-funded warrants;
- 25,023,040 shares of common stock issuable upon the exercise of stock options outstanding under our Stock Incentive Plan as of June 30, 2021, at a weighted average exercise price of \$7.04 per share;
- 4,387,793 shares of common stock issuable upon the exercise of stock options outstanding under our Inducement Equity Incentive Plan as of June 30, 2021, at a weighted average exercise price of \$4.65 per share; and
- 10,189,379 additional shares of common stock reserved for issuance under our Stock Incentive Plan, 1,479,082 additional shares of common stock reserved for issuance under our Inducement Equity Incentive Plan, and 6,056,304 additional shares of common stock reserved for issuance under our Employee Stock Purchase Plan as of June 30, 2021.

TABLE OF CONTENTS

To the extent that outstanding options or outstanding pre-funded warrants 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.

Description of pre-funded warrants

In this offering, we are offering pre-funded warrants to purchase _____ shares of our common stock. The following description is subject in all respects to the provisions contained in the form of pre-funded warrant. You should review a copy of the form of pre-funded warrant, which will be filed as an exhibit to our Current Report on Form 8-K being filed with the SEC in connection with this offering, for a complete description of the terms and conditions of the pre-funded warrants.

The pre-funded warrants will be issued as individual warrant agreements to the holders. The pre-funded warrants are exercisable at any time after their original issuance at an exercise price of \$0.01 per share. The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and by payment in full in immediately available funds for the number of shares of common stock purchased upon such exercise. As an alternative to payment in immediately available funds, the holder may, in its sole discretion, elect to exercise the pre-funded warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. No fractional shares of common stock will be issued in connection with the exercise of a pre-funded warrant. In lieu of issuing fractional shares, we will pay the holder an amount in cash equal to the fair market value of any fractional share, calculated based on the trading price of our common stock.

The exercise price per whole share of our common stock purchasable upon the exercise of the pre-funded warrants is \$0.01 per share of common stock. The exercise price of the pre-funded warrants is subject to adjustment from time to time in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock and also upon any distributions for no consideration of assets, including cash, stock or other property, to all of our stockholders.

A holder will not have the right to exercise any portion of the pre-funded warrant if the holder (together with its affiliates) would beneficially own in excess of 9.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise. However, any holder may increase or decrease such ownership percentage limit to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us.

We do not plan on applying to list the pre-funded warrants on the Nasdaq Global Select Market or any other national securities exchange or automated quotation system.

Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent.

In the event of a fundamental transaction, as defined in the pre-funded warrants and generally including, without limitation, any reclassification of our common stock into other securities, cash or property, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition by any person or group, whether in a tender offer, exchange offer, stock purchase agreement, or other business combination, of more than 50% of the voting power of our capital stock, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the same amount and kind of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction.

Except by virtue of such holder's ownership of shares of our common stock, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the pre-funded warrant.

Listing of common stock and dividend policy

Our common stock is listed on the Nasdaq Global Select Market under the symbol “BCRX.” We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market or any other national securities exchange or any other nationally recognized trading system.

The last reported sale price of our common stock on the Nasdaq Global Select Market on August 6, 2021 was \$17.61 per share. As of August 6, 2021, there were approximately 162 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 and pre-funded warrants described in this prospectus supplement through a number of underwriters. J.P. Morgan Securities LLC, Evercore Group L.L.C. and Piper Sandler & Co. are acting as joint book-running managers of the offering and as representatives 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 and pre-funded warrants listed next to its name in the following table:

Name	Number of Shares	Number of Pre-funded Warrants
J.P. Morgan Securities LLC		
Evercore Group L.L.C.		
Piper Sandler & Co.		
Total		

The underwriters are committed to purchase all the shares of common stock and pre-funded warrants offered by us if they purchase any shares or pre-funded warrants. 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 and pre-funded warrants directly to the public at the public offering prices set forth on the cover page of this prospectus supplement and to certain dealers at those prices less a concession not in excess of \$ _____ per share. After the offering of the shares and pre-funded warrants 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 _____ 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 number of shares subject to the underwriters' option will equal 15% of the total number of shares of common stock we are offering plus the shares underlying the pre-funded warrants. 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 or the public offering price per pre-funded warrant less the amount paid by the underwriters to us per pre-funded warrant, as the case may be. The underwriting fee for the common stock is \$ _____ per share and the underwriting fee for each pre-funded warrant is \$ _____. 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	\$ _____	\$ _____
Per Pre-funded Warrant	\$ _____	\$ _____
Total	\$ _____	\$ _____

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

TABLE OF CONTENTS

approximately \$500,000. We have agreed to reimburse the underwriters for certain expenses incurred in connection with the public offering in an amount of up to \$30,000. In addition, we have granted to J.P. Morgan Securities LLC the right to participate in any public offering of our common stock until December 15, 2022, 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 representatives 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, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, or submit to 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 undertake any of the foregoing, or (ii) enter into any swap or other arrangement that transfers, in whole or in part, any of the economic consequences of 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, Evercore Group L.L.C. and Piper Sandler & Co. 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, Evercore Group L.L.C. and Piper Sandler & Co., (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of 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 publicly disclose the intention to undertake any of the foregoing, (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 directors and 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; 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.

TABLE OF CONTENTS

Our common stock is listed on the Nasdaq Global Select Market under the symbol “BCRX.” We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market or any other national securities exchange or any other nationally recognized trading system.

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 representatives of the underwriters purchases common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

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

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.

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. The underwriters and certain of their affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

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 representatives; 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 representatives 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 representatives has been obtained to each such proposed offer or resale.

The Company, the representatives 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

[TABLE OF CONTENTS](#)

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.

Legal matters

The validity of the securities 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, 2020, and the effectiveness of our internal control over financial reporting as of December 31, 2020, 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, 2020 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.

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, 2020 filed with the SEC on [March 1, 2021](#) (including the sections of our proxy statement relating to our May 25, 2021 annual meeting of stockholders that are incorporated by reference therein);
- Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2021 and June 30, 2021 filed with the SEC on [May 7, 2021](#) and [August 9, 2021](#), respectively;
- Our Current Reports on Form 8-K filed with the SEC on [May 26, 2021](#), [July 28, 2021](#), [August 3, 2021](#) and [August 9, 2021](#); 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, as updated by the description of our common stock filed as [Exhibit 4.1](#) to the Annual Report on Form 10-K for the year ended December 31, 2020, and any amendments or reports filed for the purpose of updating the description of our common stock.

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.

[TABLE OF CONTENTS](#)

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.



BioCryst Pharmaceuticals, Inc.

**Common Stock
Preferred Stock
Depositary Shares
Purchase Contracts
Warrants
Debt Securities
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 to provide you with information different from that contained 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 information other than the information contained in or incorporated by reference in this prospectus or any prospectus supplement. We are not making or soliciting an offer of any securities other than the securities described in this prospectus and any prospectus supplement. We are not making or soliciting an offer of these securities in any state or jurisdiction where the offer is not permitted or in any circumstances in which such offer or solicitation is unlawful. You should not assume that the information contained or incorporated by reference in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front of those documents.

Investing in these securities involves a high degree of risk. See "Risk Factors" on page 2 of this prospectus, in the applicable prospectus supplement we will deliver with this prospectus and in the documents incorporated herein and therein by reference.

The securities may be sold by us to or through underwriters or dealers, directly to purchasers or through agents designated from time to time, or through a combination of these methods. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus. If any underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable discounts or commissions and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement. This prospectus may not be used to sell any securities unless accompanied by a prospectus supplement.

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

The date of this prospectus is March 1, 2021.

TABLE OF CONTENTS

	Page
ABOUT THIS PROSPECTUS	i
PROSPECTUS SUMMARY	1
RISK FACTORS	2
INFORMATION REGARDING FORWARD-LOOKING STATEMENTS	3
USE OF PROCEEDS	5
DESCRIPTION OF COMMON STOCK, PREFERRED STOCK AND DEPOSITARY SHARES	6
DESCRIPTION OF PURCHASE CONTRACTS	10
DESCRIPTION OF WARRANTS	11
DESCRIPTION OF DEBT SECURITIES	12
DESCRIPTION OF UNITS	17
PLAN OF DISTRIBUTION	18
LEGAL MATTERS	21
EXPERTS	21
WHERE YOU CAN FIND MORE INFORMATION	22
INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE	22

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.

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 referenced under the heading “Where You Can Find More Information.”

All references to “Company,” “BioCryst,” “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.

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 commercial-stage biotechnology company that discovers novel, oral, small-molecule medicines. We focus on oral treatments for rare diseases in which significant unmet medical needs exist and an enzyme plays the key role in the biological pathway of the disease. 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.

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 website 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 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, 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,” “predicts,” “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 preclinical development, clinical development, commercialization, or post-marketing studies of our products and product candidates, including ORLADEYO™ (berotralstat), BCX9930, BCX9250, peramivir, galidesivir, and early stage discovery programs;
- the timing and success of our commercialization of ORLADEYO in the U.S. and elsewhere;
- the potential for government stockpiling orders of our products and product candidates, including the timing or likelihood of entering into any U.S. government stockpile order and our ability to execute any such order;
- the potential funding from our contracts with the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services and the National Institute of Allergy and Infectious Diseases for the development of galidesivir;
- additional regulatory approvals, or milestones, royalties or profit from sales of our products by us or our partners;
- 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 products and product candidates;
- plans, programs, progress and potential success of our collaborations, including Torii Pharmaceutical Co., Ltd. for ORLADEYO in Japan, Shionogi & Co., Ltd. and Green Cross Corporation for peramivir in their territories, and Mundipharma International Corporation Limited for mundesine;
- our and our subsidiary guarantors’ ability to satisfy obligations under our \$200.0 million Credit Agreement with Athyrium Opportunities III Co-Invest 1 LP and to comply with the covenants as set forth in the agreements governing our debt obligations;
- the ability of our subsidiary, JPR Royalty Sub LLC, to satisfy its obligations in respect of the PhaRMA Senior Secured 14.0% Notes due 2020;
- 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, annual cash utilization, and our needs for additional financing;
- the timing or likelihood of regulatory filings or regulatory agreements, deferrals, and approvals;
- our ability to manage our liquidity needs, including our ability to raise additional capital to fund our operations or repay our recourse debt obligations;
- our financial performance; and
- competitive companies, technologies, and our industry.

[TABLE OF CONTENTS](#)

These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under “Risk Factors” and elsewhere in this prospectus, any subsequent prospectus supplement 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, and in our Current Reports on Form 8-K filed subsequent to the Annual Report, as well as any amendments we make to those filings or any future filings we make 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 commercialization, development, manufacturing and regulatory activities for ORLADEYO;
- advancing the development of other pipeline compounds for rare disease targets, including paroxysmal nocturnal hemoglobinuria (PNH) and other complement-mediated diseases and fibrodysplasia ossificans progressiva (FOP);
- post-approval commitments for RAPIVAB™;
- funding our research and development efforts; and
- capital expenditures 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 our success in commercializing and achieving market acceptance of ORLADEYO, 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 of our capital stock is based on and qualified in its entirety by reference to our Third Restated Certificate of Incorporation, as amended (the “Certificate of Incorporation”), and our Amended and Restated Bylaws, as amended (the “Bylaws”), each of which are incorporated by reference into this prospectus. See “Where You Can Find More Information.”

Authorized Capital Stock

Under the Certificate of Incorporation, we are currently authorized to issue up to 450,000,000 shares of common stock, par value \$0.01 per share, and 5,000,000 shares of preferred stock, par value \$0.01 per share. On February 24, 2021, there were 177,521,693 shares of common stock outstanding and no shares of preferred stock outstanding. The number of authorized shares of common stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of a majority of the capital stock of the Company entitled to vote.

Common Stock

Holders of our common stock are entitled to one vote per share on all matters submitted to a vote of stockholders. There are no cumulative voting rights. Directors are elected by a plurality of the votes cast by the stockholders entitled to vote. Except as provided otherwise in the Certificate of Incorporation, the Bylaws, or the General Corporation Law of the State of Delaware (the “DGCL”), the holders of a majority of our common stock present in person or represented by proxy and voting on a matter shall decide any matter to be voted upon by the stockholders at a meeting.

Holders of our common stock have the right to receive dividends as and when declared by our Board of Directors (the “Board”) from funds legally available therefor, subject to any preferential dividend rights of any Preferred Stock then outstanding. We have never paid cash dividends on our common stock.

Upon our dissolution or liquidation, whether voluntary or involuntary, holders of our common stock 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 our common stock have no preemptive rights and have no rights to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock. All outstanding shares of our common stock are validly issued, fully paid and nonassessable.

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 the Board. The Board 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 our 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

Some provisions of the Certificate of Incorporation, the Bylaws, and DGCL may have the effect of delaying, discouraging, or preventing a change in control of us or changes in our management. Pursuant to the Certificate of Incorporation and the Bylaws:

- the Board is authorized to issue “blank check” preferred stock without further stockholder approval;
- the Board is classified, with members thereof serving staggered three-year terms;
- stockholders may not cumulate votes in the election of directors;

TABLE OF CONTENTS

- vacancies on the Board may be filled only by the Board;
- stockholders may remove directors only for cause and only by the affirmative vote of the holders of at least 75 percent of the total number of votes entitled to be cast by the holders of all of the shares of our capital stock then entitled to vote generally in the election of directors (a “supermajority vote”);
- stockholders may take action only at a duly called meeting of the stockholders, and stockholders are not permitted to act by written consent;
- special meetings of stockholders may be called only by the Board; and
- stockholders must satisfy advance notice procedures to submit proposals or nominate directors for consideration at a stockholders meeting.

A supermajority vote is required to amend Article NINTH and Article TENTH of the Certificate of Incorporation, which pertain to the number, classification, and removal of our directors, the creation and filling of vacancies on the Board, the requirement that actions of stockholders be taken at a duly called meeting and not by written consent, and the requirement that special meetings only be called by the Board.

In addition, we are subject to the provisions of Section 203 of the DGCL. In general, the statute prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a period of three years after the date that the person became an interested stockholder unless, with some exceptions, the business combination or the transaction in which the person became an interested stockholder is approved in a prescribed manner. Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the stockholder, and an “interested stockholder” is a person who, together with affiliates and associates, owns (or within three years prior, did own) 15% or more of the corporation’s outstanding voting stock. This provision may have the effect of delaying, deferring, or preventing a change in control without further action by the stockholders.

Exclusive Forum for Certain Actions

The Bylaws provide that unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, stockholders, employees, or agents to us or to our stockholders; (iii) any action asserting a claim against us or any of our directors, officers, stockholders, employees, or agents arising out of or relating to any provision of the DGCL, the Certificate of Incorporation, or the Bylaws; or (iv) any action against us or any of our directors, officers, stockholders, employees, or agents governed by the internal affairs doctrine of the State of Delaware. The Bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock will be deemed to have notice of, and to have consented to, this choice of forum provision. This exclusive forum provision may limit a stockholder’s ability to choose its preferred judicial forum for disputes with us or our directors, officers, employees, or agents, which may discourage the filing of lawsuits with respect to such claims. This exclusive forum provision does not apply to establish the Delaware Court of Chancery as the forum for actions or proceedings brought to enforce a duty or liability created by the Securities Act or the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction.

Depository 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 depository shares, and each of these depository 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 depository shares will be deposited under a deposit agreement between us and a bank or trust company selected by us. The depository 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 depository share will be entitled, in proportion to the applicable fraction of a share of preferred stock underlying the depository share, to all the rights and preferences of the preferred stock underlying that depository share. Those rights may include dividend, voting, redemption, conversion and liquidation rights.

TABLE OF CONTENTS

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

TABLE OF CONTENTS

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 PURCHASE CONTRACTS

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

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

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

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

DESCRIPTION OF WARRANTS

We may issue warrants to purchase our preferred stock, depository shares, common stock or debt securities 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.

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under an indenture to be entered into between us and U.S. Bank National Association, or another trustee chosen by us that is qualified to act as such under the Trust Indenture Act of 1939, as amended (the “Trust Indenture Act”), and appointed under an indenture. The indenture will be qualified under the Trust Indenture Act. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture. We urge you to read the applicable prospectus supplement and any related free writing prospectus related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as “discount securities,” which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with “original issue discount,” or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;
- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;
- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

TABLE OF CONTENTS

- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$2,000 and multiples of \$1,000 in excess thereof;
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depository for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;
- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Events of Default and Remedies

Unless otherwise described in the applicable prospectus supplement, an event of default with respect to any series of debt securities will be defined in the indenture or applicable supplemental indenture or authorizing resolution as being:

- our failure to pay interest on any debt security of such series when the same becomes due and payable and the continuance of any such failure for a period of 30 days;
- our failure to pay the principal or premium of any debt security of such series when the same becomes due and payable at maturity, upon acceleration, redemption or otherwise;
- our failure or the failure of any restricted subsidiary to comply with any of its agreements or covenants in, or provisions of, the debt securities of such series or the indenture (as they relate thereto) and such failure continues for a period of 90 days after our receipt of notice of the default from the trustee or from the holders of at least 25% in aggregate principal amount of the then outstanding debt securities of that series (except in the case of a default with respect to the provisions of the indenture regarding the consolidation, merger, sale, lease, conveyance or other disposition of all or substantially all of our assets (or any other provision specified in the applicable supplemental indenture or authorizing resolution), which will constitute an event of default with notice but without passage of time); or
- certain events of bankruptcy, insolvency or reorganization occur with respect to us.

The indenture will provide that the trustee may withhold notice to the holders of any series of debt securities of any default, except a default in payment of principal or interest, if any, with respect to such series of debt securities, if the trustee considers it in the interest of the holders of such series of debt securities to do so.

The indenture will provide that if any event of default has occurred and is continuing with respect to any series of debt securities, the trustee or the holders of not less than 25% in principal amount of such series of debt securities then outstanding may declare the principal of all the debt securities of such series to be due and payable immediately. However, the holders of a majority in principal amount of the debt securities of such series then outstanding by notice to the trustee may waive any existing default and its consequences with respect to such series of debt securities, other than any event of default in payment of principal or interest. Holders of a majority in principal amount of the then outstanding debt securities of any series may rescind an acceleration with respect to such series and its consequences, except an acceleration due to nonpayment of principal or interest on such series, if the rescission would not conflict with any judgment or decree and if all existing events of default with respect to such series have been cured or waived.

The holders of a majority of the outstanding principal amount of the debt securities of any series will have the right to direct the time, method and place of conducting any proceedings for any remedy available to the trustee with respect to such series, subject to limitations specified in the indenture.

Defeasance

The indenture will permit us to terminate all our respective obligations under the indenture as they relate to any particular series of debt securities, other than the obligation to pay interest, if any, on and the principal of the debt securities of such series and certain other obligations, at any time by:

- depositing in trust with the trustee, under an irrevocable trust agreement, money or government obligations in an amount sufficient to pay principal of and interest, if any, on the debt securities of such series to their maturity or redemption; and
- complying with other conditions, including delivery to the trustee of an opinion of counsel to the effect that holders will not recognize income, gain or loss for federal income tax purposes as a result of our exercise of such right and will be subject to federal income tax on the same amount and in the same manner and at the same times as would have been the case otherwise.

The indenture will also permit us to terminate all of our respective obligations under the indenture as they relate to any particular series of debt securities, including the obligations to pay interest, if any, on and the principal of the debt securities of such series and certain other obligations, at any time by:

TABLE OF CONTENTS

- depositing in trust with the trustee, under an irrevocable trust agreement, money or government obligations in an amount sufficient to pay principal and interest, if any, on the debt securities of such series to their maturity or redemption; and
- complying with other conditions, including delivery to the trustee of an opinion of counsel to the effect that (A) we have received from, or there has been published by, the Internal Revenue Service a ruling, or (B) since the date such series of debt securities were originally issued, there has been a change in the applicable federal income tax law, in either case to the effect that, and based thereon such opinion of counsel shall state that, holders will not recognize income, gain or loss for federal income tax purposes as a result of our exercise of such right and will be subject to federal income tax on the same amount and in the same manner and at the same times as would have been the case otherwise.

In addition, the indenture will permit us to terminate substantially all our respective obligations under the indenture as they relate to a particular series of debt securities by depositing with the trustee money or government obligations sufficient to pay all principal and interest on such series at its maturity or redemption date if the debt securities of such series will become due and payable at maturity within one year or are to be called for redemption within one year of the deposit.

Transfer and Exchange Rights

A holder will be able to transfer or exchange debt securities only in accordance with the indenture. The registrar may require a holder, among other things, to furnish appropriate endorsements and transfer documents, and to pay any taxes and fees required by law or permitted by the indenture.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, lease, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Amendment, Supplement and Waiver

Without notice to or the consent of any holder, we and the trustee may amend or supplement the indenture or the debt securities of a series to:

- cure any ambiguity, omission, defect or inconsistency;
- comply with the provisions of the indenture regarding the consolidation, merger, sale, lease, conveyance or other disposition of all or substantially all of our assets;
- provide that specific provisions of the indenture shall not apply to a series of debt securities not previously issued or to make a change to specific provisions of the indenture that only applies to any series of debt securities not previously issued or to additional debt securities of a series not previously issued;
- create a series and establish its terms;
- provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- release a guarantor in respect of any series of debt securities which, in accordance with the terms of indenture applicable to the particular series, ceases to be liable in respect of its guarantee;
- add a guarantor subsidiary in respect of any series of debt securities;
- secure any series of debt securities;
- comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act;
- make any change that does not adversely affect the rights of any holder; or
- conform the provisions of the indenture to the final offering document in respect of any series of debt securities.

TABLE OF CONTENTS

With the exceptions discussed below, we and the trustee may amend or supplement the indenture or the debt securities of a particular series with the written consent of the holders of at least a majority in principal amount of the debt securities of such series then outstanding. In addition, the holders of a majority in principal amount of the debt securities of such series then outstanding may waive any existing default under, or compliance with, any provision of the debt securities of a particular series or of the indenture relating to a particular series of debt securities, other than any event of default in payment of interest or principal. These consents and waivers may be obtained in connection with a purchase of, or tender offer or exchange offer for, debt securities.

Without the consent of each holder affected, we and the trustee may not:

- reduce the amount of debt securities of such series whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest, including defaulted interest;
- reduce the principal of or extend the fixed maturity of any debt security or alter the provisions with respect to redemptions or mandatory offers to repurchase debt securities;
- make any change that adversely affects any right of a holder to convert or exchange any debt security into or for shares of our common shares or other securities, cash or other property in accordance with the terms of such security;
- modify the ranking or priority of the debt securities;
- make any change to any provision of the indenture relating to the waiver of existing defaults, the rights of holders to receive payment of principal and interest on the debt securities, or to the provisions regarding amending or supplementing the indenture or the debt securities of a particular series with the written consent of the holders of such series;
- waive a continuing default or event of default in the payment of principal of or interest on the debt securities; or
- make any debt security payable at a place or in money other than that stated in the debt security, or impair the right of any holder of a debt security to bring suit as permitted by the indenture.

The right of any holder to participate in any consent required or sought pursuant to any provision of the indenture, and our obligation to obtain any such consent otherwise required from such holder, may be subject to the requirement that such holder shall have been the holder of record of debt securities with respect to which such consent is required or sought as of a record date fixed by us in accordance with the indenture.

Governing Law

The laws of the State of New York will govern the indenture and the debt securities.

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, warrants or debt securities 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

TABLE OF CONTENTS

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

TABLE OF CONTENTS

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, 2020, and the effectiveness of our internal control over financial reporting as of December 31, 2020, 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, 2020 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. 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.

The SEC also maintains a website 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, 2020, filed with the SEC on March 1, 2021 (the “2020 Form 10-K”);
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2019 from our [Definitive Proxy Statement](#) (other than information furnished rather than filed) for our 2020 Annual Meeting of Stockholders, which was filed with the SEC on March 31, 2020; and
- The description of our common stock that 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, as updated by the description of our common stock filed as [Exhibit 4.1](#) to our 2020 Form 10-K, and any other amendments 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 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.

[TABLE OF CONTENTS](#)

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

Investor Relations
BioCryst Pharmaceuticals, Inc.
4505 Emperor Blvd., Suite 200
Durham, North Carolina 27703
(919) 859-1302

We have not authorized anyone to provide you with information different from that contained 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 information other than the information contained in or incorporated by reference in this prospectus or any prospectus supplement. 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.

\$200,000,000



Common stock
Pre-funded warrants to purchase shares of common stock

Prospectus supplement

J.P. Morgan

Evercore ISI

Piper Sandler

, 2021
