UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2020

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _____ to _____

Commission File Number 000-23186

BIOCRYST PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**62-1413174**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

4505 Emperor Blvd., Suite 200, Durham, North Carolina 27703

(Address of principal executive offices)

(919) 859-1302

(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.01 par value	**BCRX**	**Nasdaq Global Select Market**

Securities registered pursuant to Section 12(g) of the Act: None.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

The registrant estimates that the aggregate market value of the Common Stock on June 30, 2020 (based upon the closing price shown on the Nasdaq Global Select Market on June 30, 2020) held by non-affiliates was $832,869,919.

The number of shares of Common Stock, par value $0.01, of the registrant outstanding as of January 31, 2021 was 177,182,751 shares.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement to be filed in connection with the solicitation of proxies for its 2021 annual meeting of stockholders are incorporated by reference into Items 10, 11, 12, 13, and 14 under Part III hereof.

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When used in this report, unless otherwise indicated, "we," "our," "us," the "Company," and "BioCryst" refer to BioCryst Pharmaceuticals, Inc.

Cautionary Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K (this "report") includes forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, which are subject to the "safe harbor" created in Section 21E. In particular, statements about our expectations, beliefs, plans, objectives or assumptions of future events or performance are contained or incorporated by reference in this report. All statements other than statements of historical facts contained herein 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. Discussions containing these forward-looking statements are principally contained in the "Business," "Risk Factors," and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of this report, as well as any amendments we make to those sections in filings with the Securities and Exchange Commission ("SEC"). 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 Torii for ORLADEYO in Japan, Shionogi and Green Cross for peramivir in their territories, and Mundipharma for mundesine;
- our and our subsidiary guarantors' ability to satisfy obligations under our 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, to satisfy its obligations in respect of the PhaRMA Notes (as defined in "Business—Collaborations and In-License Relationships—Shionogi Royalty Monetization and Non-Recourse Notes Payable" in Part I, Item 1 of this report);
- 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.

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 those discussed in this report under the heading "Risk Factors" in Part I, Item 1A, some of which are summarized in the "Risk Factor Summary" below. 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 report 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.

Risk Factor Summary

An investment in the Company involves risks. You should carefully read this entire report and consider the uncertainties and risks discussed in the "Risk Factors" section in Part I, Item 1A of this report, which may adversely affect our business, financial condition, or results of operations, along with the other information included in our other filings with the Securities and Exchange Commission, before deciding to invest in the Company. A summary of the principal factors that make an investment in the Company 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 below or in the "Risk Factors" section in Part I, Item 1A of this report.
- 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. If the BARDA/HHS or the NIAID/HHS were to eliminate, reduce, or delay funding from our contracts, this would have a significant negative impact on the programs associated with such funding and could have a significant impact on our revenues and cash flows.
- 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 interest 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 result in 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 and commercialization of our products and the related expansion of our business will be delayed or stopped.

PART I

ITEM 1. *BUSINESS*

Our Business

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. 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. & Japan); MAA accepted for review and CHMP positive opinion received (European Union)	BioCryst (worldwide, except Japan); Torii Pharmaceutical Co., Ltd. (Japan)
BCX9930	Oral Factor D Inhibitor	Complement-mediated diseases	Phase 1	BioCryst (worldwide)
BCX9250	Oral Activin Receptor-like Kinase-2 Inhibitor	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)
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" for a description of our relationships with the third parties identified in this column.*

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 will continue to seek such relationships where we determine this to be an effective approach.

Products and Product Candidates

ORLADEYO (Berotralstat/BCX7353)

Hereditary Angioedema ("HAE") is a rare, severely debilitating and potentially fatal genetic condition with a prevalence of between 1 in 33,000 to 1 in 67,000 people. HAE symptoms include recurrent episodes of edema in various locations, including the hands, feet, face, genitalia and airway. Airway swelling is particularly dangerous and can lead to death by asphyxiation. In addition, patients often have bouts of severe abdominal pain, nausea and vomiting caused by swelling in the intestinal wall. By inhibiting plasma kallikrein, ORLADEYO, our HAE drug, suppresses bradykinin production. Bradykinin is the mediator of acute swelling attacks in HAE patients.

ORLADEYO is an oral, once-daily therapy discovered and developed by BioCryst for the prevention of HAE attacks. ORLADEYO, in the 110 mg and 150 mg capsule dosage forms, was approved by the U.S. Food and Drug Administration ("FDA") in December 2020 for prophylaxis to prevent attacks of HAE in adults and pediatric patients 12

years and older. On December 16, 2020, we announced that ORLADEYO is now available for shipment to patients with a prescription in the U.S. and that our exclusive specialty pharmacy provider for ORLADEYO in the U.S. began shipping to patients. Through EMPOWER Patient Services, administered by our specialty pharmacy provider, we aim to streamline access to therapy by providing each HAE patient and their healthcare provider with a single point of contact for access to ORLADEYO. A dedicated care coordinator will support access for each patient with comprehensive financial support tools and reimbursement support.

ORLADEYO, in the 150 mg capsule dosage form, also received marketing and manufacturing approval from the Ministry of Health, Labor and Welfare ("MHLW") in Japan in January 2021 for prophylactic treatment of HAE in adults and pediatric patients 12 years and older. ORLADEYO is the first and only prophylactic HAE medication approved in Japan and will be commercialized in Japan by our partner, Torii Pharmaceutical Co., Ltd. ("Torii"). See "Collaborations and In-License Relationships" below for a description of this relationship. Torii will launch ORLADEYO in Japan following the successful completion of our pricing negotiations with the Japanese National Health Insurance System. OrphanPacific, Inc. is our representative partner in Japan and holds the marketing authorization for ORLADEYO in Japan.

On March 30, 2020, we announced that the European Medicines Agency ("EMA") had validated our marketing authorization application ("MAA") submission for approval of ORLADEYO for the prevention of HAE attacks. With this validation, the EMA began its formal review of the MAA under the centralized procedure for all member states of the European Union (the "EU"), Norway, Iceland, and Liechtenstein. On February 25, 2021, we announced that the Committee for Medicinal Products for Human Use ("CHMP") of the EMA has adopted a positive opinion recommending the approval of ORLADEYO for routine prevention of recurrent attacks of HAE in adult and adolescent patients aged 12 years and older. The European Commission ("EC) will review the CHMP recommendation, and a final approval decision from the EC on the MAA for ORLADEYO is expected in the second quarter of 2021.

The United Kingdom's ("U.K.") Medicines and Healthcare products Regulatory Agency ("MHRA") has granted a Promising Innovative Medicine designation to ORLADEYO. On October 30, 2020, we announced that the MHRA has granted ORLADEYO a positive scientific opinion through the Early Access to Medicines Scheme ("EAMS"). Under the EAMS, HAE patients in the U.K. aged 12 years and older can gain access to ORLADEYO for the routine prevention of recurrent attacks of HAE before the drug is granted marketing authorization by the EC. We plan to file for a U.K. marketing authorization with the MHRA following our receipt of a positive opinion from the CHMP. This is expected to result in a U.K. marketing authorization shortly after a final decision by the EC.

On December 7, 2020, we entered into a Purchase and Sale Agreement (the "Royalty Purchase Agreement") with RPI 2019 Intermediate Finance Trust ("RPI"), pursuant to which we sold to RPI the right to receive certain royalty payments from the Company for a purchase price of $125 million in cash. Under the Royalty Purchase Agreement, RPI is entitled to receive tiered, sales-based royalties on net product sales of ORLADEYO in the U.S., certain key European markets, and other markets where we sell ORLADEYO directly or through distributors (collectively, the "Key Territories"). In addition, RPI is entitled to receive a tiered revenue share on amounts generally received by us on account of ORLADEYO sublicense revenue or net sales by licensees outside of the Key Territories. No payment will be due to RPI for any achievement milestone which may be payable under the existing out-license for ORLADEYO. See "Note 3-Royalty Monetizations-ORLADEYO Royalty Monetization" in the Notes to Consolidated Financial Statements in Part II, Item 8 of this report for additional information about our obligations under the Royalty Purchase Agreement.

We completed the build-out of our U.S. commercial infrastructure in 2020 to support the launch of ORLADEYO in the U.S. and are currently building our commercial infrastructure to support European launches. Based on proprietary analyses of HAE prevalence and market research studies with HAE patients, physicians, and payors in the U.S. and Europe, we anticipate the commercial market for ORLADEYO has the potential to reach a global peak of more than $500 million in annual sales. These expectations are subject to numerous risks and uncertainties that may cause our actual results, performance, or achievements to be materially different. There can be no assurance that our commercialization methods and strategies will succeed, or that the market for ORLADEYO will develop in line with our current expectations. See "Risk Factors—Risks Relating to Our Business—Risks Relating to Drug Development and Commercialization—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" in Part I, Item 1A of this report for further discussion of these risks.

Complement-Mediated Diseases

The complement system is part of the body's natural immune system and is responsible for helping the body eliminate microbes (including viral and bacterial infections) and damaged cells. It is comprised of proteins that are primarily produced in the liver and circulate in the blood. Once activated, the complement system stimulates inflammation, phagocytosis and cell lysis. Excessive or uncontrolled activation of the complement system can cause severe, and potentially fatal, immune and inflammatory disorders. The complement system comprises biological cascades of amplifying enzyme cleavages involving more than 30 proteins and protein fragments, and may be activated through three pathways: the classical pathway (initiated by antibody-antigen complexes), the lectin pathway (initiated by lectin binding) and the alternative pathway (initiated by microbial surfaces). The alternative pathway also provides a critical amplification loop for all three pathways, regardless of the initiating mechanism. Factor D is an essential enzyme in the alternative pathway, thus making Factor D an attractive target to address complement-mediated diseases. Several rare diseases are known to be mediated by dysregulation of the complement system.

Discovered by BioCryst, BCX9930 is a novel, oral, potent, and selective small molecule inhibitor of Factor D currently in early clinical development for the treatment of complement-mediated diseases. Based on the safety and proof-of-concept ("PoC") data generated to date in paroxysmal nocturnal hemoglobinuria ("PNH") patients, we are working closely with regulators and key opinion leaders in hematology and nephrology to map the advanced development strategy across a broad set of indications. Our goal is to develop oral BCX9930 as a monotherapy for complement-mediated diseases.

On February 25, 2021, we announced that we have completed enrollment of our ongoing dose ranging trial in treatment-naïve (no prior treatment with C5 inhibitors) PNH patients and PNH patients with an inadequate response to C5 inhibitors. The objectives of the trial are to evaluate the safety and tolerability and characterize the pharmacokinetic ("PK") and pharmacodynamic ("PD") profiles of BCX9930 after single ascending doses ("SAD") and multiple ascending doses ("MAD") in healthy subjects (parts 1 and 2). In part 3 of the trial, there is an additional objective to demonstrate PoC in treatment-naïve PNH patients and PNH patients who are inadequate responders to C5 therapy (eculizumab or ravulizumab) by evaluating key biomarkers of effectiveness and assessing the dose range in PNH patients taking BCX9930. Based on the safety, tolerability, PK and PD dose-response results from parts 1 and 2 of the phase 1 trial, we completed additional MAD dosing cohorts in healthy subjects and advanced to part 3 of the trial. We plan to present data from the 16 enrolled PNH patients (10 treatment naïve and 6 inadequate C5 responders) at our upcoming R&D day on March 22, 2021.

On September 30, 2020, we announced new data from treatment-naïve PNH patients receiving doses through 400 mg twice-daily of oral BCX9930 as monotherapy in the ongoing part 3 PoC dose-ranging trial. Oral BCX9930 was shown to drive rapid and dose-dependent reductions in key biomarkers, including lactate dehydrogenase ("LDH"), and increasing hemoglobin levels in all PNH patients in the trial. Increases in hemoglobin levels were maintained without transfusions. BCX9930 was safe and well tolerated at all doses in the trial. No drug-related serious adverse events had been reported. One subject was discontinued due to an unrelated serious adverse event.

On August 31, 2020, we announced that the FDA has granted orphan drug designation for BCX9930 for the treatment of PNH. Orphan drug designation qualifies BCX9930 for various development incentives, including tax credits for certain clinical costs, a waiver of the new drug application fee, and a designated period of market exclusivity following approval. On August 3, 2020, we announced that the FDA granted fast track designation for BCX9930 in PNH. According to the FDA, the purpose of the fast track designation is to get important new drugs to patients earlier by facilitating the development, and expediting the review, of drugs to treat serious conditions and meet an unmet medical need.

Under the Royalty Purchase Agreement, RPI will be entitled to receive 1.0% of global net sales, if any, of BCX9930. See "Note 3-Royalty Monetizations-ORLADEYO Royalty Monetization" in the Notes to Consolidated Financial Statements in Part II, Item 8 of this report for additional information about our obligations under the Royalty Purchase Agreement.

Fibrodysplasia Ossificans Progressiva ("FOP")

FOP is an ultra-rare disease that affects approximately 1 in 2 million people worldwide. It is a severely disabling condition characterized by the irregular formation of bone outside the normal skeleton, also known as heterotopic ossification ("HO"). HO can occur in muscles, tendons and soft tissue. FOP patients progressively become bound by this irregular ossification, with restricted movement and fused joints, resulting in deformities and premature mortality. In patients with FOP, minor trauma can result in rapid development of painful inflammatory masses. These progress over several weeks resulting in the replacement of the affected soft tissue by permanent bone masses. There is no cure for this condition, and there are no approved treatments for FOP.

In 2018, we announced the advancement of a program exploring activin receptor-like kinase-2 ("ALK2") inhibitors for treatment of FOP. ALK2 enzyme is a part of the normal signaling pathway for bone formation and responds to binding its specific ligands (bone morphogenic proteins, or BMPs), by stimulating normal bone growth and renewal in healthy children and adults. Specific activating mutations of the ALK2 gene are seen in all cases of FOP. An activating mutation in ALK2 is necessary for the disease to occur, making the ALK2 kinase an ideal drug target for treatment of FOP with an ALK2 kinase inhibitor.

The goal of our ALK2 inhibitor program is to discover and develop orally administered kinase inhibitor drug candidates that are able to slow or prevent HO. Our lead compound, BCX9250, reduced HO in an experimental model of ALK2-driven HO in laboratory rats, with up to 89 percent reduction in volume of HO compared to controls.

On December 21, 2020, we announced that in a phase 1 clinical trial, BCX9250 was safe and well tolerated at all doses studied, with linear and dose-proportional exposure supporting once-daily dosing. The randomized, double-blind, placebo-controlled dose-ranging trial evaluated safety, tolerability, and PK of SAD and MAD of BCX9250 in healthy subjects. The SAD study was designed to randomize four cohorts of eight subjects each to receive oral BCX9250 (n=6) or placebo (n=2) at dose levels of 5 mg, 10 mg, 15 mg, and 25 mg. Subjects in the 15 mg cohort also received a second single dose to evaluate food effect on absorption of BCX9250. The MAD study was designed to randomize 4 cohorts of 12 subjects each to receive oral BCX9250 (n=10) or placebo (n=2) at dose levels of 5 mg, 10 mg, 15 mg, and 20 mg once-daily for 7 days. Drug exposure increased with dose in an approximately linear and dose-proportional manner. Drug levels after a high fat meal were similar to those after dosing on an empty stomach. Drug exposure at 20 mg once-daily in the MAD was similar to that achieved with doses that suppressed HO in a nonclinical model of activity of orally dosed BCX9250. In both the SAD and the MAD studies, oral BCX9250 was safe and well tolerated, with no serious adverse events, no study discontinuations due to adverse events, no grade 3 or 4 adverse events, and no clinically significant changes in vital signs, electrocardiograms, or safety laboratory parameters. No safety signals were seen.

Peramivir Injection (RAPIVAB, ALPIVAB, RAPICACTA, PERAMIFLU)

RAPIVAB (peramivir injection) was developed under a $234.8 million contract from the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services ("BARDA/HHS"). In January 2010, our partner, Shionogi & Co., Ltd. ("Shionogi"), received the first approval for peramivir injection and launched it in Japan under the commercial name RAPIACTA. It is approved in Japan for the treatment of adults, children, and infants with uncomplicated seasonal influenza and those patients at high-risk for complications associated with influenza. In August 2010, our partner, Green Cross Corporation ("Green Cross"), received marketing and manufacturing approval from the Korean Food & Drug Administration under the commercial name PERAMIFLU to treat patients with influenza A & B viruses, including pandemic H1N1 and avian influenza. See "Collaborations and In-License Relationships" below for a discussion of these licensing arrangements.

Peramivir was also approved in the United States in 2014, Taiwan in 2016, Canada in 2017, and the EU and Australia in 2018. A Supplemental New Drug Application ("sNDA") was approved in the United States in February 2021, extending RAPIVAB's availability for the treatment of acute uncomplicated influenza to pediatric patients six months and older. Prior to this approval, peramivir had been indicated in the United States for pediatric patients two years and older. In the United States, peramivir is indicated for the treatment of acute uncomplicated influenza in patients who have been symptomatic for no more than two days. In May 2018, peramivir, with the brand name of ALPIVAB, received approval from the EMA, although we withdrew the ALPIVAB registration in November 2020. ALPIVAB was not commercially available in the EU at the time of the withdrawal.

In September 2018, the U.S. Department of Health and Human Services ("HHS") awarded us a $34.7 million contract for the procurement of up to 50,000 doses of RAPIVAB over a five-year period to supply the Strategic National Stockpile for use in a public health emergency. We delivered 20,000 doses of RAPIVAB under this contract in 2019 for a total price of approximately $13.9 million. On September 3, 2020, we announced that HHS exercised its option to purchase an additional 10,000 doses of RAPIVAB under this contract for $6.9 million. As a result, we expect to deliver at least one shipment of 10,000 doses within the contract in 2021.

Galidesivir (BCX4430)

Galidesivir is a broad-spectrum antiviral ("BSAV") that has been shown to be active against more than 20 RNA viruses in nine different families, including filoviruses, togaviruses, bunyaviruses, arenaviruses, paramyxoviruses, coronaviruses and flaviviruses. In animal studies, galidesivir has demonstrated survival benefits against a variety of serious pathogens, including Marburg, Yellow Fever, Ebola, and Zika viruses and from exposures to aerosolized Marburg virus,

an experimental condition designed to mimic an exposure scenario that could result during a bioterrorist attack. Our galidesivir research program is currently being developed under contracts with the National Institute of Allergy and Infectious Diseases within the HHS ("NIAID/HHS") and BARDA/HHS.

The objective of our BSAV program is to develop galidesivir as a broad-spectrum therapeutic for viruses that pose a threat to national health and security. The primary focus of the program is treatment of hemorrhagic fever viruses. NIAID/HHS funding has supported galidesivir's development as a treatment for Marburg virus, Yellow Fever and Ebola virus. Since September 2013, NIAID/HHS has supported the development of galidesivir as a therapeutic for Ebola and Marburg viruses. As of the date hereof, all options under our initial contract with NIAID/HHS have been awarded. The total amount under the initial contract, as amended, is $45.9 million, inclusive of the $2.9 million added to the contract in August 2020 to support the development of galidesivir. Since March 2015, BARDA/HHS has supported the development of galidesivir as a potential treatment for filoviruses. The total BARDA/HHS contract value to advance the program through toxicology studies and manufacturing work to support a new drug application is $39.1 million if all contract options are exercised. As of the date hereof, a total of $20.6 million has been awarded under exercised options within this contract.

In April 2020, we agreed with NIAID/HHS to add a group of COVID-19 patients to an ongoing clinical trial in Yellow Fever. On April 9, 2020, we announced that we had opened a randomized, double-blind, placebo-controlled clinical trial in Brazil to assess the safety, clinical impact, and antiviral effects of galidesivir in patients with COVID-19.

On August 31, 2020, we announced that NIAID/HHS awarded us a new $43.9 million contract for the manufacture and evaluation of the safety, efficacy, and tolerability of galidesivir and that it also added $2.9 million to its existing contract with us to support the development of galidesivir. NIAID/HHS made an initial award of $6.3 million under the new contract.

On December 22, 2020, we announced that data from part 1 of the clinical trial in Brazil showed that galidesivir was safe and generally well tolerated in patients infected with SARS-Cov-2, the virus that causes COVID-19. The trial was not designed or sized to demonstrate clinical efficacy, and no clinical efficacy benefit with galidesivir treatment compared to placebo treatment was observed in the trial. Based on our ongoing discussions with NIAID/HHS, we expect NIAID/HHS to continue its support for the development of galidesivir with a focus on biodefense threats, such as Marburg virus disease, and to discontinue the pursuit of a COVID-19 indication for galidesivir.

Mundesine (forodesine)

Mundesine is a Purine Nucleoside Phosphorylase ("PNP") inhibitor developed by Mundipharma International Corporation Limited ("Mundipharma") as a treatment for cancer under a world-wide license agreement. PNP is a purine salvage pathway enzyme. High doses of PNP inhibitors could be useful in the treatment of hematological malignancies. Mundipharma has received orphan drug status for Mundesine, and following its successful completion of a phase 2 pivotal study in recurrent/refractory peripheral T-cell lymphoma ("PTCL") patients in Japan, Mundesine was approved in April 2017 by the MHLW in Japan. We are currently entitled to receive royalties on Mundesine.

Collaborations and In-License Relationships

Torii Pharmaceutical Co., Ltd. ("Torii")

On November 5, 2019, we entered into a Commercialization and License Agreement with Torii (the "Torii Agreement"), granting Torii the exclusive right to commercialize ORLADEYO for the prevention of HAE attacks in Japan.

Under the Torii Agreement, we received an upfront, non-refundable payment of $22.0 million and are eligible to receive an additional milestone payment of $15.0 million upon receipt from Japan's National Health Insurance system of a reimbursement price approval for ORLADEYO in excess of the threshold specified in the Torii Agreement.

In addition, under the Torii Agreement, we are entitled to receive tiered royalty payments, ranging from 20% to 40% of annual net sales of ORLADEYO in Japan during each calendar year. Torii's royalty payment obligations are subject to customary reductions in certain circumstances, but may not be reduced by more than 50% of the amount that otherwise would have been payable to us in the applicable calendar quarter. Torii's royalty payment obligations commence upon the first commercial sale of ORLADEYO in Japan and expire upon the later of (i) the tenth anniversary of the date of first commercial sale of ORLADEYO in Japan, (ii) the expiration of our patents covering ORLADEYO, and (iii) the expiration of regulatory exclusivity for ORLADEYO in Japan. We will be responsible for supplying Torii with its required amounts of ORLADEYO. The activities of the parties pursuant to the Torii Agreement will be overseen by a joint steering committee,

to be composed of an equal number of representatives from each party to coordinate the development and commercialization of ORLADEYO in Japan.

Under the Torii Agreement, we granted Torii a right of first negotiation ("ROFN") to commercialize ORLADEYO in Japan for the acute treatment of HAE attacks if we develop ORLADEYO for such indication and to commercialize any additional kallikrein inhibitor that we may develop in the future for use in HAE in Japan. Under both ROFNs, if the parties do not agree to terms with respect to a definitive amendment to the Torii Agreement or new agreement, as applicable, the terms of the amendment or agreement would be set by a third-party arbitrator.

Seqirus UK Limited

In June 2015, we entered into a license agreement (the "SUL Agreement") with CSL Limited ("CSL"), a company organized under the laws of Australia, granting Seqirus UK Limited ("SUL"), a limited company organized under the laws of the United Kingdom and a subsidiary of CSL, and its affiliates worldwide rights to develop, manufacture, and commercialize peramivir for the treatment of influenza, except for the rights to conduct such activities in Israel, Japan, Korea and Taiwan. On March 4, 2020, the International Court of Arbitration of the International Chamber of Commerce ("ICC Tribunal") delivered a Partial Arbitration Award (the "Partial Arbitration Award") in an arbitration matter between us and SUL with respect to the SUL Agreement. In the Partial Arbitration Award, the ICC Tribunal found that, during the term, SUL materially breached and abandoned its core duties to us under the Diligent Efforts (as defined in the SUL Agreement) requirements of the SUL Agreement as applicable in the U.S. The ICC Tribunal granted a declaratory judgment in favor of us terminating the SUL Agreement and restoring all rights to peramivir to us. We agreed with SUL on a transition process for the product, with a full transition of commercialization of the product in the U.S. and Australia returned to us as of August 1, 2020 and November 1, 2020, respectively. The ICC Tribunal also awarded us attorneys' fees and expenses incurred in securing the declaratory judgment as well as the costs incurred by us in the arbitration. Finally, the ICC Tribunal found that SUL breached the SUL Agreement by failing to pay a milestone payment due to us within 30 days of the approval of peramivir for adult use in the EU and awarded us $5.0 million (plus interest) for this claim. The ICC Tribunal retained jurisdiction for further proceedings relating to the award of attorneys' fees and for any dispute relating to the return to us of all rights to peramivir in the Territory.

Shionogi & Co., Ltd. ("Shionogi")

In February 2007, we entered into a License, Development and Commercialization Agreement (as amended, supplemented or otherwise modified, the "Shionogi Agreement"), an exclusive license agreement with Shionogi to develop and commercialize peramivir in Japan for the treatment of seasonal and potentially life-threatening human influenza. In October 2008, we and Shionogi amended the Shionogi Agreement to expand the territory covered by the agreement to include Taiwan. Under the terms of the Shionogi Agreement, Shionogi obtained rights to injectable formulations of peramivir in Japan in exchange for a $14.0 million upfront payment. The license provided for development milestone payments (up to $21.0 million), which have all been paid, and for commercial milestone payments (up to $95.0 million) in addition to double-digit (between 10% and 20%) royalty payments on product sales of peramivir.

In December 2017, we, on behalf of JPR Royalty Sub LLC, a wholly-owned subsidiary of BioCryst ("Royalty Sub"), instituted arbitration proceedings against Shionogi in order to resolve a dispute with Shionogi under the Shionogi Agreement regarding the achievement of sales milestones and escalating royalties. The arbitration proceedings concluded with the decision that no sales milestones had been achieved and that royalties would remain the same. The costs associated with the arbitration proceedings are recoverable from the assets of Royalty Sub in accordance with the terms of the indenture and servicing agreement relating to the PhaRMA Notes (as defined below under "Shionogi Royalty Monetization and Non-Recourse Notes Payable").

Generally, all payments under the Shionogi Agreement are non-refundable and non-creditable, but they are subject to audit. Shionogi is responsible for all development, regulatory, and marketing costs in Japan. The term of the Shionogi Agreement is from February 28, 2007 until terminated. Either party may terminate the Shionogi Agreement in the event of an uncured breach. Shionogi has the right of termination without cause. In the event of termination, all license and rights granted to Shionogi shall terminate and shall revert back to us. We developed peramivir under a license from the University of Alabama Birmingham ("UAB") and have paid sublicense payments to UAB on the upfront payments and will owe sublicense payments on any future event payments and/or royalties received by us from Shionogi.

Shionogi Royalty Monetization and Non-Recourse Notes Payable.

On March 9, 2011, we completed a $30.0 million financing transaction to monetize certain future royalty and milestone payments under the Shionogi Agreement. Pursuant to the transaction, Royalty Sub issued $30.0 million in aggregate principal amount of its PhaRMA Senior Secured 14.0% Notes due 2020 (the "PhaRMA Notes") in a private placement to institutional investors. The PhaRMA Notes were issued under an indenture, dated as of March 9, 2011 (the "Indenture"), by and between Royalty Sub and U.S. Bank National Association, as Trustee. We received net proceeds of $22.7 million from this transaction.

As part of the transaction, we entered into a purchase and sale agreement, dated as of March 9, 2011, with Royalty Sub, whereby we transferred to Royalty Sub, among other things, (i) our rights to receive commercial royalty and milestone payments from Shionogi under the Shionogi Agreement and (ii) the right to receive payments under a Japanese yen/US dollar foreign currency hedge arrangement (as further described below under "Foreign Currency Hedge," the "Currency Hedge Agreement") put into place by us in connection with the transaction. Royalty payments are paid by Shionogi in Japanese yen, and milestone payments are paid in U.S. dollars. Our collaboration with Shionogi was not impacted by this transaction.

Principal and interest on the PhaRMA Notes are payable from, and are secured by, (i) the rights to royalty and milestone payments under the Shionogi Agreement, which were transferred by us to Royalty Sub, and (ii) payments, if any, made to Royalty Sub under the Currency Hedge Agreement. The PhaRMA Notes bear interest at 14.0% per annum, payable annually in arrears on September 1st of each year (the "Payment Date"). We remain entitled to receive any royalties and milestone payments related to sales of peramivir by Shionogi following repayment by Royalty Sub of the PhaRMA Notes.

Royalty Sub's obligations to pay principal and interest on the PhaRMA Notes are obligations solely of Royalty Sub and are without recourse to any other person, including the Company, except to the extent of our pledge of our equity interests in Royalty Sub in support of the PhaRMA Notes. We may, but are not obligated to, make capital contributions to a capital account that may be used to redeem, or on up to one occasion pay any interest shortfall on, the PhaRMA Notes.

In September 2014, Royalty Sub was unable to pay the full amount of interest payable in September 2013 by the next succeeding payment date for the PhaRMA Notes, which was September 1, 2014. This inability constituted an event of default under the terms of the Indenture. Accordingly, we have classified the PhaRMA Notes and related accrued interest as current liabilities on our balance sheet since that time. The PhaRMA Notes matured on December 1, 2020, at which time the outstanding principal amount of the PhaRMA Notes of $30.0 million, together with all accrued and unpaid interest of $20.6 million, was due in full. As of December 31, 2020, the PhaRMA Notes remained in default, and we will continue to record the liability and accrued interest owed until it is determined that we are no longer the financial obligor.

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. As a result of the continuing events of default under the PhaRMA Notes, the holders of the PhaRMA Notes may foreclose on the collateral securing the PhaRMA Notes and our equity interests in Royalty Sub, and they may exercise other remedies available to them under the Indenture in respect of the PhaRMA Notes. In such event, we may not realize the benefit of future royalty payments that might otherwise accrue to us following repayment of the PhaRMA Notes and we might otherwise be adversely affected. Due to the non-recourse nature of the PhaRMA Notes, in the event of any potential foreclosure, we believe the primary impact to us would be the loss of future royalty payments from Shionogi and the legal costs associated with retiring the PhaRMA Notes. 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, there can be no assurance that this will be the case or that we will not otherwise be adversely affected as a result of the continuing events of default under the PhaRMA Notes.

The Indenture does not contain any financial covenants. The Indenture includes customary representations and warranties of Royalty Sub, affirmative and negative covenants of Royalty Sub, events of default and related remedies, and provisions regarding the duties of the Trustee, indemnification of the Trustee, and other matters typical for indentures used in structured financings of this type.

Foreign Currency Hedge

In connection with the issuance by Royalty Sub of the PhaRMA Notes, we entered into the Currency Hedge Agreement to hedge certain risks associated with changes in the value of the Japanese yen relative to the U.S. dollar. Under

the Currency Hedge Agreement, we had the right to purchase dollars and sell yen at a rate of 100 yen per dollar. The final tranche of the options under the Currency Hedge Agreement expired in November 2020.

The Currency Hedge Agreement did not qualify for hedge accounting treatment; therefore, mark-to-market adjustments are recognized in our Consolidated Statements of Comprehensive Loss. Cumulative mark-to-market adjustments resulted in losses of $0.6 million, $0.4 million, and $1.0 million for the twelve months ended December 30, 2020, 2019, and 2018, respectively. In addition, realized currency exchange gains of $0.7 million, $0.9 million, and $1.0 million were recognized in 2020, 2019, and 2018, respectively, related to the exercise of the U.S. dollar/Japanese yen currency option under the Currency Hedge Agreement.

Green Cross Corporation ("Green Cross")

In June 2006, we entered into an agreement with Green Cross to develop and commercialize peramivir in Korea. Under the terms of the agreement, Green Cross is responsible for all development, regulatory, and commercialization costs in Korea. Under the agreement, we received a one-time license fee of $250,000. The license provides that we will share in profits resulting from the sale of peramivir in Korea, including the sale of peramivir to the Korean government for stockpiling purposes. Furthermore, Green Cross will pay us a premium over its cost to supply peramivir for development and any future marketing of peramivir products in Korea. Both parties have the right to terminate the agreement in the event of an uncured material breach. In the event of termination, all rights, data, materials, products, and other information would be transferred to us.

In August 2010, we announced that Green Cross had received marketing and manufacturing approval from the Korean Food & Drug Administration for i.v. peramivir, under the commercial name PERAMIFLU. PERAMIFLU is intended to treat patients with influenza A & B viruses, including pandemic H1N1 and avian influenza. Green Cross received the indication of single dose administration of 300 mg i.v. peramivir.

Mundipharma

We are party to an exclusive, royalty bearing right and license agreement with Mundipharma for the development and commercialization of Mundesine for use in oncology. The agreement, as amended and restated, provides for the possibility of future event payments totaling $15.0 million for achieving specified regulatory events for certain indications and provides that we will receive tiered royalties ranging from mid-to high-single digit percentages of net product sales in each country where Mundesine is sold by Mundipharma. We licensed forodesine and other PNP inhibitors from AECOM/IRL (as defined below) and will owe sublicense payments to AECOM/IRL on all milestone payments and royalties received by us from Mundipharma.

Albert Einstein College of Medicine of Yeshiva University and Industrial Research, Ltd. ("AECOM" and "IRL," respectively)

In June 2000, we licensed a series of potent inhibitors of PNP from AECOM and IRL (together, the "Licensors"). The lead product candidate from this collaboration is forodesine. We have obtained worldwide exclusive rights to develop and ultimately distribute it, or any other, product candidates that might arise from research on these inhibitors. We have the option to expand our license agreement with the Licensors to include other inventions in the field made by the investigators or employees of the Licensors. Under this agreement, as amended and restated, we have agreed to use commercially reasonable efforts to develop these drugs and to pay certain milestone payments for each licensed product (which range in the aggregate from $1.4 million to almost $4.0 million per indication) for future development, single digit royalties on net sales of any resulting product made by us, and to share a portion of future payments received from other third-party partners, if any. In addition, we have agreed to pay annual license fees, which can range from $150,000 to $500,000, that are creditable against actual royalties and other payments due to the Licensors. The Licensors have also granted us an exclusive worldwide license of galidesivir for any antiviral use.

The University of Alabama at Birmingham ("UAB")

We currently have agreements with UAB for influenza neuraminidase and complement inhibitors. Under the terms of these agreements, UAB performed specific research for us in return for research payments and license fees. UAB has granted us certain rights to any discoveries in these areas resulting from research developed by UAB or jointly developed with us. We have agreed to pay single digit royalties on sales of any resulting product and to share in future payments received from other third-party partners. We have completed the research under the UAB agreements. These two agreements have initial 25-year terms, are automatically renewable for five-year terms throughout the life of the last patent, and are

terminable by us upon three months' notice and by UAB under certain circumstances. Upon termination, both parties shall cease using the other parties' proprietary and confidential information and materials, the parties shall jointly own joint inventions, and UAB shall resume full ownership of all UAB licensed products. There is currently no activity between us and UAB on these agreements, but when we license this technology, such as in the case of the Shionogi and Green Cross agreements, or commercialize products related to these programs, we will owe sublicense fees or royalties on amounts received.

Government Contracts

RAPIVAB (Peramivir Injection)

In September 2018, HHS awarded us a $34.7 million contract for the procurement of up to 50,000 doses of RAPIVAB over a five-year period, including an initial base order of 10,000 doses. In each of September 2019 and 2020, HHS exercised its options to purchase an additional 10,000 doses of RAPIVAB. We delivered a total of 20,000 doses of RAPIVAB and recorded approximately $13.9 million of product sales in 2019. We expect to deliver at least one shipment of 10,000 doses within the contract in 2021, totaling approximately $6.9 million in product sales. The RAPIVAB purchases by HHS will supply the Strategic National Stockpile, the nation's largest supply of life-saving pharmaceuticals and medical supplies for use in a public health emergency.

Galidesivir

In March 2015, BARDA/HHS awarded us a contract for the continued development of galidesivir as a potential treatment for diseases caused by RNA pathogens, including filoviruses. This BARDA/HHS contract has a potential value of $39.1 million if all contract options are exercised. As of the date of this report, a total of $20.6 million has been awarded under exercised options within this contract.

In September 2013, NIAID/HHS contracted with us for the development of galidesivir as a treatment for Marburg, and subsequently, Yellow Fever and Ebola virus disease. All options under this contract have been awarded, and the total value of the contract, as amended, is $45.9 million, inclusive of the $2.9 million added to the contract in August 2020 to support the development of galidesivir. In August 2020, NIAID/HHS awarded us a new $43.9 million contract for the manufacture and evaluation of the safety, efficacy, and tolerability of galidesivir. NIAID/HHS made an initial award of $6.3 million under this new contract. See "Products and Product Candidates -- Galidesivir" above. Based on our ongoing discussions with NIAID/HHS, we expect NIAID to continue its support for the development of galidesivir with a focus on biodefense threats, such as Marburg virus disease, and to discontinue the pursuit of a COVID-19 indication for galidesivir.

The contracts with BARDA/HHS and NIAID/HHS are cost-plus-fixed-fee contracts. That is, we are entitled to receive reimbursement for all costs incurred in accordance with the contracts provisions that are related to the development of peramivir and galidesivir plus a fixed fee, or profit. BARDA/HHS and NIAID/HHS will make periodic assessments of progress and the continuation of the contract is based on our performance, the timeliness and quality of deliverables, and other factors. The government has rights under certain contract clauses to terminate these contracts. These contracts are also terminable by the government at any time for breach or without cause.

Patents and Proprietary Information

Our success will depend in part on our ability to obtain and enforce patent protection for our products, methods, processes, and other proprietary technologies, preserve our trade secrets, and operate without infringing on the proprietary rights of other parties, both in the United States and in other countries. We own or have rights to certain proprietary information, proprietary technology, issued and allowed patents and patent applications which relate to compounds we are developing. We actively seek, when appropriate, protection for our products, proprietary technology, and proprietary information by means of U.S. and foreign patents, trademarks, and contractual arrangements. In addition, we rely upon trade secrets and contractual arrangements to protect certain of our proprietary information, proprietary technology, and products and product candidates.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. Our ability to maintain and solidify our proprietary position for our technology will depend on our success in obtaining effective patent claims and enforcing those claims once granted. We do not know whether any of our patent applications or those patent applications that we license will result in the issuance of any patents. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, invalidated, rendered unenforceable or circumvented, which could limit our ability to stop competitors from marketing related products or the length of term of patent protection that we

may have for our products. In addition, the rights granted under any issued patents may not provide us with competitive advantages against competitors with similar compounds or technology. Furthermore, our competitors may independently develop similar technologies or duplicate any technology developed by us in a manner that does not infringe our patents or other intellectual property. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our product candidates or those developed by our partners can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent.

As of December 31, 2020, we have been issued approximately 21 U.S. patents that expire between 2021 and 2039 and that relate to our kallikrein inhibitor compounds, neuraminidase inhibitor compounds, BSAV compounds and PNP inhibitor compounds. We have licensed a number of compounds protected by certain composition of matter patents from AECOM and IRL, totaling three additional U.S. patents that expire between 2023 and 2029. Additionally, we have approximately 24 Patent Cooperation Treaty or U.S. patent applications pending related to kallikrein inhibitor compounds, neuraminidase inhibitor compounds, BSAV compounds, PNP inhibitor compounds, FOP program compounds, and complement-mediated disease program compounds. Our pending applications may not result in issued patents, our patents may not cover the products of interest or may not be enforceable in all, or any jurisdictions and our patents may not provide us with sufficient protection against competitive products or otherwise be commercially viable. After expiration of composition of matter patents for our products and product candidates, we may rely on data exclusivity, or in some cases, method of use patents. The enforceability of these patents varies from jurisdiction to jurisdiction and may not be allowed or enforceable in some territories where we may seek approval. We may not have the funds to continue patent prosecution or to defend all of our existing patents in our current patent estate and may selectively abandon patents or patent families worldwide or in certain territories.

Our success is also dependent upon the skills, knowledge and experience of our scientific and technical personnel, none of which is patentable. To help protect our rights, we require all employees, consultants, advisors and partners to enter into confidentiality agreements, which prohibit the disclosure of confidential information to anyone outside of BioCryst and, where possible, 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.

Competition

The pharmaceutical and biotechnology industries are intensely competitive. Many companies, including biotechnology, chemical and pharmaceutical companies, are actively engaged in activities similar to ours, including research, development, and commercialization of drugs for the treatment of rare medical conditions. Many of these companies have substantially greater financial and other resources, larger research and development staffs, and more extensive commercial and manufacturing organizations than we do. In addition, many have considerable experience in preclinical testing, clinical trials, and other regulatory approval procedures. In addition, there are also academic institutions, governmental agencies and other research organizations who conduct research in areas in which we are working. We expect to encounter significant competition for any of the pharmaceutical products we plan to develop. Companies that successfully complete clinical trials, obtain required regulatory approvals, and commence commercial marketing and sales of their products may achieve a significant competitive advantage.

HAE

HAE is an autosomal dominant disease characterized by painful, unpredictable, recurrent attacks of inflammation affecting the hands, feet,face, abdomen, urogenital tract, and the larynx. The inflammation can be disfiguring, debilitating, or in the case of laryngeal attacks, life-threatening. Prevalence for HAE is uncertain but is estimated to be approximately 1 case per 33,000 to 67,000 persons without known differences among ethnic groups and is caused by deficient (Type I) or dysfunctional (Type II) levels of C1-Inhibitor ("C1-INH"), a naturally occurring molecule that is known to inhibit kallikrein, bradykinin, and other serine proteases in the blood. If left untreated, HAE can result in a mortality rate as high as 40% primarily due to upper airway obstruction. There are several licensed therapies for HAE, including the following:

- C1-INH replacement therapy is available as an acute therapy (Berinert®) and as a prophylactic therapy (Haegarda® and Cinryze®). These therapies are dosed subcutaneously and intravenously. Recombinant C1-INH (Ruconest®) is also available as an acute therapy.
- Kallikrein Inhibitors - Kalbitor® (ecallantide) is a specific recombinant plasma kallikrein inhibitor that is dosed subcutaneously by healthcare providers to treat acute HAE attacks. Takhzyro™ (lanadelumab-flyo) is a

monoclonal antibody approved for prophylaxis of HAE attacks and can be self-administered as a subcutaneous injection.

- Bradykinin receptor antagonist - Firazyr® (icatibant) is the treatment of acute attacks and is administered by subcutaneous administration. To date, there have been seven generic forms of icatibant approved by the FDA.
- Other medications - Prophylactic administration of synthetic attenuated androgens (generically available as danazol or stanozolol) has been utilized to reduce the frequency or severity of attacks. However, long-term use of danazol or stanozolol may result in liver damage, virilization and arterial hypertension. Six-month liver function tests, annual lipid profiles, and biennial hepatic ultrasound are recommended for patients on chronic androgen therapy.

We are aware of a number of HAE therapies in clinical development that, if approved, may compete with ORLADEYO. These include:

Company	Asset	Mechanism of Action	Route of Administration	Trial Phase	Role in Therapy
KalVista	KVD-900	Kallikrein inhibitor	Oral	II	Acute treatment
	KVD-824	Kallikrein inhibitor	Oral	I	Prophylaxis
Pharvaris	PHA121 (PHVS416/PHVS719)	B2 bradykinin antagonist	Oral	II	Acute and Prophylaxis
Attune	ATN-249	Kallikrein inhibitor	Oral	I	Prophylaxis
CSL	CSL312	Anti-factor XII mAb	IV/Subcutaneous	III	Prophylaxis
Ionis	IONIS-PKK-LRx	Antisense inhibitor of prekallikrein	Subcutaneous	II	Prophylaxis

Complement-Mediated Diseases

Several rare diseases are known to be mediated by defects of the complement system, including PNH, atypical hemolytic uremic syndrome ("aHUS"), complement 3 glomerulopathy ("C3G"), and myasthenia gravis. Alexion Pharmaceuticals, Inc.'s Soliris® (eculizumab) is a C5 inhibitor approved for PNH, aHUS, myasthenia gravis, and neuromyelitis optica spectrum disorder. Soliris had global sales of over $3.9 billion in 2019. Alexion also recently received FDA approval for Ultomiris™ (ravulizumab), a longer-acting C5 inhibitor, as a treatment for PNH in late 2018 and aHUS in late 2019. Global sales for Ultomiris were $339 million in 2019. In addition, Alexion acquired Achillion, a developer of oral Factor D inhibitors, in early 2020. In December 2020, Alexion agreed to be acquired by AstraZeneca, with the deal expected to close in the third quarter of 2021.

In addition to BCX9930, we are aware of a number of complement pathway-based products in development, which include:

Company	Asset	Mechanism of Action	Route of Administration	Trial Phase
Apellis	Pegcetacoplan (APL-2)	C3 Inhibitor	Subcutaneous	NDA
Akari	Nomacopan	C5 Inhibitor	Subcutaneous	III
Roche	Crovalimab (RG6107)	C5 Inhibitor	IV / Subcutaneous	III
Regeneron	Pozelimab	C5 Inhibitor	IV / Subcutaneous	III
Omeros	Narsoplimab	MASP-2	IV / Subcutaneous	BLA
	OMS906	MASP-3	Subcutaneous	I
Alexion	Danicopan (ALXN2040)	Factor D Inhibitor	Oral	III
	Vermicopan (ALXN2050)	Factor D Inhibitor	Oral	II
Novartis	Iptacopan (LNP023)	Factor B Inhibitor	Oral	III
	Tesidolumab	C5 Inhibitor	IV	II
ChemoCentryx	Avacopan	C5aR Inhibitor	Oral	NDA
Ra / UCB	Zilucoplan	C5 Inhibitor	Subcutaneous	II
Alnylam	Cemdisiran	C5 Inhibitor	Subcutaneous	II

Amgen (Phase 3), Samsung, and Isu Abxis are also in clinical trials developing biosimilars of eculizumab.

FOP

FOP is a rare, severely disabling condition characterized by HO. HO can occur in muscles, tendons, and soft tissue. FOP patients progressively become bound by this irregular ossification, with restricted movement and fused joints, resulting in deformities and premature mortality. There are currently no approved treatments for FOP.

In addition to BCX9250, we are aware of a number of FOP therapies in clinical development, which include:

Company	Asset	Mechanism of Action	Route of Administration	Trial Phase
Ipsen	Palovarotene	Retinoic Acid Receptor (RAR) Gamma Agonist	Oral	III
	BLU-782	ALK-2 Inhibitor	Oral	I
Regeneron	Garetosmab	Anti-activin A	IV	II
Incyte	INCB00928	ALK-2 Inhibitor	Oral	I
Keros	KER-047	ALK-2 Inhibitor	Oral	I

Antivirals

The pharmaceutical market for products that prevent or treat influenza is very competitive. Key competitive factors for RAPIVAB(peramivir injection) include, among others, efficacy, ease of use, safety, price and cost-effectiveness, storage and handling requirements, and reimbursement. A number of products are currently available in the U.S. and/or other counties, including Japan, for the prevention or treatment of influenza, including seasonal flu vaccines, F. Hoffmann-La Roche Ltd.'s ("Roche") TAMIFLU® (oseltamivir), generic oseltamivir, GlaxoSmithKline plc's ("GSK") RELENZA®, Genentech and Shiongi's XOFLUZA™ and Daiichi Sankyo Co., Ltd.'s INAVIR®. In addition, FUJIFILM Corporation's favipiravir, a polymerase inhibitor, is approved in Japan.

Various government entities throughout the world are offering incentives, grants, and contracts to encourage additional investment into preventative and therapeutic agents against influenza, which may have the effect of further increasing the number of our competitors and/or providing advantages to certain competitors.

Galidesivir is a product candidate in our BSAV research program and is currently being developed under contracts with NIAID/HHS and BARDA/HHS. The objective of our BSAV program is to develop galidesivir as a broad-spectrum therapeutic for viruses that pose a threat to national health and security. The U.S. Government is investing in a number of programs intended to address gaps in its medical countermeasure plan. Currently, there are five investigational therapeutics under a compassionate use/expanded access framework that can be available in an outbreak setting to treat Ebola virus disease.

In order to compete successfully in these and other therapeutic areas, we must develop proprietary positions in patented drugs for therapeutic markets that have not been satisfactorily addressed by conventional research strategies and, in the process, expand our expertise in structure-based drug design. Our product candidates, even if successfully tested and developed, may not be adopted by physicians over other products and may not offer economically feasible alternatives to other therapies.

Research and Development

We initiated our research and development activities in 1986. We have assembled a scientific research staff with expertise in a broad base of advanced research technologies, including protein biochemistry, X-ray crystallography, chemistry, and pharmacology. Our research facilities, located in Birmingham, Alabama, include protein biochemistry and organic synthesis laboratories, testing facilities, X-ray crystallography, computer and graphics equipment and facilities to make product candidates on a small scale for early-stage clinical trials.

Compliance

We conduct our business in an ethical, fair, honest, and lawful manner. We act responsibly, respectfully, and with integrity in our relationships with patients, health care professionals, collaborators, governments, regulatory entities, stockholders, suppliers, and vendors.

In order to ensure compliance with applicable laws and regulations, our Chief Financial Officer, Chief Legal Officer, and Senior Vice President of Human Resources oversee compliance training, education, auditing, and monitoring; enforce

disciplinary guidelines for any infractions of our corporate polices; implement new policies and procedures; respond to any detected issues; and undertake corrective action procedures. Our controls address compliance with laws and regulations that govern public pharmaceutical companies, including, but not limited to, the following: federal and state law, such as the Sarbanes-Oxley Act of 2002 and the U.S. Foreign Corrupt Practices Act of 1977; Nasdaq listing requirements; the regulations of the Financial Industry Regulatory Authority, the SEC, the FDA, and HHS; and applicable laws and regulations administered by foreign regulatory authorities, including those of the EU, the U.K., and Japan. Our standard operating procedures are designed to provide a framework for corporate governance in accordance with ethical standards and best legal practices.

Government Regulation

The FDA regulates the pharmaceutical and biotechnology industries in the U.S., and our product candidates are subject to extensive and rigorous domestic government regulations prior to commercialization. The FDA regulates, among other things, the development, testing, manufacture, safety, efficacy, record-keeping, labeling, storage, approval, advertising, promotion, sale and distribution of pharmaceutical products. In foreign countries, our products are also subject to extensive regulation by foreign governments. These government regulations are a significant factor in the production and marketing of any pharmaceutical products that we develop. Failure to comply with applicable FDA and other regulatory requirements at any stage during the regulatory process may subject us to sanctions, including:

- delays;
- warning letters;
- fines;
- product recalls or seizures;
- injunctions;
- penalties;
- refusal of the FDA to review pending market approval applications or supplements to approval applications;
- total or partial suspension of production;
- civil penalties;
- withdrawals of previously approved marketing applications; and
- criminal prosecutions.

The regulatory review and approval process is lengthy, expensive, and uncertain. Before obtaining regulatory approvals for the commercial sale of any products, we or our partners must demonstrate that our product candidates are safe and effective for use in humans. The approval process takes many years, substantial expenses may be incurred, and significant time may be devoted to clinical development.

The policies of the FDA and foreign regulatory authorities may change, and additional government regulations may be enacted which could prevent or delay regulatory approval of our product candidates or approval of new indications for our existing products. We cannot predict the likelihood, nature, or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the United States or abroad.

FDA Regulation

Before testing potential product candidates in humans, we carry out laboratory and animal studies to determine safety and biological activity. After completing preclinical trials, we must file an investigation new drug application ("IND"), including a proposal to begin clinical trials, with the FDA. Thirty days after filing an IND, a phase 1 human clinical trial can start, unless the FDA places a hold on the trial.

Clinical trials to support a new drug application ("NDA") are typically conducted in three sequential phases, but the phases may overlap.

Phase 1 — During phase 1, which involves the initial introduction of the drug into healthy volunteers, the drug is tested to assess metabolism, PK, and pharmacological actions and safety, including side effects associated with increasing doses.

Phase 2 — Phase 2 usually involves trials in a limited patient population to: (1) assess the efficacy of the drug in specific, targeted indications; (2) assess dosage tolerance and optimal dosage; and (3) identify possible adverse effects and safety risks.

Phase 3 (pivotal) — If a compound is found to be potentially effective and to have an acceptable safety profile in phase 2 evaluations, phase 3 clinical trials, also called pivotal studies, major studies, or advanced clinical trials, are undertaken to further demonstrate clinical efficacy and to further test for safety within an expanded patient population at geographically dispersed clinical trial sites. In general, the FDA requires that at least two adequate and well-controlled phase 3 clinical trials be conducted.

Initiation and completion of the clinical trial phases are dependent on several factors, including things that are beyond our control. For example, the clinical trials cannot begin at a particular site until that site receives approval from its Institutional Review Board ("IRB"), which reviews the protocol and related documents. This process can take several weeks to several months. In addition, clinical trials are dependent on patient enrollment, but the rate at which patients enroll in the study depends on:

- willingness of investigators to participate in a study;
- ability of clinical sites to obtain approval from their IRB;
- the availability of the required number of eligible subjects to be enrolled in a given trial;
- the availability of existing or other experimental drugs for the disease we intend to treat;
- the willingness of patients to participate; and
- the patients meeting the eligibility criteria.

Delays in planned patient enrollment may result in increased expense and longer development timelines.

After successful completion of the required clinical testing, generally an NDA is submitted. Upon receipt of the NDA, the FDA will review the application for completeness. Within 60 days, the FDA will determine if the application is sufficiently complete to warrant full review and will consider the application "filed" at that time. Also upon receipt of the application, the FDA will assign a review priority to the application. Priority review applications are usually reviewed within 6 months; standard review applications are usually reviewed within 10 months. The FDA may refer NDAs for new molecular entities to an appropriate advisory committee for review and evaluation in regard to providing a recommendation as to whether the application should be approved. The FDA is not bound to follow the recommendation of an advisory committee.

Following the review of the application, which may include requests for additional information from the sponsor and results from inspections of manufacturing and clinical sites, the FDA will issue an "action letter" on the application. The action letter will either be an "approval letter," in which case the product may be lawfully marketed in the United States, or a "complete response letter." A complete response letter will state that the FDA cannot approve the NDA in its present form and, usually, will describe all of the specific deficiencies that the FDA has identified in the application. The complete response letter, when possible, will include the FDA's recommended actions to place the application in a condition for approval. Deficiencies can be minor (e.g., labeling changes) or major (e.g., requiring additional clinical trials). A complete response letter may also be issued before the FDA conducts the required facility inspection and/or reviews labeling, leaving the possibility that additional deficiencies in the original NDA could be subsequently cited. An applicant receiving a complete response letter is permitted to resubmit the NDA addressing the identified deficiencies (in which case a new two- or six-month review cycle will begin), or withdraw the NDA. The FDA may consider a failure to take action within one year of a complete response letter to be a request to withdraw, unless the applicant has requested an extension of time in which to resubmit the NDA. If the FDA approves an NDA, the marketing of the product will be limited to the particular disease states and conditions of use that are described in the product label.

We and all of our contract manufacturers are also required to comply with the applicable FDA current Good Manufacturing Practice, or cGMP, regulations during clinical development and to ensure that the product can be consistently manufactured to meet the specifications submitted in an NDA. The cGMP regulations include requirements relating to product quality, as well as the corresponding maintenance of records and documentation. Manufacturing facilities must be approved by the FDA before they can be used to manufacture our products. Based on an inspection, the FDA determines whether manufacturing facilities are in compliance with applicable regulations. Manufacturing facilities in non-United States countries that are utilized to manufacture drugs for distribution into the United States are also subject to inspection by the FDA. Additionally, failure to comply with local regulatory requirements could affect production and availability of product in relevant markets.

Foreign Regulation

In addition to regulations in the United States, we are subject to a variety of foreign regulatory requirements governing human clinical trials and marketing approval for drugs. The foreign regulatory approval process includes all of the risks associated with FDA approval set forth above, as well as additional country-specific regulations. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary greatly from country to country.

For example, under EU regulatory systems, we may submit marketing authorizations either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all EU member states. The decentralized procedure provides for mutual recognition of national approval decisions, and the holder of a national marketing authorization may submit an application to the remaining member states. The U.K.'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.

Under the Japanese regulatory system administered by the Japanese Pharmaceuticals and Medical Devices Agency ("PMDA"), pre-marketing approval and clinical studies are required for all pharmaceutical products. To obtain manufacturing/marketing approval, we must submit an application for approval to the MHLW with results of nonclinical and clinical studies to show the quality, efficacy, and safety of a new drug. A data compliance review, good Clinical Practices, or GCP, on-site inspection, cGMP audit, and detailed data review are undertaken by the PMDA. The application is then discussed by the committees of the Pharmaceutical Affairs and Food Sanitation Council ("PAFSC"). Based on the results of these reviews, the final decision on approval is made by MHLW. In Japan, the National Health Insurance system maintains a Drug Price List specifying which pharmaceutical products are eligible for reimbursement, and the MHLW sets the prices of the products on this list. Following the January 2021 approval of ORLADEYO in Japan, negotiations regarding the reimbursement price with MHLW have begun. The price will be determined within 60 to 90 days following approval unless the applicant disagrees, which may result in extended pricing negotiations. The government generally introduces price cut rounds every other year and also mandates price decreases for specific products. New products judged innovative or useful, that are indicated for pediatric use, or that target orphan or small population diseases, however, may be eligible for a pricing premium. The Japanese government has also promoted the use of generics, where available.

Human Capital Resources

As of January 31, 2021, we had approximately 246 employees, of whom approximately 119 employees were engaged in the research and development function of our operations. Our research and development staff, approximately 48 of whom hold Ph.D. or M.D. degrees, have diversified experience in biochemistry, pharmacology, X-ray crystallography, synthetic organic chemistry, computational chemistry, medicinal chemistry, clinical development and regulatory affairs.

We believe that our ability to successfully execute on our strategic initiatives is highly dependent upon our ability to recruit, retain, and reward our employees. We engage in targeted recruitment strategies to fill highly skilled positions. Our employees enjoy competitive salaries and benefits, as well as equity participation. Our compensation philosophy is designed to provide an appealing, competitive, and rewarding compensation program that encourages high personal and company performance, strong cultural and ethical behavior, and incentives aligned with stockholder interests.

We are committed to providing a workplace that protects the health and wellbeing of our employees. All employees are required to abide by our Code of Conduct and Compliance Plan and health and safety parameters and to contribute to a positive, inclusive, and friendly company culture. Where we believe such arrangements can be effective, we have implemented flexible working arrangements, including work from home arrangements, for our employees, in part, to encourage employee health and wellness during the global COVID-19 pandemic. We consider our relations with our employees to be satisfactory.

Corporate Information

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 our 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 into this Form 10-K.

Financial Information

For information related to our revenues, profits, net loss and total assets, in addition to other financial information, please refer to the Consolidated Financial Statements and Notes to Consolidated Financial Statements contained in Part II, Item 8 of this report. Financial information about revenues derived from foreign countries is included in Note 1 to Consolidated Financial Statements contained in this report.

Available Information

Our website address is www.biocryst.com. We make available, free of charge, at our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. We also make available at our website copies of our audit committee charter, compensation committee charter, corporate governance and nominating committee charter and our code of business conduct, which applies to all our employees as well as the members of our Board of Directors. Any amendment to, or waiver from, our code of business conduct will be posted on our website.

ITEM 1A. *RISK FACTORS*

An investment in our stock involves risks. You should carefully read this entire report and consider the following uncertainties and risks, which may adversely affect our business, financial condition or results of operations, along with all of the other information included in our other filings with the SEC, before deciding to buy our common stock.

Risks Relating to Our Business

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 recent 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 COVID-19 pandemic has spread to multiple countries around the world, is affecting 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 FDA, EMA, 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, if interruptions related to COVID-19 were to impair our or Torii's ability to perform under the Torii Agreement to complete our regulatory interactions in Japan, including with respect to the pending approval of a reimbursement price for ORLADEYO for the treatment of HAE, then the timing and success of our development and commercialization of ORLADEYO in Japan could be severely impacted.

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 future 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. 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 plans and timelines.

We have implemented 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 rapidly. The ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly 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 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 RPI royalties on certain ORLADEYO and BCX9930 revenues under the Royalty Purchase Agreement, 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 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 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 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, milestones 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 MHLW or the 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.

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.

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.

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. 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 (as defined under "Management's Discussion and Analysis of Financial Condition and Results of Operations -- Overview -- Recent Corporate Highlights -- Financing Transactions" in Part II, Item 7 of this report). 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 they might limit or place burdensome conditions upon future transactions with us. Also, it is possible that suppliers may be negatively impacted. Any such unfavorable outcomes in our current programs or unfavorable economic conditions could place severe downward pressure on the price of our common stock and may decrease opportunities to raise capital in the capital or credit markets, and further could reduce the return available on invested corporate cash, which, if severe and sustained, could have a material and adverse impact on our results of operations and cash flows and limit our ability to continue development 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 products through the various stages of development, especially through the clinical trial process, and to receive regulatory approval for the commercial sale of our products," 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. If we receive approval to market our potential products, whether in the United States or internationally, we will continue to be subject to extensive regulatory requirements. These requirements are wide ranging and govern, among other things:

- adverse drug experience reporting regulations;
- product promotion;
- product manufacturing, including good manufacturing practice requirements; and
- product changes or modifications.

Our failure to comply with existing or future regulatory requirements 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 PNH has received Fast Track and Orphan Drug designations from the FDA, and ORLADEYO has a Promising Innovative Medicine designation from the MHRA, as well as orphan drug status from the EMA, 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 ORLADEYO, 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 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.

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 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;
- 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 SUL, 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 towards 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 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, 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. 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 potential milestone or royalty payments, is subject to a number of risks, including that applicable regulatory agencies may not provide reimbursement approvals on a timely basis or at all, 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 for a potential milestone payment upon receipt of a reimbursement price approval from Japan's National Health Insurance system in excess of the threshold specified in the Torii Agreement, which we may not receive on a timely basis or at all. The Torii Agreement also 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 expect 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, fail to receive reimbursement authorization in excess of the specified threshold, 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 of, 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 obtain reimbursement price approval for ORLADEYO in Japan and 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.

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 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 product candidates 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 and our products and product candidates;
- we may fail to employ a comprehensive and effective regulatory strategy, which could result in a delay or failure in commercialization of our products;
- our ability to successfully commercialize our products is affected by the competitive landscape, which cannot be fully known at this time;
- 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.

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 and train 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 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 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, 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 product candidates at a cost or in quantities necessary to make them commercially viable. Our raw materials, drug substances, and product candidates are manufactured by a limited group of suppliers, including some at a single facility. If any of these suppliers were unable to produce these items, this could significantly impact our supply of product candidate material for further preclinical

testing and clinical trials. 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 our partners and may result in little to no milestones or royalties to us;
- effectiveness of marketing and commercialization efforts for our products by our partners;
- market satisfaction with existing alternative therapies;
- perceived efficacy relative to other available therapies;
- disease prevalence;
- cost of treatment;
- pricing and availability of alternative products;
- marketing and sales activities of competitors;
- shifts in the medical community to new treatment paradigms or standards of care; and
- relative convenience and ease of administration.

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, in December 2020. 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® and Ultomiris™), 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 this report 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.

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, 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.

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.

We have a number of outstanding post-approval commitments to the FDA and EMA that we retain, which we may not complete successfully or on time for any number of reasons, including but not limited to lack of funds to complete the studies and insufficient interest by appropriate sites, investigators or study subjects. For example, as a condition of the approval of RAPIVAB, we were required to complete pediatric patient trials and to submit the final results of these clinical trials to the FDA and EMA. We may be subject to penalties if we fail to comply with post-approval legal and regulatory requirements, and our products could be subject to continual recordkeeping and reporting requirements, review and periodic inspections by the FDA and other regulatory bodies. Regulatory approval of a product may be subject to limitations on the indicated uses for which the product may be marketed or to the other restrictive conditions of approval that limit our ability to promote, sell or distribute a product. Furthermore, the approval of 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 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, 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. 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 the product candidates to produce revenue would diminish. Additionally, if our products, methods, processes, and other technologies or our commercial use of such products, processes, and other technologies, including but not limited to any trade name, trademark or commercial strategy infringe the proprietary rights of other parties, we could incur substantial costs. The USPTO and the patent offices of other jurisdictions have issued to us a number of patents for our various inventions and we have in-licensed several patents from various institutions. We have filed additional patent applications and provisional patent applications with the USPTO. We have filed a number of corresponding foreign patent applications and intend to file additional foreign and U.S. patent applications, as appropriate. We have also filed certain trademark and trade name applications worldwide. We cannot assure you as to:

- the degree and range of protection any patents will afford against competitors with similar products;
- if and when patents will issue;
- if patents do issue, we cannot be sure that we will be able to adequately defend such patents and whether or not we will be able to adequately enforce such patents; or
- whether or not others will obtain patents claiming aspects similar to those covered by our patent applications.

If the USPTO or other foreign patent office upholds patents issued to others or if the USPTO grants patent applications filed by others, we may have to:

- obtain licenses or redesign our products or processes to avoid infringement;
- stop using the subject matter claimed in those patents; or
- pay damages.

We may initiate, or others may bring against us, litigation or administrative proceedings related to intellectual property rights, including proceedings before the USPTO or other foreign patent office. Any judgment adverse to us in any litigation or other proceeding arising in connection with a patent or patent application could materially and adversely affect our business, financial condition and results of operations. In addition, the costs of any such proceeding may be substantial whether or not we are successful.

Our success is also dependent upon the skills, knowledge and experience, none of which is patentable, of our scientific and technical personnel. To help protect our rights, we require all employees, consultants, advisors and partners to enter into confidentiality agreements that prohibit the disclosure of confidential information to anyone outside of our company and require disclosure and assignment to us of their ideas, developments, discoveries and inventions. These agreements may not provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information, and if any of our proprietary information is disclosed, our business will suffer because our revenues depend upon our ability to license or commercialize our product candidates and any such events would significantly impair the value of such product candidates.

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 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; if BARDA/HHS or NIAID/HHS were to eliminate, reduce or delay funding from our contracts, this would have a significant negative impact on the programs associated with such funding and could have a significant negative impact on our revenues and cash flows.

We have completed work under a contract with BARDA/HHS for the development of RAPIVAB and have entered into contracts with BARDA/HHS and NIAID/HHS for the development of galidesivir as a treatment for diseases caused by RNA pathogens, including Marburg virus disease, 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, significant negative impact on our cash flows and operations could result.

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, significant negative impact on our cash flows and operations could result.

As a U.S. Government contractor, we are required to comply with applicable laws, regulations and standards relating to our accounting practices and are subject to periodic audits and reviews. As part of any such audit or review, the U.S. Government may review the adequacy of, and our compliance with, our internal control systems and policies, including those relating to our purchasing, property, estimating, compensation and management information systems. Audits 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 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 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 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 pursue acceleration of the PhaRMA Notes and 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 December 31, 2020, we had an outstanding principal balance under our Credit Agreement of $125.0 million. 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;
- 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.

Risks 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;
- 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 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 European 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 samples could result in significant delays in our drug development process.

In addition, we store most of our preclinical and clinical data at our facilities. Duplicate copies of most critical data are secured off-site. Any significant degradation or failure of our computer systems could cause us to inaccurately calculate or lose our data. Loss of data could result in significant delays in our drug development process and any system failure could harm our business and operations.

A significant disruption in our information technology systems or a 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

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 December 31, 2020, the 52-week range of the market price of our stock was from $1.58 to $8.99 per share. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock:

- announcements of technological innovations or new products by us or our competitors;
- developments or disputes concerning patents or proprietary rights;
- additional dilution through sales of our common stock or other derivative securities;
- status of new or existing licensing or collaborative agreements and government contracts;
- announcements relating to the status of our programs;
- developments and announcements regarding new and virulent strains of influenza;
- we or our partners achieving or failing to achieve development milestones;
- publicity regarding actual or potential medical results relating to products under development by us or our competitors;
- publicity regarding certain public health concerns for which we are or may be developing treatments;
- regulatory developments in both the United States and foreign countries;
- public concern as to the safety of pharmaceutical products;
- actual or anticipated fluctuations in our operating results;
- changes in financial estimates or recommendations by securities analysts;
- changes in the structure of healthcare payment systems, including developments in price control legislation;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- additions or departures of key personnel or members of our board of directors;
- purchases or sales of substantial amounts of our stock by existing stockholders, including officers or directors;
- economic and other external factors or other disasters or crises; and
- period-to-period fluctuations in our financial results.

Future sales and issuances of securities may dilute 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 January 31, 2021, there were 177,182,751 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 January 31, 2021, there were 24,780,638 stock options outstanding and 4,587,872 shares available for issuance under our Amended and Restated Stock Incentive Plan, 4,307,668 stock options outstanding and 92,332 shares available for issuance under our Amended and Restated Inducement Equity Incentive Plan and 2,679,554 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.

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 pre-funded warrants to purchase 3,511,111 shares of our common stock at a price of $4.49 per warrant, including pre-funded warrants acquired by certain of the Baker Entities to purchase 3,252,375 shares of our common stock. 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 Securities Exchange Act of 1934, as amended, 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.

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 recent COVID-19 pandemic on us or on third parties with whom we conduct business, including without limitation our development partners, manufacturers, CROs, and others, as well as on the regulatory and government agencies with whom we work."

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

From time to time, we may be involved in disputes, called upon to initiate legal proceedings or to defend ourselves in such legal proceedings relating to our business. 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. If our stock price is volatile, we may become involved in securities class action lawsuits in the future. Any current or future dispute resolution or legal proceeding, regardless of the merits of any such proceeding, could 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 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 and commercialization of our products and the related expansion of our business will be delayed or stopped.

We are highly dependent upon our senior management and scientific team, the unexpected loss of whose services might impede the achievement of our development and commercial objectives. 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.

ITEM 1B. *UNRESOLVED STAFF COMMENTS*

None.

ITEM 2. *PROPERTIES*

We lease property in both Durham, North Carolina and Birmingham, Alabama. Our headquarters, including our clinical and regulatory operations, are based in Durham, while our principal research facility is located in Birmingham. We currently lease approximately 33,000 square feet in Durham through June 30, 2021 and approximately 34,000 square feet in Birmingham through October 31, 2026. We also lease smaller office spaces in Ireland, Germany, and France. We believe that our facilities are adequate for our current and planned future operations.

ITEM 3. *LEGAL PROCEEDINGS*

None.

ITEM 4. *MINE SAFETY DISCLOSURES*

Not applicable.

PART II

ITEM 5. *MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES*

Market Information

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

Holders

As of January 31, 2021, there were approximately 167 holders of record of our common stock.

Dividends

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

Stock Performance Graph

This performance graph is not "soliciting material," is not deemed filed with the SEC and is not to be incorporated by reference in any filing by us under the Securities Act or the Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing. The stock price performance shown on the graph is not necessarily indicative of future price performance.

PERFORMANCE GRAPH FOR BIOCRYST

Indexed Comparison Since 2015

	Beginning Investment at 12/31/15	Investment at 12/31/16	Investment at 12/31/17	Investment at 12/31/18	Investment at 12/31/19	Investment at 12/31/20
BioCryst Pharmaceuticals, Inc.	$ 100.00	$ 61.34	$ 47.58	$ 78.20	$ 33.43	$ 72.19
Nasdaq Stock Market (U.S.).....	100.00	113.01	137.17	129.71	170.14	206.32
Nasdaq Pharmaceutical Stocks.....	100.00	98.91	117.83	127.20	145.65	160.97

The above graph measures the change in a $100 investment in our common stock based on its closing price of $10.32 on December 31, 2015 and its year-end closing price thereafter. Our relative performance is then compared with the CRSP Total Return Indexes for the Nasdaq Stock Market (U.S.) and Nasdaq Pharmaceutical Stocks.

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

There were no repurchases of our common stock or shares surrendered to satisfy tax obligations during the fourth quarter of 2020.

ITEM 6. *SELECTED FINANCIAL DATA*

The selected Statement of Operations Data and Balance Sheet data with respect to the years ended December 31, 2020, 2019, 2018, 2017, and 2016 set forth below are derived from our consolidated financial statements. The selected financial data set forth below should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" contained in Part II, Item 7 of this report and our consolidated financial statements and the notes thereto appended to this report.

	Years Ended December 31,				
	2020	2019	2018	2017	2016
	(In thousands, except per share amounts)				
Statement of Operations Data:					
Total revenues	$ 17,812	$ 48,835	$ 20,653	$ 25,186	$ 26,353
Cost of product sold	1,550	3,726	-	1,142	2,297
Research and development expenses	122,964	107,068	84,888	66,962	61,008
Selling, general and administrative expenses	67,929	37,121	29,514	13,933	11,253
Royalty expense	126	375	471	560	402
Loss from operations	(174,757)	(99,455)	(94,220)	(57,411)	(48,607)
Net loss	(182,814)	(108,897)	(101,252)	(65,782)	(55,144)
Basic and diluted net loss per share	$ (1.09)	$ (0.94)	$ (0.98)	$ (0.78)	$ (0.75)
Weighted average shares outstanding	167,267	115,600	103,185	84,451	73,699

	As of December 31,				
	2020	2019	2018	2017	2016
	(In thousands)				
Balance Sheet Data:					
Cash, cash equivalents, restricted cash and investments	$ 302,587	$ 137,777	$ 128,387	$ 158,978	$ 65,122
Receivables	8,646	22,146	4,293	6,117	8,768
Inventory	7,039	-	1,649	-	500
Total assets	334,715	175,282	146,841	178,259	89,847
Long-term deferred revenue	-	-	-	-	8,184
Non-recourse notes payable	30,000	29,561	29,121	28,682	28,243
Royalty financing obligation	124,717	-	-	-	-
Senior credit facility	-	50,309	29,952	23,214	22,777
Secured term loan	119,735	-	-	-	-
Accumulated deficit	(1,023,442)	(840,628)	(731,969)	(631,843)	(566,061)
Total stockholders' (deficit) equity	(19,262)	38,252	49,235	83,767	1,578

ITEM 7. *MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS*

The following Management's Discussion and Analysis ("MD&A") is intended to help the reader understand our results of operations and financial condition. MD&A is provided as a supplement to, and should be read in conjunction with, our audited financial statements and the accompanying notes to the financial statements and other disclosures included in this report (including the "Cautionary Note Regarding Forward-Looking Statements" at the beginning of this report and the "Risk Factors" section in Part I, Item 1A of this report).

Overview

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. In addition to these discovery and development efforts, our business strategy includes the efficient commercialization of these drugs in the U.S. 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.

Our revenues are difficult to predict and depend on several factors, including those discussed in the "Risk Factors" section in Part I, Item 1A of this report. For example, our revenues depend, in part, on regulatory approval decisions for our products and product candidates, the effectiveness of our and our collaborative partners' commercialization efforts, market acceptance of our products, particularly ORLADEYO, the resources dedicated to our products by us and our collaborative partners, and ongoing discussions with government agencies regarding contract awards for development and procurement, as well as entering into, or modifying, licensing agreements for our product candidates. Furthermore, revenues related to our collaborative development activities are dependent upon the progress toward and the achievement of developmental milestones by us or our collaborative partners.

Our operating expenses are also difficult to predict and depend on several factors, including research and development expenses (and whether these expenses are reimbursable under government contracts), drug manufacturing, and clinical research activities, the ongoing requirements of our development programs, the availability of capital and direction from regulatory agencies, which are difficult to predict, and the factors discussed in the "Risk Factors" section in Part I, Item 1A of this report. Management may be able to control the timing and level of research and development and selling, general and administrative expenses, but many of these expenditures will occur irrespective of our actions due to contractually committed activities and/or payments.

As a result of these factors, we believe that period-to-period comparisons are not necessarily meaningful and you should not rely on them as an indication of future performance. Due to all of the foregoing factors, it is possible that our operating results will be below the expectations of market analysts and investors. In such event, the prevailing market price of our common stock could be materially adversely affected.

Critical Accounting Policies and Estimates

The accompanying discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements and the related disclosures, which have been prepared in accordance with U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues, expenses and related disclosure of contingent assets and liabilities. We evaluate our estimates, judgments and the policies underlying these estimates on a periodic basis, as situations change, and regularly discuss financial events, policies, and issues with members of our audit committee and our independent registered public accounting firm. In particular, we routinely evaluate our estimates and policies regarding revenue recognition, administration, inventory and manufacturing, taxes, stock-based compensation, research and development, consulting and other expenses and any associated liabilities. Our estimates are based on historical experience and on various other assumptions that are believed to be reasonable under the circumstances. The results of our estimates form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. See "Critical Accounting Policies" at the end of this "Management's Discussion and Analysis of Financial Condition and Results of Operations" for a description of accounting policies that we believe are the most critical to aid you in fully understanding and evaluating our reported financial results and that affect the more significant judgments and estimates that we use in the preparation of our financial statements.

Recent Corporate Highlights

COVID-19

The outbreak of COVID-19 has severely impacted global economic activity and caused significant volatility in financial markets. To date, our financial condition, results of operations, and liquidity have not been materially impacted by the direct effects of the COVID-19 pandemic. However, as discussed under "Risk Factors-Risks Related to Our Business-Risks Related to COVID-19" in Part I, Item 1A of this report, the acceleration of COVID-19 slowed startup of the inadequate responder cohorts in our complement oral Factor D inhibitor program. The COVID-19 pandemic is constantly evolving, and its full impact to our business is uncertain. We are continuing to monitor developments with respect to the COVID-19 pandemic and to make adjustments as needed to assist in protecting the safety of our employees and communities while continuing our business activities. Our remote working arrangements are ongoing where possible, and we continue to restrict business-related travel. To date, implementation of these measures has not required material expenditures or significantly impacted our ability to operate our business or our internal control over financial reporting and disclosure controls and procedures. We are continuing to monitor the potential impacts of COVID-19 on our operations and those of our partners, suppliers, customers, and regulators.

ORLADEYO (berotralstat)

ORLADEYO is an oral, once-daily therapy discovered and developed by BioCryst for the prevention of HAE attacks. ORLADEYO, in both 110 mg and 150 mg capsule dosage forms, was approved by the FDA in December 2020 for prophylaxis to prevent attacks of HAE in adults and pediatric patients 12 years and older. On December 16, 2020, we announced that ORLADEYO is now available for shipment to patients with a prescription in the U.S. and that our exclusive specialty pharmacy provider for ORLADEYO in the U.S. began shipping to patients. We completed the build-out of our U.S. commercial infrastructure in 2020 to support the launch of ORLADEYO in the U.S. and are currently building our commercial infrastructure to support European launches.

ORLADEYO, in the 150 mg capsule dosage form, also received marketing and manufacturing approval from the MHLW in Japan in January 2021 for prophylactic treatment of HAE in adults and pediatric patients 12 years and older. Torii, our collaborative partner, will launch ORLADEYO in Japan following the successful completion of our pricing negotiations with the Japanese National Health Insurance System.

On March 30, 2020, we announced that the EMA had validated our MAA submission for approval of ORLADEYO for the prevention of HAE attacks. With this validation, the EMA began its formal review of the MAA under the centralized procedure for all member states of the EU, Norway, Iceland, and Liechtenstein. On February 25, 2021, we announced that the CHMP has adopted a positive opinion recommending the approval of ORLADEYO for routine prevention of recurrent attacks of HAE in adult and adolescent patients aged 12 years and older. The EC will review the CHMP recommendation, and a final approval decision from the EC on the MAA for ORLADEYO is expected in the second quarter of 2021.

On October 30, 2020, we announced that the MHRA has granted ORLADEYO a positive scientific opinion through the EAMS. Under the EAMS, HAE patients in the U.K. aged 12 years and older can gain access to ORLADEYO for the routine prevention of recurrent attacks of HAE before the drug is granted marketing authorization. We plan to file for a U.K. marketing authorization with the MHRA following our receipt of a positive opinion from the CHMP. This is expected to result in a U.K. marketing authorization shortly after a final decision by the EC.

We completed the build-out of our U.S. commercial infrastructure in 2020 to support the launch of ORLADEYO in the U.S. and are currently building our commercial infrastructure to support European launches. Based on proprietary analyses of HAE prevalence and market research studies with HAE patients, physicians, and payors in the U.S. and Europe, we anticipate the commercial market for ORLADEYO has the potential to reach a global peak of more than $500 million in annual sales. These expectations are subject to numerous risks and uncertainties that may cause our actual results, performance, or achievements to be materially different. There can be no assurance that our commercialization methods and strategies will succeed, or that the market for ORLADEYO will develop in line with our current expectations. See "Risk Factors-Risks Relating to Our Business-Risks Relating to Drug Development and Commercialization-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" in Part I, Item 1A of this report for further discussion of these risks.

Complement-Mediated Diseases

Discovered by BioCryst, BCX9930 is a novel, oral, potent, and selective small molecule inhibitor of Factor D currently in early clinical development for the treatment of complement-mediated diseases. Based on the safety and PoC data generated to date in PNH patients, we are working closely with key opinion leaders in hematology and nephrology to map the development strategy across a broad set of indications. Our goal is to develop BCX9930 as a monotherapy for complement-mediated diseases.

On February 25, 2021, we announced that we have completed enrollment of our ongoing dose ranging trial in treatment-naïve (no prior treatment with C5 inhibitors) PNH patients and PNH patients with an inadequate response to C5 inhibitors. We plan to present data from the 16 enrolled PNH patients (10 treatment naïve and 6 inadequate C5 responders) at our upcoming R&D day on March 22, 2021.

On September 30, 2020, we announced new data from treatment-naïve PNH patients receiving doses through 400 mg twice-daily of oral BCX9930 as monotherapy in the ongoing part 3 PoC dose-ranging trial. Oral BCX9930 was shown to drive rapid and dose-dependent reductions in key biomarkers, including LDH, and increasing hemoglobin levels in all PNH patients in the trial. Increases in hemoglobin levels were maintained without transfusions. BCX9930 was safe and well tolerated at all doses in the trial. No drug-related serious adverse events had been reported. One subject was discontinued due to an unrelated serious adverse event.

On August 31, 2020, we announced that the FDA granted orphan drug designation for BCX9930 for the treatment of PNH. Orphan drug designation qualifies BCX9930 for various development incentives, including tax credits for certain clinical costs, a waiver of the new drug application fee, and a designated period of market exclusivity following approval. On August 3, 2020, we announced that the FDA granted fast track designation for BCX9930 in PNH.

FOP

The goal of our ALK2 inhibitor is to discover and develop orally administered kinase inhibitor drug candidates that are able to slow or prevent HO. On December 21, 2020, we announced that in a phase 1 clinical trial, BCX9250, our lead compound, was safe and well tolerated at all doses studied, with linear and dose-proportional exposure supporting once-daily dosing. The randomized, double-blind, placebo-controlled dose-ranging trial evaluated safety, tolerability, and PK of SAD and MAD of BCX9250 in healthy subjects. The SAD study was designed to randomize four cohorts of eight subjects each to receive oral BCX9250 (n=6) or placebo (n=2) at dose levels of 5 mg, 10 mg, 15 mg, and 25 mg. Subjects in the 15 mg cohort also received a second single dose to evaluate food effect on absorption of BCX9250. The MAD study was designed to randomize 4 cohorts of 12 subjects each to receive oral BCX9250 (n=10) or placebo (n=2) at dose levels of 5 mg, 10 mg, 15 mg, and 20 mg once-daily for 7 days. Drug exposure increased with dose in an approximately linear and dose-proportional manner. Drug levels after a high fat meal were similar to those after dosing on an empty stomach. Drug exposure at 20 mg once-daily in the MAD was similar to that achieved with doses that suppressed HO in a nonclinical model of activity of orally dosed BCX9250. In both the SAD and the MAD studies, oral BCX9250 was safe and well tolerated, with no serious adverse events, no study discontinuations due to adverse events, no grade 3 or 4 adverse events, and no clinically significant changes in vital signs, electrocardiograms, or safety laboratory parameters. No safety signals were seen.

Peramivir Injection (RAPIVAB, ALPIVAB, RAPICACTA, PERAMIFLU)

On March 4, 2020, the ICC Tribunal delivered a Partial Arbitration Award in the arbitration matter between the Company and SUL with respect to the SUL Agreement. In the Partial Arbitration Award, the ICC Tribunal found that, during the term, SUL materially breached and abandoned its core duties to us under the Diligent Efforts (as defined in the SUL Agreement) requirements of the SUL Agreement as applicable in the U.S. The ICC Tribunal granted a declaratory judgment in favor of us terminating the SUL Agreement and restoring all rights to peramivir to us. We agreed with SUL on a transition process for the product, with a full transition of commercialization of the product in the U.S. and Australia returned to us as of August 1, 2020 and November 1, 2020, respectively. The ICC Tribunal also awarded us attorneys' fees and expenses incurred in securing the declaratory judgment as well as the costs incurred by us in the arbitration. Finally, the ICC Tribunal found that SUL breached the SUL Agreement by failing to pay a milestone payment due to us within 30 days of the approval of peramivir for adult use in the EU and awarded us $5.0 million (plus interest) for this claim. The ICC Tribunal retained jurisdiction for further proceedings relating to the award of attorneys' fees and for any dispute relating to the return to us of all rights to peramivir in the Territory.

On September 3, 2020, we announced that HHS has exercised its option to purchase an additional 10,000 doses of our antiviral influenza therapy, RAPIVAB (peramivir injection), for $6.9 million. As a result, we expect to deliver at least one shipment of 10,000 doses in 2021. The order is part of a $34.7 million contract awarded to us in 2018 for the procurement of up to 50,000 doses of RAPIVAB over a five-year period for the Strategic National Stockpile.

Galidesivir (formerly BCX4430)

In April 2020, we agreed with NIAID/HHS to add a group of COVID-19 patients to an ongoing clinical trial in Yellow Fever. On April 9, 2020, we announced that we had opened a randomized, double-blind, placebo-controlled clinical trial in Brazil to assess the safety, clinical impact, and antiviral effects of galidesivir in patients with COVID-19. NIAID/HHS awarded us a new $43.9 million contract for the manufacture and evaluation of the safety, efficacy, and tolerability of galidesivir in August 2020, and it also added $2.9 million to its existing contract with us to support the development of galidesivir. NIAID/HHS made an initial award of $6.3 million under the new contract.

On December 22, 2020, we announced that data from part 1 of the clinical trial in Brazil showed that galidesivir was safe and generally well tolerated in patients infected with SARS-Cov-2, the virus that causes COVID-19. The trial was not designed or sized to demonstrate clinical efficacy, and no clinical efficacy benefit with galidesivir treatment compared to placebo treatment was observed in the trial. Based on our ongoing discussions with NIAID/HHS, we expect NIAID/HHS to continue its support for the development of galidesivir with a focus on biodefense threats, such as Marburg virus disease, and to discontinue the pursuit of a COVID-19 indication for galidesivir.

Financing Transactions

Royalty Monetization. On December 7, 2020, we entered into the Royalty Purchase Agreement with RPI, pursuant to which we sold to RPI the right to receive certain royalty payments from the Company for a purchase price of $125 million in cash (the "Royalty Sale"). Under the Royalty Purchase Agreement, RPI is entitled to receive tiered, sales-based royalties on net product sales of ORLADEYO in the Key Territories. In addition, RPI is entitled to receive a tiered revenue share on amounts generally received by us on account of ORLADEYO sublicense revenue or net sales by licensees outside of the Key Territories. No payment will be due to RPI for any achievement milestone which may be payable under the existing out-license for ORLADEYO. Under the Royalty Purchase Agreement, RPI will also be entitled to receive 1.0% of global net sales, if any, of BCX9930. See "Note 3-Royalty Monetizations-ORLADEYO Royalty Monetization" in the Notes to Consolidated Financial Statements in Part II, Item 8 of this report for additional information about our obligations under the Royalty Purchase Agreement.

Credit Agreement. On December 7, 2020, we entered into a $200.0 million Credit Agreement with Athyrium Opportunities III Co-Invest 1 LP ("Athyrium" and such agreement, the "Credit Agreement"), as lender and as administrative agent for the lenders. BioCryst Ireland Limited, BioCryst US Sales Co., LLC, and BioCryst UK Limited, each of which is a wholly-owned subsidiary of ours, are guarantors to the Credit Agreement. The Credit Agreement provides for an initial term loan in the principal amount of $125.0 million (the "Term A Loan"), which was received by us on December 7, 2020 and is classified as "Secured term loan" on our balance sheet as of December 31, 2020. We used a portion of the proceeds from the Term A Loan to repay the approximate $43.3 million of outstanding indebtedness, including accrued interest, under our secured credit facility with MidCap Financial Trust ("MidCap"), which terminated in December 2020 upon such repayment. We intend to use the remaining proceeds to support the launch of ORLADEYO in the United States and Europe and to advance the development of BCX9930 into clinical trials in multiple complement-mediated diseases, and for other general corporate purposes.

The Credit Agreement also provides for two additional term loans, at our option, in the respective principal amounts of $25.0 million (the "Term B Loan") and $50.0 million (the "Term C Loan"). The Term B Loan and the Term C Loan may be drawn upon if, among other conditions, we reach 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. The maturity date of the Credit Agreement is December 7, 2025. See "Note 4-Credit Agreement" in the Notes to Consolidated Financial Statements in Part II, Item 8 of this report for additional information about our obligations under the Credit Agreement.

Results of Operations

The discussion below presents a summary of our results of operations for fiscal years 2020 and 2019. See Part II, Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations-Results of Operations" of our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, filed with the Securities and Exchange Commission on March 13, 2020, for a summary of our results of operations for the fiscal year ended December 31, 2018.

Year Ended December 31, 2020 Compared to 2019

Total revenues in 2020 were $17.8 million, compared to $48.8 million in 2019. The decrease in revenue was primarily due to the recognition of $20.1 million of revenue related to a one-time $22.0 million upfront milestone payment we received in 2019 upon execution of the Torii Agreement, with the remaining amount of $1.9 million recognized in 2020. Additionally, we recognized $13.9 million of RAPIVAB product sales under our HHS contract in 2019. We did not have any RAPIVAB product sales under our HHS contract in 2020.

Revenues in 2020 included $3.3 million of product revenue, the majority of which was from peramivir inventory sales to our commercial partners, $3.2 million of royalty revenue from Shionogi, Green Cross and SUL associated with sales of peramivir in Japan, Taiwan, Korea and the United States, $1.9 million of deferred revenue amortization related to the Torii Agreement and $9.2 million of reimbursement of collaborative expenses from NIAID/HHS and BARDA/HHS related to the development of galidesivir. Revenues in 2019 included $6.1 million of royalty revenue from SUL, Shionogi and Green Cross associated with sales of peramivir in the United States, Japan and Korea, $4.9 million of reimbursement of collaborative expenses from NIAID/HHS and BARDA/HHS under U.S. Government development contracts, $3.7 million of peramivir product revenue from inventory sales to our commercial partners, $13.9 million of RAPIVAB product revenue from inventory sales to BARDA/HHS under our Government procurement contract and $20.1 million related to the Torii Agreement upfront milestone payment.

Research and development expenses ("R&D expenses") increased to $123.0 million in 2020 from $107.1 million in 2019. The increase in 2020 R&D expenses, as compared to 2019, was primarily due to increased spending on our complement-mediated diseases and galidesivir programs, as well as an increase in other research, preclinical and development activities, partially offset by a reduction in spend on the ORLADEYO program, which launched commercially in the U.S. during December 2020.

The following table summarizes our R&D expenses for the periods indicated (amounts are in thousands):

	2020	2019	2018
R&D expenses by program:			
BCX7353	$ 44,329	$ 57,059	$ 53,993
BCX9930	35,265	26,640	10,189
FOP	2,583	6,167	8,871
Galidesivir	9,705	4,680	2,428
Peramivir	1,613	2,143	1,936
Other 2nd generation HAE compounds	–	6	357
Other research, preclinical and development costs	29,469	10,373	7,114
Total R&D expenses	$ 122,964	$ 107,068	$ 84,888

R&D expenses include all direct and indirect expenses and are allocated to specific programs at the point of development of a lead product candidate. Direct expenses are charged directly to the program to which they relate, and indirect expenses are allocated based upon internal direct labor hours dedicated to each respective program. Direct expenses consist of compensation for R&D personnel and costs of outside parties to conduct laboratory studies, develop manufacturing processes, manufacture the product candidates, conduct and manage clinical trials, as well as other costs related to our clinical and preclinical studies. Indirect R&D expenses consist of lab supplies and services, facility expenses, depreciation of development equipment and other overhead of our research and development efforts. R&D expenses vary according to the number of programs in clinical development and the stage of development of our clinical programs. Later stage clinical programs tend to cost more than earlier stage programs due to the longer length of time of the clinical trials and the higher number of patients enrolled in these clinical trials.

Selling, general and administrative ("SG&A") expenses increased to $67.9 million in 2020 compared to $37.1 million in 2019. The increase of $30.8 million was primarily due to increased spending on commercial activities, including building a sales organization, as well as increases in medical affairs activities to support the U.S. commercial launch of ORLADEYO in 2020.

Interest and other income was $9.4 million in 2020, compared to $1.9 million in 2019. The increase was primarily due to recognition of other income related to our arbitration proceedings.

Interest expense is related to the non-recourse PhaRMA Notes issued in March 2011, borrowings under our secured credit facility with MidCap, the Royalty Sale, and the $125.0 million Term A Loan under our new Credit Agreement with Athyrium. The Royalty Purchase Agreement requires us to recognize a liability (the "Royalty Financing Obligation") for the future sale of royalties under the agreement. This liability is amortized using the effective interest rate method, resulting in the recognition of non-cash interest expense over the estimated term of the Royalty Purchase Agreement. Interest expense increased to $14.5 million in 2020, compared to $11.9 million in 2019, primarily due to the amortization of interest associated with the royalty financing obligation, which resulted in $2.1 million of non-cash interest expense, and interest expense of $0.9 million associated with the Term A Loan borrowing under the Credit Agreement. In December 2020, we repaid the outstanding indebtedness under our secured credit facility with MidCap.

Loss on debt extinguishment is comprised of the write-off of unamortized deferred financing costs and original issue discount of $1.2 million and a prepayment fee of $0.8 million associated with the repayment of the outstanding indebtedness under our secured credit facility with MidCap.

We realized a currency exchange gain of $0.7 million in 2020, compared to a $0.9 million currency exchange gain in 2019 related to the exercise of a U.S. dollar/Japanese yen currency option under the Currency Hedge Agreement. A mark-to-market loss of $0.6 million was recognized in 2020, compared to a mark-to-market loss of $0.4 million recognized in 2019, related to the Currency Hedge Agreement, resulting from changes in the U.S. dollar/Japanese yen exchange rate during the year. The final tranche of the options under the Currency Hedge Agreement expired in November 2020. Additionally, we realized currency exchange losses in 2020 of $1.0 million as a result of expanded international operating activities.

Liquidity and Capital Resources

Our operations have principally been funded through public offerings and private placements of equity securities; cash from collaborative and other research and development agreements, including U.S. Government contracts for RAPIVAB and galidesivir; to a lesser extent, the PhaRMA Notes financing and our secured credit facility with MidCap, which terminated in December 2020 when we repaid the outstanding indebtedness under the facility with a portion of the net proceeds from the Term A Loan under the Credit Agreement; and more recently, the Credit Agreement and the Royalty Sale. To date, we have been awarded a BARDA/HHS RAPIVAB development contract totaling $234.8 million, which expired on June 30, 2014, a NIAID/HHS galidesivir development contract totaling $45.9 million, which is ongoing, a second NIAID/HHS galidesivir development contract totaling $43.9 million, which is ongoing, and a BARDA/HHS galidesivir development contract totaling $39.1 million, which is also ongoing. The total amount of NIAID/HHS and BARDA/HHS galidesivir funding obligated under awarded options is $52.2 million and $20.6 million, respectively. In addition to the above, we have previously received funding from other sources, including other collaborative and other research and development agreements, government grants, equipment lease financing, facility leases, research grants, and interest income on our investments.

On June 1, 2020, we issued 22,044,447 shares of common stock to the public at a purchase price of $4.50 per share and pre-funded warrants to purchase 3,511,111 shares of common stock at a purchase of $4.49 per pre-funded warrant, for total net proceeds to us of $108.1 million after deducting underwriting discounts and commissions and other offering expenses payable by us. The pre-funded warrants are exercisable in accordance with the terms in the warrant agreement and have an exercise price of $0.01 per share, which is subject to adjustment 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 of assets to our stockholders.

On December 7, 2020, we entered into the Royalty Purchase Agreement with RPI, pursuant to which we sold to RPI the right to receive certain royalty payments from us on account of ORLADEYO and BCX9930 for a purchase price of $125.0 million in cash. We also entered into the Credit Agreement with Athyrium on December 7, 2020, pursuant to which we received a $125.0 million Term A Loan. We used a portion of the net proceeds from the Term A Loan to repay the approximate $43.3 million of outstanding indebtedness, including accrued interest, under our secured credit facility with MidCap. We intend to use the remaining proceeds to support the launch of ORLADEYO in the U.S. and Europe and to advance the development of BCX9930 into clinical trials in multiple complement-mediated diseases, and for other general corporate purposes. The Credit Agreement also provides for two additional term loans, at our option, in the respective principal amounts of $25.0 million for the Term B Loan and $50.0 million for the Term C Loan. The Term B Loan and the Term C Loan may be drawn upon if, among other conditions, we reach 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. The maturity date of the Credit Agreement is December 7, 2025. See "Note 3-Royalty Monetizations-ORLADEYO Royalty Monetization" and "Note 4-Credit Agreement" in the Notes to Consolidated Financial Statements in Part II, Item 8 of this report for additional information about the Royalty Sale and the Credit Agreement, respectively.

As of December 31, 2020, we had net working capital of $218.1 million, an increase of approximately $146.1 million from $72.0 million at December 31, 2019. The increase in working capital was primarily due to cash provided from the Royalty Sale and the Credit Agreement in December 2020, as well as the June 2020 public offering of our common stock and pre-funded warrants to purchase our common stock, partially offset by our normal operating expenses associated with the development of our product candidates and expenses incurred in anticipation of our launch and commercialization of ORLADEYO. Our principal sources of liquidity at December 31, 2020 were approximately $272.1 million in cash and cash equivalents and approximately $28.2 million in investments considered available-for-sale.

We intend to contain costs and cash flow requirements by closely managing our third-party costs and headcount, leasing scientific equipment and facilities, contracting with other parties to conduct certain research and development projects, and using consultants. We expect to incur additional expenses, potentially resulting in significant losses, as we continue to pursue our research and development activities and commercialize ORLADEYO. We may incur additional expenses related to the filing, prosecution, maintenance, defense, and enforcement of patent and other intellectual property

claims and additional regulatory costs as our clinical programs advance through later stages of development. The objective of our investment policy is to ensure the safety and preservation of invested funds, as well as maintaining liquidity sufficient to meet cash flow requirements. We place our excess cash with high credit quality financial institutions, commercial companies, and government agencies in order to limit the amount of our credit exposure. We have not realized any significant losses on our investments.

We plan to finance our needs principally from the following:

- lease, royalty, or loan financing and future public or private equity or debt financing;
- our existing capital resources and interest earned on that capital;
- revenues from product sales;
- payments under existing, and executing new, contracts with the U.S. Government; and
- payments under current or future collaborative and licensing agreements with corporate partners.

As our commercialization activities and research and development programs continue to advance, our costs will increase. Our current and planned clinical trials, plus the related development, manufacturing, regulatory approval process requirements, and additional personnel resources and testing required for the continuing development of our product candidates and the commercialization of our products will consume significant capital resources and will increase our expenses. Our expenses, revenues and cash utilization rate could vary significantly depending on many factors, including our ability to raise additional capital, the development progress of our collaborative agreements for our product candidates, the amount and timing of funding we receive from existing U.S. Government contracts for galidesivir, the amount of funding or assistance, if any, we receive from new U.S. Government contracts or other new partnerships with third parties for the development and/or commercialization of our products and product candidates, the progress and results of our current and proposed clinical trials for our most advanced product candidates, the progress made in the manufacturing of our lead product candidates, commercialization and market acceptance of our products, and the overall progression of our other programs. The impact of the ongoing COVID-19 pandemic on one or more of the foregoing factors could negatively affect our expenses, revenues, and cash utilization rate.

Based on our expectations for revenue, operating expenses and our option to access an additional $75 million under the Credit Agreement, we believe our financial resources will be sufficient to fund our operations into 2023. However, 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 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 successful commercialization of our products and the future progression of our product candidates. We also may consider other plans to fund future operations, including: (1) securing or increasing U.S. Government funding of our programs, including obtaining procurement contracts; (2) out-licensing rights to certain of our products or product candidates, pursuant to which the we would receive cash milestones; (3) raising additional capital through 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, milestones and cash flow; (5) reducing spending on one or more research and development programs, including by discontinuing development; and/or (6) restructuring operations to change our overhead structure. We may issue securities, including common stock, preferred stock, depositary shares, purchase contracts, warrants, debt securities, and units, through private placement transactions or registered public offerings. Our future liquidity needs, and ability to address those needs, will largely be determined by the success of our products and product candidates; the timing, scope, and magnitude of our commercial expenses; and key development and regulatory events and our decisions in the future.

Our long-term capital requirements and the adequacy of our available funds will depend upon many factors, including:

- market acceptance of approved products and successful commercialization by either us or our partners;
- our ability to perform under our government contracts and to receive reimbursement and stockpiling procurement contracts;
- the magnitude of work under our government contracts;
- the progress and magnitude of our research, drug discovery and development programs;
- changes in existing collaborative relationships or government contracts;
- our ability to establish additional collaborative relationships with academic institutions, biotechnology or pharmaceutical companies and governmental agencies or other third parties;
- the extent to which our partners, including governmental agencies, will share in the costs associated with the development of our programs or run the development programs themselves;

- our ability to negotiate favorable development and marketing strategic alliances for certain products and product candidates;
- any decision to build or expand internal development and commercial capabilities;
- the scope and results of preclinical studies and clinical trials to identify and develop product candidates;
- our ability to engage sites and enroll subjects in our clinical trials;
- the scope of manufacturing of our products to support our commercial operations and of our product candidates to support our preclinical research and clinical trials;
- increases in personnel and related costs to support the development and commercialization of our products and product candidates;
- the scope of manufacturing of our drug substance and product candidates required for future NDA filings;
- competitive and technological advances;
- the time and costs involved in obtaining regulatory approvals;
- post-approval commitments for ORLADEYO, RAPIVAB, and other products that receive regulatory approval; and
- the costs involved in all aspects of intellectual property strategy and protection, including the costs involved in preparing, filing, prosecuting, maintaining, defending, and enforcing patent claims.

We expect that we will be required to raise additional capital to complete the development and commercialization of our current products and product candidates, and we may seek to raise capital in the future. Additional funding, whether through additional sales of equity or debt securities, collaborative or other arrangements with corporate partners or from other sources, including governmental agencies in general and existing government contracts specifically, may not be available when needed or on terms acceptable to us. The issuance of preferred or common stock or convertible securities, with terms and prices significantly more favorable than those of the currently outstanding common stock, could have the effect of diluting or adversely affecting the holdings or rights of our existing stockholders. In addition, collaborative arrangements may require us to transfer certain material rights to such corporate partners. Insufficient funds may require us to delay, scale back or eliminate certain of our research and development programs. Our future working capital requirements, including the need for additional working capital, will be largely determined by the advancement of our portfolio of product candidates and commercialization of ORLADEYO, as well as rate of reimbursement by U.S. Government agencies of our galidesivir expenses and any future decisions regarding the future of the RAPIVAB and galidesivir programs, including those relating to stockpiling procurement. More specifically, our working capital requirements will be dependent on the number, magnitude, scope and timing of our development programs; regulatory approval of our product candidates; obtaining funding from collaborative partners; the cost, timing and outcome of regulatory reviews, regulatory investigations, and changes in regulatory requirements; the costs of obtaining patent protection for our product candidates; the timing and terms of business development activities; the rate of technological advances relevant to our operations; the efficiency of manufacturing processes developed on our behalf by third parties; the timing, scope and magnitude of commercial spending, and the level of required administrative support for our daily operations.

The restrictive covenants contained in the Credit Agreement with Athyrium could cause us to be unable to pursue business opportunities that we or our stockholders may consider beneficial without the lender's permission or without repaying all obligations outstanding under the Credit Agreement. 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. A breach of any of these covenants could result in an event of default under the Credit Agreement. As of December 31, 2020, we were in compliance with the covenants under the Credit Agreement.

Financial Outlook for 2021

In the launch period for ORLADEYO, the Company is not providing specific revenue or operating guidance. Based on our expectations for revenue, operating expenses, and our option to access an additional $75 million from our existing credit facility, we believe our current cash runway takes us into 2023.

Off-Balance Sheet Arrangements

As of December 31, 2020, we are not involved in any unconsolidated entities or off–balance sheet arrangements.

Contractual Obligations

In the table below, we set forth our enforceable and legally binding obligations and future commitments and obligations related to all contracts that we are likely to continue regardless of the fact that they are cancelable as of December 31, 2020. Some of the amounts we include in this table are based on management's estimates and assumptions about these obligations, including their duration, the possibility of renewal, anticipated actions by third parties, and other factors. Because these estimates and assumptions are necessarily subjective, the obligations we will actually pay in future periods may vary from those reflected in the table.

	Payments Due by Period (In thousands)				
Contractual Obligations	**Total**	**Less Than 1 Year**	**1-3 Years**	**3-5 Years**	**More Than 5 Years**
Operating lease obligations	$ 11,165	$ 1,302	$ 1,378	$ 1,158	$ 7,327
Purchase obligations(1)	99,741	99,741	-	-	-
Contingent license obligations	1,050	150	300	300	300
Non-recourse notes payable(2)	53,331	53,331	-	-	-
Secured term loan	209,339	-	16,080	193,259	-
Total	$ 374,626	$ 154,524	$ 17,758	$ 194,717	$ 7,627

(1) Purchase obligations include commitments related to clinical development, manufacturing and research operations and other purchase commitments.

(2) The PhaRMA Notes had a final legal maturity date of December 1, 2020, at which time the outstanding principal, together with accrued and unpaid interest, was due in full. As of December 31, 2020, the PhaRMA Notes remain outstanding and in default and the Company will continue to record the liability and accrued interest owed until the Company is determined to no longer be the financial obligor.

The above amounts exclude future potential payments under our Royalty Purchase Agreement with RPI, pursuant to which we are required to make certain royalty payments to RPI based on net product sales of ORLADEYO and BCX9930, as well as on certain ORLADEYO sublicense revenue. Due to the nature of this arrangement, the future potential payments related to the attainment of additional regulatory approvals and sales-based milestones over a period of several years are inherently uncertain, and accordingly, no amounts have been presented for these future potential payments.

In addition to the above, we have committed to make potential future "sublicense" payments to third parties as part of in-licensing and development programs. Payments under these agreements generally become due and payable only upon achievement of certain developmental, regulatory and/or commercial milestones. Because the achievement of these milestones is neither probable nor reasonably estimable, such contingencies have not been recorded on our balance sheet.

Critical Accounting Policies

We have established various accounting policies that govern the application of U.S. GAAP, which were utilized in the preparation of our consolidated financial statements. Certain accounting policies involve significant judgments and assumptions by management that have a material impact on the carrying value of certain assets and liabilities. Management considers such accounting policies to be critical accounting policies. The judgments and assumptions used by management are based on historical experience and other factors, which are believed to be reasonable under the circumstances. Because of the nature of the judgments and assumptions made by management, actual results could differ from these judgments and estimates, which could have a material impact on the carrying values of assets and liabilities and the results of operations.

While our significant accounting policies are more fully described in "Note 1-Significant Accounting Policies and Concentrations of Risk" to the Consolidated Financial Statements in Part II, Item 8 of this report, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our reported financial results and affect the more significant judgments and estimates that we use in the preparation of our financial statements.

Inventory

Our inventories consist of peramivir finished goods and work in process, which are valued at the lower of cost or net realizable value using the first-in, first-out (i.e., FIFO) method. Cost includes materials, labor, overhead, shipping and

handling costs. Our inventories are subject to expiration dating. We regularly evaluate the carrying value of our inventories and provide valuation reserves for any estimated obsolete, short-dated or unmarketable inventories. In addition, we may experience spoilage of our raw materials and supplies. Our determination that a valuation reserve might be required, in addition to the quantification of such reserve, requires us to utilize significant judgment. In connection with the FDA approval of RAPIVAB and other regulatory approvals, we began capitalizing costs associated with the production of peramivir inventories.

Accrued Expenses

We enter into contractual agreements with third-party vendors who provide research and development, manufacturing, and other services in the ordinary course of business. Some of these contracts are subject to milestone-based invoicing and services are completed over an extended period of time. We record liabilities under these contractual commitments when an obligation has been incurred. This accrual process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed and estimating the level of service performed and the associated cost when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date based on the facts and circumstances known to us. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued expenses include:

- fees paid to CROs in connection with preclinical and toxicology studies and clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- fees paid to contract manufacturers in connection with the production of our raw materials, drug substance, drug products, and product candidates; and
- professional fees.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we will adjust the accrual accordingly. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of these costs, our actual expenses could differ from our estimates.

Revenue Recognition

We adopted the provisions of ASC 606 as of January 1, 2018 using the modified retrospective method as applied to contracts that were not completed as of that date. As a result, financial information for reporting periods beginning after January 1, 2018 are presented under ASC 606, while comparative financial information has not been adjusted and continues to be reported in accordance with our historical accounting policy for revenue recognition prior to the adoption of ASC 606.

Collaborative and Other Research and Development Arrangements and Royalties

We recognize revenue when we satisfy a performance obligation by transferring promised goods or services to a customer. Revenue is measured at the transaction price that is based on the amount of consideration that we expect to receive in exchange for transferring the promised goods or services to the customer. The transaction price includes estimates of variable consideration to the extent it is probable that a significant reversal of revenue recognized will not occur.

We have collaboration and license agreements with a number of third parties as well as research and development agreements with certain government entities. Our primary sources of revenue are license, service, royalty and product sale revenues from these collaborative and other research and development arrangements.

Revenue from license fees, royalty payments, milestone payments, and research and development fees are recognized as revenue when the earnings process is complete and we have no further continuing performance obligations or we have completed the performance obligations under the terms of the agreement.

Arrangements that involve the delivery of more than one performance obligation are initially evaluated as to whether the intellectual property licenses granted by us represent distinct performance obligations. If they are determined to be distinct, the value of the intellectual property licenses would be recognized up-front while the research and development service fees

would be recognized as the performance obligations are satisfied. Variable consideration is assessed at each reporting period as to whether it is not subject to significant future reversal and, therefore, should be included in the transaction price at the inception of the contract. If a contract includes a fixed or minimum amount of research and development support, this also would be included in the transaction price. Changes to collaborations, such as the extensions of the research term or increasing the number of targets or technology covered under an existing agreement, are assessed for whether they represent a modification or should be accounted for as a new contract. For contracts with multiple performance obligations, revenue is allocated to each performance obligation based on its relative standalone selling price. Standalone selling prices are based on observable prices at which we separately sell the products or services. If a standalone selling price is not directly observable, then we estimate the standalone selling price considering market conditions and entity-specific factors. Analyzing the arrangement to identify performance obligations requires the use of judgment, and each may be an obligation to deliver services, a right or license to use an asset, or another performance obligation.

Milestone payments are recognized as licensing revenue upon the achievement of specified milestones if (i) the milestone is substantive in nature and the achievement of the milestone was not probable at the inception of the agreement; and (ii) we have a right to payment. Any milestone payments received prior to satisfying these revenue recognition criteria are recorded as deferred revenue.

Reimbursements received for direct out-of-pocket expenses related to research and development costs are recorded as revenue in the Consolidated Statements of Comprehensive Loss rather than as a reduction in expenses. Under our contracts with BARDA/HHS and NIAID/HHS, revenue is recognized as reimbursable direct and indirect costs are incurred.

Under certain of our license agreements, we receive royalty payments based upon our licensees' net sales of covered products. Royalties are recognized at the later of when (i) the subsequent sale or usage occurs, or (ii) the performance obligation to which some or all of the sales-based or usage-based royalty has been satisfied.

Product Sales

Our principal sources of product sales are sales of peramivir to our licensing partners and sales of RAPIVAB to HHS under our procurement contract. In December 2020, we launched ORLADEYO and began recording product revenue. We recognize revenue for sales when the customer obtains control of the product, which generally occurs upon delivery.

Contract Balances

The timing of revenue recognition, billings and cash collections results in billed accounts receivable, unbilled receivables (contract assets) and deferred revenue and billings in excess of revenue recognized (contract liabilities) on the Consolidated Balance Sheets.

Contract assets. Our long-term contracts are billed as work progresses in accordance with the contract terms and conditions, either at periodic intervals or upon achievement of certain milestones. Often this results in billing occurring subsequent to revenue recognition, resulting in contract assets. Contract assets are generally classified as current assets in the Consolidated Balance Sheets.

Contract liabilities. We often receive cash payments from customers in advance of our performance, resulting in contract liabilities. These contract liabilities are classified as either current or long-term in the Consolidated Balance Sheets based on the timing of when we expect to recognize the revenue.

Contract Costs

We may incur direct and indirect costs associated with obtaining a contract. Incremental contract costs that we expect to recover are capitalized and amortized over the expected term of the contract. Non-incremental contract costs and costs that we expect to recover are expensed as incurred.

Research and Development Expenses

Our research and development costs are charged to expense when incurred. Advance payments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are recognized as expense when the related goods are delivered or the related services are performed. Research and development expenses include, among other items, personnel costs, including salaries and benefits, manufacturing costs, clinical, regulatory, and toxicology services performed by CROs, materials and supplies, and overhead allocations consisting of

various administrative and facilities related costs. Most of our manufacturing and clinical and preclinical studies are performed by third-party CROs. Costs for studies performed by CROs are accrued by us over the service periods specified in the contracts and estimates are adjusted, if required, based upon our on-going review of the level of services actually performed.

Additionally, we have license agreements with third parties, such as AECOM, IRL, and UAB, which require fees related to sublicense agreements or maintenance fees. We expense sublicense payments as incurred unless they are related to revenues that have been deferred, in which case the expenses are deferred and recognized over the related revenue recognition period. We expense maintenance payments as incurred.

Deferred collaboration expenses represent sub-license payments paid to our academic partners upon receipt of consideration from various commercial partners, and other consideration to our academic partners for modification to existing license agreements. These deferred expenses would not have been incurred without receipt of such payments or modifications from our commercial partners and are being expensed in proportion to the related revenue being recognized. We believe that this accounting treatment appropriately matches expenses with the associated revenue.

We group our R&D expenses into two major categories: direct external expenses and indirect expenses. Direct expenses consist of compensation for R&D personnel and costs of outside parties to conduct laboratory studies, develop manufacturing processes and manufacture the product candidate, conduct and manage clinical trials, as well as other costs related to our clinical and preclinical studies. These costs are accumulated and tracked by active program. Indirect expenses consist of lab supplies and services, facility expenses, depreciation of development equipment and other overhead of our research and development efforts. These costs apply to work on non-active product candidates and our discovery research efforts.

Stock-Based Compensation

All share-based payments, including grants of stock option awards and restricted stock unit awards, are recognized in our Consolidated Statements of Comprehensive Loss based on their fair values. Stock-based compensation cost is estimated at the grant date based on the fair value of the award and is recognized as expense on a straight-line basis over the requisite service period of the award. Determining the appropriate fair value model and the related assumptions for the model requires judgment, including estimating the life of an award, the stock price volatility, and the expected term. We utilize the Black-Scholes option-pricing model to value our awards and recognize compensation expense on a straight-line basis over the vesting periods. The estimation of share-based payment awards that will ultimately vest requires judgment, and to the extent actual results or updated estimates differ from our current estimates, such amounts will be recorded as a cumulative adjustment in the period estimates are revised. In addition, we have outstanding performance-based stock options for which no compensation expense is recognized until “performance” has occurred. Significant management judgment is also required in determining estimates of future stock price volatility and forfeitures to be used in the valuation of the options. Actual results, and future changes in estimates, may differ substantially from our current estimates.

Interest Expense and Royalty Financing Obligation

The royalty financing obligation is eligible to be repaid based on royalties from net sales of ORLADEYO. Interest expense is accrued using the effective interest rate method over the estimated period the related liability will be paid. This requires us to estimate the total amount of future royalty payments to be generated from product sales over the life of the agreement. We impute interest on the carrying value of the royalty financing obligation and record interest expense using an imputed effective interest rate. We will reassess the expected royalty payments each reporting period and account for any changes through an adjustment to the effective interest rate on a prospective basis. The assumptions used in determining the expected repayment term of the debt and amortization period of the issuance costs requires that we make estimates that could impact the carrying value of the liability, as well as the period over which associated issuance costs will be amortized. A significant increase or decrease in forecasted net sales could materially impact the liability balance, interest expense and the time period for repayment.

Foreign Currency Hedge

In connection with our issuance of the PhaRMA Notes, we entered into a foreign Currency Hedge Agreement to hedge certain risks associated with changes in the value of the Japanese yen relative to the U.S. dollar. Under the Currency Hedge Agreement, we have the right to purchase dollars and sell yen at a rate of 100 yen per dollar. The final tranche of the options under the Currency Hedge Agreement expired in November of 2020.

The Currency Hedge Agreement did not qualify for hedge accounting treatment and therefore mark-to-market adjustments were recognized in our Consolidated Statements of Comprehensive Loss. Mark-to-market adjustments were determined by quoted prices in markets that are not actively traded and for which significant inputs are observable directly or indirectly, representing Level 2 in the fair value hierarchy as defined by generally accepted accounting principles ("U.S. GAAP").

Tax

We account for uncertain tax positions in accordance with U.S. GAAP. Significant management judgment is required in determining our provision for income taxes, deferred tax assets and liabilities and any valuation allowance recorded against net deferred tax assets. We have recorded a valuation allowance against all potential tax assets, due to uncertainties in our ability to utilize deferred tax assets, primarily consisting of certain net operating losses carried forward, before they expire. The valuation allowance is based on estimates of taxable income in each of the jurisdictions in which we operate and the period over which our deferred tax assets will be recoverable.

Impact of Inflation

We do not believe that our operating results have been materially impacted by inflation during the past three years. However, we cannot be assured that our operating results will not be adversely affected by inflation in the future. We will continually seek to mitigate the adverse effects of inflation on the services that we use through improved operating efficiencies and cost containment initiatives.

Recent Accounting Pronouncements

"Note 1-Significant Accounting Policies and Concentrations of Risk" to the Consolidated Financial Statements included in Part II, Item 8 of this report discusses accounting pronouncements recently issued or proposed but not yet required to be adopted.

ITEM 7A. *QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.*

Interest Rate Risk

We are subject to interest rate risk on our investment portfolio and borrowings under our Credit Agreement. The Term A Loan under the Credit Agreement bears interest each quarter at a rate equal to the three-month LIBOR rate, which is capped to be no less than 1.75% and no more than 3.50% ("LIBOR"), plus 8.25% or, for each quarterly interest period in which a PIK Interest Payment is made, the LIBOR plus 10.25%. Accordingly, increases in interest rates could increase the associated interest payments that we are required to make on the term loans. As of December 31, 2020, interest was accrued at 12.2% on the $125.0 million Term A Loan under the Credit Agreement.

We invest in marketable securities in accordance with our investment policy. The primary objectives of our investment policy are to preserve capital, maintain proper liquidity to meet operating needs and maximize yields. Our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure to any single issue, issuer or type of investment. We place our excess cash with high credit quality financial institutions, commercial companies, and government agencies in order to limit the amount of credit exposure. Some of the securities we invest in may have market risk. This means that a change in prevailing interest rates may cause the principal amount of the investment to fluctuate.

Our investment exposure to market risk for changes in interest rates relates to the increase or decrease in the amount of interest income we can earn on our portfolio, changes in the market value due to changes in interest rates and other market factors as well as the increase or decrease in any realized gains and losses. Our investment portfolio includes only marketable securities and instruments with active secondary or resale markets to help ensure portfolio liquidity. A hypothetical 100 basis point increase or decrease in interest rates along the entire interest rate yield curve would not significantly affect the fair value of our interest sensitive financial instruments, including our borrowings, but may affect our future earnings and cash flows. We generally have the ability to hold our fixed-income investments to maturity and therefore do not expect that our operating results, financial position or cash flows will be materially impacted due to a sudden change in interest rates. However, our future investment income may fall short of expectations due to changes in interest rates, or we may suffer losses in principal if forced to sell securities which have declined in market value due to changes in interest rates or other factors, such as changes in credit risk related to the securities' issuers. To minimize this risk, we schedule our investments to have maturities that coincide with our expected cash flow needs, thus avoiding the need to redeem an investment prior to its maturity date. Accordingly, we do not believe that we have material exposure to interest rate risk arising from our

investments. Generally, our investments are not collateralized. We have not realized any significant losses from our investments.

We do not use interest rate derivative instruments to manage exposure to interest rate changes. We ensure the safety and preservation of invested principal funds by limiting default risk, market risk and reinvestment risk. We reduce default risk by investing in investment grade securities.

Foreign Currency Risk

The majority of our transactions and the greatest magnitude of these transactions occur in U.S. dollars and we do not have significant operating subsidiaries or significant investments in foreign countries as of December 31, 2020. Therefore, we are not subject to significant foreign currency exchange risk in our normal operations.

In connection with the issuance by Royalty Sub of the PhaRMA Notes, we had entered into a Currency Hedge Agreement to hedge certain risks associated with changes in the value of the Japanese yen relative to the U.S. dollar. The final tranche of the options under the Currency Hedge Agreement expired in November 2020.

ITEM 8. ***FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA***

BIOCRYST PHARMACEUTICALS, INC.

CONSOLIDATED BALANCE SHEETS
(In thousands, except per share amounts)

	December 31,	
	2020	**2019**
ASSETS		
Cash and cash equivalents	$ 272,127	$ 114,172
Restricted cash	2,221	1,551
Investments	28,239	22,054
Receivables	8,646	22,146
Inventory	7,039	-
Prepaid expenses and other current assets	5,528	4,422
Total current assets	323,800	164,345
Property and equipment, net	7,113	7,347
Other assets	3,802	3,590
Total assets	$ 334,715	$ 175,282
LIABILITIES AND STOCKHOLDERS' EQUITY		
Accounts payable	$ 18,713	$ 13,988
Accrued expenses	33,942	21,365
Interest payable	21,670	14,904
Deferred collaboration revenue	150	2,120
Lease financing obligation	1,179	1,377
Senior credit facility	-	9,020
Non-recourse notes payable	30,000	29,561
Total current liabilities	105,654	92,335
Royalty financing obligation	124,717	-
Lease financing obligation	3,871	3,406
Senior credit facility	-	41,289
Secured term loan	119,735	-
Stockholders' equity:		
Preferred stock, $0.01 par value; shares authorized — 5,000; no shares outstanding	-	-
Common stock, $0.01 par value; shares authorized — 450,000; shares issued and outstanding — 176,883 at December 31, 2020 and 154,082 at December 31, 2019	1,769	1,541
Additional paid-in capital	1,002,408	877,300
Accumulated other comprehensive income (loss)	3	39
Accumulated deficit	(1,023,442)	(840,628)
Total stockholders' (deficit) equity	(19,262)	38,252
Total liabilities and stockholders' equity	$ 334,715	$ 175,282

See accompanying notes to consolidated financial statements.

BIOCRYST PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(In thousands, except per share amounts)

	Year Ended December 31,		
	2020	**2019**	**2018**
Revenues			
Product sales, net	$ 3,301	$ 17,533	$ –
Royalty revenue	3,381	6,303	6,101
Collaborative and other research and development	11,130	24,999	14,552
Total revenues	17,812	48,835	20,653
Expenses			
Cost of products sold	1,550	3,726	–
Research and development	122,964	107,068	84,888
Selling, general and administrative	67,929	37,121	29,514
Royalty	126	375	471
Total operating expenses	192,569	148,290	114,873
Loss from operations	(174,757)	(99,455)	(94,220)
Interest and other income	9,420	1,933	2,252
Interest expense	(14,501)	(11,892)	(9,176)
Loss on extinguishment of debt	(2,011)	-	-
Gain (loss) on foreign currency	(965)	517	(108)
Net loss	$ (182,814)	$ (108,897)	$ (101,252)
Unrealized gain (loss) on available for sale investments	$ (36)	$ 336	$ (54)
Net comprehensive loss	$ (182,850)	$ (108,561)	$ (101,306)
Basic and diluted net loss per common share	**$ (1.09)**	**$ (0.94)**	**$ (0.98)**
Weighted average shares outstanding	**167,267**	**115,600**	**103,185**

See accompanying notes to consolidated financial statements.

BIOCRYST PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands, except per share amounts)

	Year Ended December 31,		
	2020	**2019**	**2018**
Operating activities:			
Net loss	$ (182,814)	$ (108,897)	$ (101,252)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	748	724	770
Loss (gain) on disposal of property and equipment	–	–	7
Stock-based compensation expense	14,794	17,719	9,396
Amortization of debt issuance costs	2,428	1,278	885
Amortization of premium/discount on investments	121	117	110
Change in fair value of foreign currency derivative	632	347	1,049
Changes in operating assets and liabilities:			
Receivables	13,903	(17,853)	1,824
Inventory	(7,039)	1,649	(1,649)
Prepaid expenses and other assets	(2,140)	(1,364)	(866)
Accounts payable and accrued expenses	17,355	11,741	4,487
Interest payable	6,766	3,056	(247)
Deferred revenue	(1,970)	1,899	(7,079)
Net cash used in operating activities:	**(137,216)**	**(89,584)**	**(92,565)**
Investing activities:			
Acquisition of property and equipment	(514)	(343)	(366)
Purchases of investments	(49,818)	(3,018)	(62,614)
Sales and maturities of investments	43,475	81,295	67,748
Realized gain on investments	1	-	-
Net cash provided by (used in) investing activities:	**(6,856)**	**77,934**	**4,768**
Financing activities:			
Sale of common stock, net	93,279	58,500	53,400
Sale of pre-funded warrants	14,817	19,882	–
Net proceeds from common stock issued under stock-based compensation plans	2,446	1,239	2,852
Proceeds from senior credit facility	-	19,477	10,353
Payment of senior credit facility	(52,420)	–	(4,025)
Net proceeds from secured term loan	119,867	–	–
Net proceeds from royalty financing obligation	124,708	–	–
(Decrease) increase in lease financing obligation	–	–	(76)
Net cash provided by financing activities:	**302,697**	**99,098**	**62,504**
Increase (decrease) in cash, cash equivalents and restricted cash	158,625	87,448	(25,293)
Cash, cash equivalents and restricted cash at beginning of year	115,723	28,275	53,568
Cash, cash equivalents and restricted cash at end of year	**$ 274,348**	**$ 115,723**	**$ 28,275**

See accompanying notes to consolidated financial statements.

BIOCRYST PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands, except per share amounts)

	Common Stock	Additional Paid-In Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2017	**$ 984**	**$ 714,869**	**$ (243)**	**$ (631,843)**	**$ 83,767**
Impact to retained earnings from adoption of ASC 606	–	–	–	1,126	1,126
Net loss	–	–	–	(101,252)	(101,252)
Other comprehensive (loss)	–	–	(54)	–	(54)
Exercise of stock options, 1,106 shares, net	11	2,490	–	–	2,501
Employee stock purchase plan sales, 92 shares, net	1	350	–	–	351
Issuance of common stock, 10,455 shares, net	105	53,295	–	–	53,400
Stock-based compensation expense	-	9,396	–	–	9,396
Balance at December 31, 2018	**$ 1,101**	**$ 780,400**	**$ (297)**	**$ (731,969)**	**$ 49,235**
Impact to retained earnings from adoption of ASC 842	–	–	–	238	238
Net loss	–	–	–	(108,897)	(108,897)
Other comprehensive income	–	–	336	–	336
Exercise of stock options, 283 shares, net	3	832	–	–	835
Employee stock purchase plan sales, 115 shares, net	1	403	–	–	404
Issuance of common stock, 43,621 shares, net	436	58,064	–	–	58,500
Issuance of pre-funded warrants, 11,765 warrants	–	19,882	–	–	19,882
Stock-based compensation expense	–	17,719	–	–	17,719
Balance at December 31, 2019	**$ 1,541**	**$ 877,300**	**$ 39**	**$ (840,628)**	**$ 38,252**
Net loss	–	–	–	(182,814)	(182,814)
Other comprehensive (loss)	–	–	(36)	–	(36)
Exercise of stock options, 510 shares, net	5	1,809	–	–	1,814
Employee stock purchase plan sales, 246 shares, net	3	629	–	–	632
Issuance of common stock, 22,044 shares, net	220	93,059	–	–	93,279
Issuance of pre-funded warrants, 3,511 warrants	–	14,817	–	–	14,817
Stock-based compensation expense	–	14,794	–	–	14,794
Balance at December 31, 2020	**$ 1,769**	**$1,002,408**	**$ 3**	**$ (1,023,442)**	**$ (19,262)**

See accompanying notes to consolidated financial statements.

Note 1 — Significant Accounting Policies and Concentrations of Risk

The Company

BioCryst Pharmaceuticals, Inc. (the "Company") is a commercial-stage biotechnology company that discovers novel, oral, small-molecule medicines. The Company focuses on the treatment of rare diseases in which significant unmet medical needs exist and an enzyme plays the key role in the biological pathway of the disease. The Company was founded in 1986 and incorporated in Delaware in 1991, and its headquarters is located in Durham, North Carolina. The Company integrates 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. The Company has incurred losses and negative cash flows from operations since inception.

Based on the Company's expectations for revenue, operating expenses, and its option to access an additional $75 million from its existing credit facility, the Company believes its financial resources available at December 31, 2020 will be sufficient to fund its operations into 2023. The Company has sustained operating losses for the majority of its corporate history and expects that its 2021 expenses will exceed its 2021 revenues. The Company expects to continue to incur operating losses and negative cash flows until revenues reach a level sufficient to support ongoing operations. The Company's liquidity needs will be largely determined by the success of operations in regard to the successful commercialization of its products and the progression of its product candidates in the future. The Company also may consider other plans to fund future operations, including: (1) securing or increasing U.S. Government funding of its programs, including obtaining procurement contracts; (2) out-licensing rights to certain of its products or product candidates, pursuant to which the Company would receive cash milestones; (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, milestones and cash flow; (5) reducing spending on one or more research and development programs, including by discontinuing development; and/or (6) restructuring operations to change its overhead structure. The Company may issue securities, including common stock, preferred stock, depositary shares, purchase contracts, warrants, debt securities and units, through private placement transactions or registered public offerings in the future. The Company's future liquidity needs, and ability to address those needs, will largely be determined by the success of its products and product candidates, timing, scope and magnitude of its commercial expenses and key development and regulatory events and its decisions in the future.

Basis of Presentation

The consolidated financial statements include the accounts of the Company and its subsidiaries. All intercompany transactions and balances among the consolidated entities have been eliminated from the consolidated financial statements.

The Company's consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP"). Such consolidated financial statements reflect all adjustments that are, in management's opinion, necessary to present fairly, in all material respects, the Company's consolidated financial position, results of operations, and cash flows. There were no adjustments other than normal recurring adjustments.

Cash and Cash Equivalents

The Company generally considers cash equivalents to be all cash held in commercial checking accounts, certificates of deposit, money market accounts or investments in debt instruments with maturities of three months or less at the time of purchase. The carrying value of cash and cash equivalents approximates fair value due to the short-term nature of these items.

Restricted Cash

Restricted cash as of December 31, 2020 and 2019 reflects $796 and $134, respectively, in royalty revenue paid by Shionogi & Co., Ltd. ("Shionogi") designated for interest on the PhaRMA Notes (defined in Note 3) and $1,425 and $1,417,

respectively, the Company is required to maintain as collateral for a letter of credit associated with the lease execution and build-out of its new Birmingham research facilities.

Investments

The Company invests in high credit quality investments in accordance with its investment policy, which is designed to minimize the possibility of loss. The objective of the Company's investment policy is to ensure the safety and preservation of invested funds, as well as maintaining liquidity sufficient to meet cash flow requirements. The Company places its excess cash with high credit quality financial institutions, commercial companies, and government agencies in order to limit the amount of its credit exposure. In accordance with its policy, the Company is able to invest in marketable debt securities that may consist of U.S. Government and government agency securities, money market and mutual fund investments, municipal and corporate notes and bonds, commercial paper and asset or mortgage-backed securities, among others. The Company's investment policy requires it to purchase high-quality marketable securities with a maximum individual maturity of three years and requires an average portfolio maturity of no more than 18 months. Some of the securities the Company invests in may have market risk. This means that a change in prevailing interest rates may cause the principal amount of the investment to fluctuate. To minimize this risk, the Company schedules its investments with maturities that coincide with expected cash flow needs, thus avoiding the need to redeem an investment prior to its maturity date. Accordingly, the Company does not believe it has a material exposure to interest rate risk arising from its investments. Generally, the Company's investments are not collateralized. The Company has not realized any significant losses from its investments.

The Company classifies all of its investments as available-for-sale. Unrealized gains and losses on investments are recognized in comprehensive loss, unless an unrealized loss is considered to be other than temporary, in which case the unrealized loss is charged to operations. The Company periodically reviews its investments for other than temporary declines in fair value below cost basis and whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. The Company believes the individual unrealized losses represent temporary declines primarily resulting from interest rate changes. Realized gains and losses are reflected in interest and other income in the Consolidated Statements of Comprehensive Loss and are determined using the specific identification method with transactions recorded on a settlement date basis. Investments with original maturities at date of purchase beyond three months and which mature at or less than 12 months from the balance sheet date are classified as current. Investments with a maturity beyond 12 months from the balance sheet date are classified as long-term. At December 31, 2020, the Company believes that the cost of its investments is recoverable in all material respects.

The following tables summarize the fair value of the Company's investments by type. The estimated fair values of the Company's fixed income investments are classified as Level 2 in the fair value hierarchy as defined in U.S. GAAP. These valuations are based on observable direct and indirect inputs, primarily quoted prices of similar, but not identical, instruments in active markets or quoted prices for identical or similar instruments in markets that are not active. These fair values are obtained from independent pricing services which utilize Level 2 inputs.

	December 31, 2020				
	Amortized Cost	Accrued Interest	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Obligations of U.S. Government and its agencies	$ 24,986	$ 14	$ 3	$ (3)	$ 25,000
Certificates of deposit	3,225	11	3	–	3,239
Total Investments	$ 28,211	$ 25	$ 6	$ (3)	$ 28,239

	December 31, 2019				
	Amortized Cost	Accrued Interest	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Obligations of U.S. Government and its agencies	$ 10,488	$ 50	$ 23	$ –	$ 10,561
Corporate debt securities	9,742	59	10	(1)	9,810
Certificates of deposit	1,669	7	7	–	1,683
Total Investments	$ 21,899	$ 116	$ 40	$ (1)	$ 22,054

The Company's investments at December 31, 2020 and 2019 have maturities of one year or less.

Receivables from Collaborations

Receivables from collaborations are recorded for amounts due to the Company related to reimbursable research and development costs from the U.S. Department of Health and Human Services, royalty receivables from Shionogi, Green Cross Corporation ("Green Cross"), Mundipharma International Holdings Limited ("Mundipharma") and Seqirus UK Limited ("SUL"), and product sales to SUL. These receivables are evaluated to determine if any reserve or allowance should be established at each reporting date based on historical collection experience or specific circumstances and no amounts were recorded at December 31, 2020 and 2019.

At December 31, 2020 and December 31, 2019, the Company had the following receivables:

	December 31, 2020		
	Billed	**Unbilled**	**Total**
U.S. Department of Health and Human Services	$ –	$ 5,402	$ 5,402
Shionogi & Co. Ltd.	2,037	4	2,041
Green Cross Corporation	740	21	761
Mundipharma International Holdings Limited	39	–	39
Total receivables	$ 2,816	$ 5,427	$ 8,243

	December 31, 2019		
	Billed	**Unbilled**	**Total**
U.S. Department of Health and Human Services	$ 1,353	$ 15,023	$ 16,376
Shionogi & Co. Ltd.	1,336	4	1,340
Green Cross Corporation	2,924	8	2,932
Mundipharma International Holdings Limited	56	-	56
Seqirus UK Limited	1,091	351	1,442
Total receivables	$ 6,760	$ 15,386	$ 22,146

Monthly invoices are submitted to the U.S. Department of Health and Human Services related to reimbursable research and development costs. The Company is also entitled to monthly reimbursement of indirect costs based on rates stipulated in the underlying contract. The Company's calculations of its indirect cost rates are subject to audit by the U.S. Government.

Receivables from Product Sales

Receivables from product sales are recorded for amounts due to the Company related to sales of RAPIVAB and ORLADEYO. At December 31, 2020, receivables related to sales of RAPIVAB and ORLADEYO were $254 and $149, respectively. There were no receivables from product sales as of December 31, 2019. Receivables from product sales are evaluated to determine if any reserve or allowance should be recorded based on consideration of the current economic environment, expectations of future economic conditions and the Company's own historical collection experience. No reserve or allowance amounts were recorded at December 31, 2020.

Inventory

At December 31, 2020 and 2019, the Company's inventory related to peramivir which is being manufactured for the Company's partners and the U.S. Government. Inventory as of December 31, 2020, consisted of raw materials of $206, work-in-process of $2,555 and finished goods of $4,548. As of December 31, 2019, the Company inventory consisted of peramivir finished goods of $276. Inventory is stated at the lower of cost and net realizable value, determined under the first-in, first-out ("FIFO") method, or market. As of December 31, 2020 and 2019, the Company had inventory reserves of $270 and $276, respectively, for estimated unrecoverable capitalized inventory costs.

The Company expenses costs related to the production of inventories as research and development expenses in the period incurred until such time it is believed that future economic benefit is expected to be recognized, which generally is reliant upon receipt of regulatory approval. Upon regulatory approval, the Company capitalizes subsequent costs related to the production of inventories.

Property and Equipment

Property and equipment are recorded at cost. Depreciation is computed using the straight-line method over the estimated useful lives of the assets. Computer equipment is depreciated over a life of three years. Laboratory equipment, office equipment, and software are depreciated over a life of five years. Furniture and fixtures are depreciated over a life of seven years. Leasehold improvements are amortized over their estimated useful lives or the expected lease term, whichever is less.

In accordance with U.S. GAAP, the Company periodically reviews its property and equipment for impairment when events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Determination of recoverability is based on an estimate of undiscounted future cash flows resulting from the use of the asset and its eventual disposition. In the event that such cash flows are not expected to be sufficient to recover the carrying amount of the assets, the assets are written down to their estimated fair values. Property and equipment to be disposed of are reported at the lower of carrying amount or fair value less cost to sell.

Patents and Licenses

The Company seeks patent protection on all internally developed processes and products. All patent related costs are expensed to selling, general and administrative expenses when incurred as recoverability of such expenditures is uncertain.

Accrued Expenses

The Company generally enters into contractual agreements with third-party vendors who provide research and development, manufacturing, distribution, and other services in the ordinary course of business. Some of these contracts are subject to milestone-based invoicing and services are completed over an extended period of time. The Company records liabilities under these contractual commitments when it determines an obligation has been incurred, regardless of the timing of the invoice. This process involves reviewing open contracts and purchase orders, communicating with applicable Company personnel to identify services that have been performed on its behalf and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of actual cost. The majority of service providers invoice the Company monthly in arrears for services performed. The Company makes estimates of accrued expenses as of each balance sheet date in its financial statements based on the facts and circumstances. The Company periodically confirms the accuracy of its estimates with the service providers and makes adjustments if necessary. Examples of estimated accrued expenses include:

- fees paid to Clinical Research Organizations ("CROs") in connection with preclinical and toxicology studies and clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- fees paid to contract manufacturers in connection with the production of the Company's raw materials, drug substance, drug products, and product candidates; and
- professional fees.

The Company bases its expenses related to clinical trials on its estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical trials on the Company's behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company will adjust the accrual accordingly. As of December 31, 2020 and December 31, 2019, the carrying value of accrued expenses approximates their fair value due to their short-term settlement.

Accrued expenses were comprised of the following:

	December 31,	
	2020	2019
Compensation and benefits	$ 11,030	$ 6,190
Development costs	15,150	11,302
Inventory	2,453	29
Professional fees	333	326
Duties and taxes	80	67
Other	4,896	3,451
Total accrued expenses	$ 33,942	$ 21,365

Income Taxes

The liability method is used in the Company's accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse.

Accumulated Other Comprehensive Loss

Accumulated other comprehensive loss is comprised of unrealized gains and losses on available-for-sale investments and is disclosed as a separate component of stockholders' equity. Amounts reclassified from accumulated other comprehensive loss are recorded as interest and other income on the Consolidated Statements of Comprehensive Loss. For the year ended December 31, 2020, realized gains of $1 were reclassified out of accumulated other comprehensive loss. No reclassifications out of accumulated other comprehensive loss were recorded in 2019.

Revenue Recognition

Collaborative and Other Research and Development Arrangements and Royalties

The Company recognizes revenue when it satisfies a performance obligation by transferring promised goods or services to a customer. Revenue is measured at the transaction price that is based on the amount of consideration that the Company expects to receive in exchange for transferring the promised goods or services to the customer. The transaction price includes estimates of variable consideration to the extent it is probable that a significant reversal of revenue recognized will not occur.

The Company has collaboration and license agreements with a number of third parties as well as research and development agreements with certain government entities. The Company's primary sources of revenue are license, service, royalty and product sale revenues from these collaborative and other research and development arrangements.

Revenue from license fees, royalty payments, milestone payments, and research and development fees are recognized as revenue when the earnings process is complete and the Company has no further continuing performance obligations or the Company has completed the performance obligations under the terms of the agreement.

Arrangements that involve the delivery of more than one performance obligation are initially evaluated as to whether the intellectual property licenses granted by the Company represent distinct performance obligations. If they are determined to be distinct, the value of the intellectual property licenses would be recognized up-front while the research and development service fees would be recognized as the performance obligations are satisfied. For performance obligations based on services performed, the Company measures progress using an input method based on the effort we expend or costs we incur toward the satisfaction of performance obligation in relation to the total estimated effort of costs. Variable consideration is assessed at each reporting period as to whether it is not subject to significant future reversal and, therefore, should be included in the transaction price at the inception of the contract. If a contract includes a fixed or minimum amount of research and development support, this also would be included in the transaction price. Changes to collaborations, such as the extensions of the research term or increasing the number of targets or technology covered under an existing agreement, are assessed for whether they represent a modification or should be accounted for as a new contract. For contracts with multiple performance obligations, revenue is allocated to each performance obligation based on its relative standalone selling price. Standalone selling prices are based on observable prices at which the Company separately sells the products or services. If a standalone selling price is not directly observable, then the Company estimates the standalone selling price using either an adjusted

market assessment approach or an expected cost plus margin approach, representing the amount that the Company believes the market is willing to pay for the product or service. Analyzing the arrangement to identify performance obligations requires the use of judgment, and each may be an obligation to deliver services, a right or license to use an asset, or another performance obligation.

Milestone payments are recognized as licensing revenue upon the achievement of specified milestones if (i) the milestone is substantive in nature and the achievement of the milestone was not probable at the inception of the agreement; and (ii) the Company has a right to payment. Any milestone payments received prior to satisfying these revenue recognition criteria are recorded as deferred revenue.

Reimbursements received for direct out-of-pocket expenses related to research and development costs are recorded as revenue in the Consolidated Statements of Comprehensive Loss rather than as a reduction in expenses. Under the Company's contracts with the Biomedical Advanced Research and Development Authority within the United States Department of Health and Human Services ("BARDA/HHS") and the National Institute of Allergy and Infectious Diseases ("NIAID/HHS"), revenue is recognized as reimbursable direct and indirect costs are incurred.

Under certain of the Company's license agreements, the Company receives royalty payments based upon its licensees' net sales of covered products. Royalties are recognized at the later of when (i) the subsequent sale or usage occurs, or (ii) the performance obligation to which some or all of the sales-based or usage-based royalty has been satisfied.

Product Sales

The Company's principal sources of product sales are sales of peramivir to our licensing partners and sales of RAPIVAB to the U.S. Department of Health and Human Services under the Company's procurement contract. In December 2020, the Company launched ORLADEYO and began recording product revenue. The Company recognizes revenue for sales when the customer obtains control of the product, which generally occurs upon delivery.

The Company recorded the following revenues for the years ended December 31:

	2020	2019	2018
Product sales, net	$ 3,301	$ 17,533	$ –
Royalty revenue	3,381	6,303	6,101
Collaborative and other research and development revenues:			
U.S. Department of Health and Human Services	9,231	4,898	2,552
Torii Pharmaceutical Co., Ltd.	1,899	20,101	–
Seqirus UK Limited	–	–	12,000
Total collaborative and other research and development revenues	11,130	24,999	14,552
Total revenues	$ 17,812	$ 48,835	$ 20,653

Advertising

The Company engages in very limited distribution and direct-response advertising when promoting RAPIVAB. Advertising and promotional costs are expensed in "Selling, general and administrative" as the costs are incurred. Advertising expenses related to the launch of ORLADEYO were $6,567 for year ended December 31, 2020. The Company did not incur advertising and product promotion expenses in 2019 and 2018.

Research and Development Expenses

The Company's research and development costs are charged to expense when incurred. Research and development expenses include all direct and indirect development costs related to the development of the Company's portfolio of product candidates. Advance payments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are recognized as expense when the related goods are delivered or the related services are performed. Research and development expenses include, among other items, personnel costs, including salaries and benefits, manufacturing costs, clinical, regulatory, and toxicology services performed by CROs, materials and supplies, and overhead allocations consisting of various administrative and facilities related costs. Most of the Company's manufacturing and clinical and preclinical studies are performed by third-party CROs. Costs for studies performed by CROs are accrued by the Company over the service periods specified in the contracts and estimates are adjusted, if required, based upon the Company's on-going review of the level of services actually performed.

Additionally, the Company has license agreements with third parties, such as Albert Einstein College of Medicine of Yeshiva University ("AECOM"), Industrial Research, Ltd. ("IRL"), and the University of Alabama at Birmingham ("UAB"), which require fees related to sublicense agreements or maintenance fees. The Company expenses sublicense payments as incurred unless they are related to revenues that have been deferred, in which case the expenses are deferred and recognized over the related revenue recognition period. The Company expenses maintenance payments as incurred.

Deferred collaboration expenses represent sub-license payments, paid to the Company's academic partners upon receipt of consideration from various commercial partners, and other consideration paid to the Company's academic partners for modification to existing license agreements. These deferred expenses would not have been incurred without receipt of such payments or modifications from the Company's commercial partners and are being expensed in proportion to the related revenue being recognized. The Company believes that this accounting treatment appropriately matches expenses with the associated revenue.

Stock-Based Compensation

All share-based payments, including grants of stock option awards and restricted stock unit awards, are recognized in the Company's Consolidated Statements of Comprehensive Loss based on their fair values. The fair value of stock option awards is estimated using the Black-Scholes option pricing model. The fair value of restricted stock unit awards is based on the grant date closing price of the common stock. Stock-based compensation cost is recognized as expense on a straight-line basis over the requisite service period of the award. In addition, we have outstanding performance-based stock options for which no compensation expense is recognized until "performance" is deemed to have occurred.

Interest Expense and Royalty Financing Obligation

The royalty financing obligation is eligible to be repaid based on royalties from net sales of ORLADEYO. Interest expense is accrued using the effective interest rate method over the estimated period the related liability will be paid. This requires the Company to estimate the total amount of future royalty payments to be generated from product sales over the life of the agreement. The Company imputes interest on the carrying value of the royalty financing obligation and records interest expense using an imputed effective interest rate. The Company will reassess the expected royalty payments each reporting period and account for any changes through an adjustment to the effective interest rate on a prospective basis. The assumptions used in determining the expected repayment term of the debt and amortization period of the issuance costs requires that the Company make estimates that could impact the carrying value of the liability, as well as the period over which associated issuance costs will be amortized. A significant increase or decrease in forecasted net sales could materially impact the liability balance, interest expense and the time period for repayment.

Interest Expense and Deferred Financing Costs

Interest expense for the years ended December 31, 2020, 2019 and 2018 was $14,501 $11,892 and $9,176, respectively, and primarily relates to the issuance of the PhaRMA Notes (defined in Note 3) and the Prior Credit Facility and Amended and Restated Senior Credit Facility (each defined in Note 4). Costs directly associated with the issuance of the PhaRMA Notes, the Prior Credit Facility and the Amended and Restated Senior Credit Facility have been capitalized and are netted against the non-recourse notes payable and senior credit facility on the Consolidated Balance Sheets. These costs are being amortized to interest expense over the terms of the PhaRMA Notes and the Amended and Restated Senior Credit Facility (as subsequently amended and restated) using the effective interest rate method. In December 2020, the Company incurred costs directly associated with its royalty monetization (defined in Note 3) and borrowings under the Credit Agreement (defined in Note 4). These costs have been deferred and are being amortized to interest expense over the terms of the respective arrangements. Amortization of deferred financing costs and original issue discount included in interest expense was $1,217, $1,278 and $885 for each of the years ended December 31, 2020, 2019 and 2018, respectively. In December 2020, the outstanding principal balance of the Senior Credit Facility was repaid and related unamortized deferred financing costs and original issue discount of $1,211 were fully expensed as part of loss on debt extinguishment.

Currency Hedge Agreement

In connection with the issuance by Royalty Sub of the PhaRMA Notes, the Company entered into a Currency Hedge Agreement to hedge certain risks associated with changes in the value of the Japanese yen relative to the U.S. dollar. The final tranche of the options under the Currency Hedge Agreement expired in November of 2020. The Currency Hedge Agreement did not qualify for hedge accounting treatment; therefore mark-to-market adjustments were recognized in the Company's Consolidated Statements of Comprehensive Loss. Cumulative mark-to-market adjustments for the years ended December 31, 2020, 2019 and 2018 resulted in losses of $632, $347 and $1,049, respectively. Mark-to-market adjustments

were determined by a third-party pricing model which uses quoted prices in markets that are not actively traded and for which significant inputs are observable directly or indirectly, representing Level 2 in the fair value hierarchy as defined by U.S. GAAP. In addition, realized currency exchange gains of $662, $863 and $941 were recognized in 2020, 2019 and 2018, respectively, related to the exercise of a U.S. dollar/Japanese yen currency option under the Company's foreign currency hedge.

Net Loss Per Share

Net loss per share is based upon the weighted average number of common shares outstanding during the period. Diluted loss per share is equivalent to basic net loss per share for all periods presented herein because common equivalent shares from unexercised stock options, outstanding warrants, and common shares expected to be issued under the Company's employee stock purchase plan were anti-dilutive. The calculation of diluted earnings per share for the years ended December 31, 2020, 2019, and 2018 does not include 14,957, 2,805, and 2,274, respectively, of potential common shares as their impact would be anti-dilutive.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent assets and liabilities. The most significant estimates in the Company's consolidated financial statements relate to the valuation of stock options, the royalty financing and the valuation allowance for deferred tax assets resulting from net operating losses. These estimates are based on historical experience and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results could differ from those estimates.

Significant Customers and Other Risks

Significant Customers

Other than royalty revenues, the Company's primary sources of revenue that have an underlying cash flow stream are the reimbursement of galidesivir (formerly BCX4430) development expenses earned under cost-plus-fixed-fee contracts with BARDA/HHS and NIAID/HHS and sales of RAPIVAB (peramivir injection) under our procurement contract with the Assistant Secretary for Preparedness and Response within the United States Department of Health and Human Services. The Company relies on BARDA/HHS and NIAID/HHS to reimburse predominantly all of the development costs for its galidesivir program. Accordingly, reimbursement of these expenses represents a significant portion of the Company's collaborative and other research and development revenues. The completion or termination of the NIAID/HHS and BARDA/HHS galidesivir contracts could negatively impact the Company's future Consolidated Statements of Comprehensive Loss and Cash Flows. The Company recognizes royalty revenue from the net sales of RAPIACTA by Shionogi; however, the underlying cash flow from these royalty payments, except for Japanese government stockpiling sales, goes directly to pay the interest, and then the principal, on the Company's non-recourse notes payable. Payment of the interest and the ultimate repayment of principal of these notes will be entirely funded by future royalty payments derived from net sales of RAPIACTA. Further, the Company's drug development activities are performed by a limited group of third-party vendors. If any of these vendors were unable to perform their services, this could significantly impact the Company's ability to complete its drug development activities.

Risks from Third Party Manufacturing and Distribution Concentration

The Company relies on single source manufacturers for active pharmaceutical ingredient and finished drug product manufacturing of product candidates in development and on single source distributors for distribution of approved drug products. Delays in the manufacture or distribution of any product could adversely impact the commercial revenue and future procurement stockpiling of the Company's product candidates in development.

Credit Risk

Cash equivalents and investments are financial instruments which potentially subject the Company to concentration of risk to the extent recorded on the Consolidated Balance Sheets. The Company deposits excess cash with major financial institutions in the United States. Balances may exceed the amount of insurance provided on such deposits. The Company believes it has established guidelines for investment of its excess cash relative to diversification and maturities that maintain safety and liquidity. To minimize the exposure due to adverse shifts in interest rates, the Company maintains a portfolio of investments with an average maturity of approximately 18 months or less. Other than product sale and collaborative partner

receivables discussed above, the majority of the Company's receivables from collaborations are due from the U.S. Government, for which there is no assumed credit risk.

Recent Accounting Pronouncements

In June 2016, the FASB issued Accounting Standards Update No. 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"). ASU 2016-13 requires a financial asset (or a group of financial assets) measured at amortized cost basis to be presented at the net amount expected to be collected. In addition, ASU 2016-13 requires credit losses relating to available-for-sale debt securities to be recorded through an allowance for credit losses. ASU 2016-13 requires consideration of a broader range of reasonable and supportable information to develop credit loss estimates. ASU 2016-13 is effective for public companies for interim and annual periods beginning after December 15, 2019. The Company adopted ASU 2016-02 as of January 1, 2020. Given the nature of the Company's receivables from collaborators, investment portfolio and other financial assets, adoption of this standard did not have a material effect on the Company's financial position, results of operations or cash flows.

In August 2018, the FASB issued Accounting Standards Update No. 2018-15, *Intangibles - Goodwill and Other - Internal-Use Software (Subtopic 350-40)* ("ASU 2018-15"). ASU 2018-15 aligns the requirements for capitalizing implementation costs incurred in a hosting arrangement that is a service contract with the requirements for capitalizing implementation costs incurred to develop or obtain internal-use software. The guidance requires entities to capitalize costs for certain implementation activities in the application development stage and expense the capitalized implementation costs over the expected term of the hosting arrangement. ASU 2018-15 is effective for fiscal years beginning after December 15, 2019, with early adoption permitted. The Company elected to adopt this standard early, beginning October 1, 2019 on a prospective basis. Adoption did not have a material effect on the Company's financial position, results of operations or cash flows.

The Company has reviewed other new accounting pronouncements that were issued as of December 31, 2020 and does not believe that these pronouncements are either applicable to the Company, or that they will have a material impact on its financial position or results of operations.

Note 2 — Property and Equipment

Property and equipment consisted of the following at December 31:

	2020	2019
Furniture and fixtures	$ 722	$ 602
Office equipment	211	184
Software	1,159	1,159
Laboratory equipment	3,774	3,462
Leasehold improvements	8,583	8,528
	14,449	13,935
Less accumulated depreciation and amortization	(7,336)	(6,588)
Property and equipment, net	$ 7,113	$ 7,347

Depreciation and amortization expense for the years ended December 31, 2020, 2019, and 2018 was $748, $724, and $770, respectively.

Note 3—Royalty Monetizations

RAPIACTA Royalty Monetizations

Overview

On March 9, 2011, the Company completed a $30,000 financing transaction to monetize certain future royalty and milestone payments under the Company's agreement with Shionogi (the "Shionogi Agreement"), pursuant to which Shionogi licensed from the Company the rights to market RAPIACTA in Japan and Taiwan. The Company received net proceeds of $22,691 from the transaction after transaction costs of $4,309 and the establishment of a $3,000 interest reserve account by

Royalty Sub, available to help cover interest shortfalls in the future. All of the interest reserve account has been fully utilized with the September 2012 interest payment.

As part of the transaction, the Company entered into a purchase and sale agreement dated as of March 9, 2011 with JPR Royalty Sub, LLC, a wholly-owned subsidiary of the Company ("Royalty Sub"), whereby the Company transferred to Royalty Sub, among other things, (i) its rights to receive certain royalty and milestone payments from Shionogi arising under the Shionogi Agreement, and (ii) the right to receive payments under a Japanese yen/US dollar foreign currency hedge arrangement (as further described below, the "Currency Hedge Agreement") put into place by the Company in connection with the transaction. Royalty payments are paid by Shionogi in Japanese yen, and any milestone payments will be paid in U.S. dollars. The Company's collaboration with Shionogi was not impacted as a result of this transaction.

Non-Recourse Notes Payable

On March 9, 2011, Royalty Sub completed a private placement to institutional investors of $30,000 in aggregate principal amount of its PhaRMA Senior Secured 14.0% Notes due on December 1, 2020 (the "PhaRMA Notes"). The PhaRMA Notes were issued by Royalty Sub under an Indenture, dated as of March 9, 2011 (the "Indenture"), by and between Royalty Sub and U.S. Bank National Association, as Trustee. Principal and interest on the PhaRMA Notes issued are payable from, and are secured by, the rights to royalty and milestone payments under the Shionogi Agreement transferred by the Company to Royalty Sub and payments, if any, made to Royalty Sub under the Currency Hedge Agreement. The PhaRMA Notes bear interest at 14% per annum, payable annually in arrears on September 1st of each year. The Company remains entitled to receive any royalties and milestone payments related to sales of peramivir by Shionogi following repayment of the PhaRMA Notes.

Royalty Sub's obligations to pay principal and interest on the PhaRMA Notes are obligations solely of Royalty Sub and are without recourse to any other person, including the Company, except to the extent of the Company's pledge of its equity interests in Royalty Sub in support of the PhaRMA Notes. The Company may, but is not obligated to, make capital contributions to a capital account that may be used to redeem, or on up to one occasion pay any interest shortfall on, the PhaRMA Notes.

In September 2014, Royalty Sub was unable to pay the accrued interest obligation due September 3, 2013. Under the terms of the Indenture, Royalty Sub's inability to pay the full amount of interest payable in September 2013 by the next succeeding payment date for the PhaRMA Notes, which was September 1, 2014, constituted an event of default. Accordingly, the PhaRMA Notes and related accrued interest have been classified as current liabilities on the December 31, 2014 balance sheet, and thereafter. As a result of the event of default under the PhaRMA Notes, the holders of the PhaRMA Notes may foreclose on the collateral securing the PhaRMA Notes and the equity interest in Royalty Sub and exercise other remedies available to them under the Indenture in respect of the PhaRMA Notes. In such event, the Company may not realize the benefit of future royalty payments that might otherwise accrue to it following repayment of the PhaRMA Notes and it might otherwise be adversely affected. Due to the non-recourse nature of the PhaRMA Notes, in the event of any potential foreclosure, the primary impact to the Company would be the loss of future royalty payments from Shionogi and legal costs associated with retiring the PhaRMA Notes. As the PhaRMA Notes are the obligation of Royalty Sub and non-recourse to the Company, the event of default of the PhaRMA Notes is not expected to have a significant impact on the Company's future results of operations or cash flows. 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 $30,000, together with accrued and unpaid interest of $20,614, was due in full. As of December 31, 2020, the PhaRMA Notes remain outstanding and in default and the Company will continue to record the liability and accrued interest owed until the Company is determined to no longer be the financial obligor.

The Indenture does not contain any financial covenants. The Indenture includes customary representations and warranties of Royalty Sub, affirmative and negative covenants of Royalty Sub, Events of Default and related remedies, and provisions regarding the duties of the Trustee, indemnification of the Trustee, and other matters typical for indentures used in structured financings of this type.

As of December 31, 2020, the aggregate fair value of the PhaRMA Notes was estimated to be approximately 3% of its carrying value of $30,000. The estimated fair value of the PhaRMA Notes is classified as Level 3 in the fair value hierarchy as defined in U.S. GAAP.

Foreign Currency Hedge

In connection with the issuance by Royalty Sub of the PhaRMA Notes, the Company entered into a Currency Hedge Agreement to hedge certain risks associated with changes in the value of the Japanese yen relative to the U.S. dollar. Under the Currency Hedge Agreement, the Company had the right to purchase dollars and sell yen at a rate of 100 yen per dollar. The final tranche of the options under the Currency Hedge Agreement expired in November of 2020.

The Currency Hedge Agreement did not qualify for hedge accounting treatment; therefore mark-to-market adjustments were recognized in the Company's Consolidated Statements of Comprehensive Loss. Cumulative mark-to-market adjustments in 2020, 2019 and 2018 resulted in losses of $632, $347 and $1,049, respectively. In addition, realized currency exchange gains of $662, $863 and $941 were recognized in 2020, 2019 and 2018, respectively, related to the exercise of a U.S. dollar/Japanese yen currency option under the Company's foreign currency hedge.

ORLADEYO Royalty Monetization

On December 7, 2020, the Company and RPI 2019 Intermediate Finance Trust ("RPI") entered into a Purchase and Sale Agreement (the "Royalty Purchase Agreement"), pursuant to which the Company sold to RPI the right to receive certain royalty payments from the Company for a purchase price of $125,000 in cash (the "Royalty Sale"). Under the Royalty Purchase Agreement, RPI is entitled to receive tiered, sales-based royalties on net product sales of ORLADEYO in the United States, certain key European markets, and other markets where the Company sells ORLADEYO directly or through distributors (collectively, the "Key Territories") in an amount equal to: (i) 8.75% of aggregate annual net sales of ORLADEYO in the Key Territories for annual net sales up to $350,000 and (ii) 2.75% of annual net sales in the Key Territories for annual net sales between $350,000 and $550,000. No royalty payments are payable on annual net sales in the Key Territories over $550,000. In addition, RPI will be entitled to receive 1.0% of global net sales, if any, of BCX9930.

Under the Royalty Purchase Agreement, RPI is also entitled to receive a tiered revenue share on ORLADEYO sublicense revenue or net sales by licensees outside of the Key Territories (the "Other Markets") equal to: (i) 20% of the proceeds received by the Company for upfront license fees and development milestones for ORLADEYO in the Other Markets; (ii) 20% of proceeds received on annual net sales of up to $150,000 in the Other Markets; and (iii) 10% of proceeds received by the Company on annual net sales between $150,000 and $230,000 in the Other Markets. No royalty payments are payable on annual net sales above $230,000 in the Other Markets. No payment will be due to RPI for any achievement milestone which may be payable under the existing out-license for ORLADEYO.

The Company will be required to make royalty payments of amounts owed to RPI each calendar quarter following the first commercial sale of ORLADEYO in any country.

Under the Royalty Purchase Agreement, the Company has agreed to specified affirmative and negative covenants, including covenants regarding periodic reporting of information by the Company to RPI, third-party audits of royalties paid under the Royalty Purchase Agreement, and restrictions on the ability of the Company or any of its subsidiaries to incur indebtedness other than certain royalty sales and as is permitted to be incurred under the terms of the Company's Credit Agreement with Athyrium Opportunities III Co-Invest 1 LP. Refer to Note 4 for further details on the Credit Agreement. The restrictions on the ability of the Company or any of its subsidiaries to incur indebtedness are eliminated after the achievement of certain specified milestones in the Royalty Purchase Agreement.

The cash consideration of $125,000 obtained pursuant to the Royalty Purchase Agreement is recorded in "Royalty financing obligation" on the Company's consolidated balance sheet as of December 31, 2020. The fair value for the royalty financing obligation at the time of the transaction was based on the Company's estimates of future royalties expected to be paid to RPI over the life of the arrangement. The estimates of future net product sales (and resulting royalty payments) are based on key assumptions including population, penetration and sales price and are determined using forecasts from market data sources, which are considered Level 3 inputs. Deferred issuance costs, which consist primarily of advisory and legal fees, totaled $2,370 as of December 31, 2020. The liability and the deferred issuance costs are amortized using the effective interest method over the term of the arrangement, in accordance with the respective guidance. The effective interest rate as of December 31, 2020 was approximately 24%. For 2020, accrued interest expense in the amount of $2,108 was added to the initial balance of the liability. The Company will utilize the prospective method to account for subsequent changes in the estimated future payments to be made to RPI.

Note 4 — Credit Agreement

On December 7, 2020, the Company entered into a $200,000 Credit Agreement with Athyrium Opportunities III Co-Invest 1 LP ("Athyrium"), as lender and as administrative agent for the lenders. BioCryst Ireland Limited, BioCryst US Sales Co., LLC, and BioCryst UK Limited, each of which is a wholly-owned subsidiary of the Company, are guarantors to the Credit Agreement. The Credit Agreement provides for an initial term loan in the principal amount of $125,000 (the "Term A Loan"), which was received by the Company on December 7, 2020 and is recorded in "Secured term loan" on the Company's balance sheet as of December 31, 2020. The Company used a portion of the proceeds from the Term A Loan to repay $43,298 of outstanding indebtedness, including accrued interest, under its existing credit facility with MidCap Financial Trust. The Company intends to use the remaining proceeds to support the launch of ORLADEYO in the United States and Europe and to advance the development of BCX9930 into clinical trials in multiple complement-mediated diseases, and for other general corporate purposes.

The Credit Agreement also provides for two additional term loans, at the Company's option, in the respective principal amounts of $25,000 (the "Term B Loan") and $50,000 (the "Term C Loan"). The Term B Loan and the Term C Loan may be drawn upon 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. The maturity date of the Credit Agreement is December 7, 2025.

The Credit Agreement provides for quarterly interest-only payments until the maturity date, with the unpaid principal amount of the outstanding Term Loans due and payable on the maturity date. For each of the first eight full fiscal quarters following December 7, 2020, the Company has the option to make the applicable interest payment-in-kind (a "PIK Interest Payment") 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. The Term Loans will bear interest at a rate equal to the three-month LIBOR rate, which shall be no less than 1.75% and no more than 3.50% ("LIBOR"), plus 8.25%, or for each interest period in which a PIK Interest Payment is made, the LIBOR plus 10.25%.

Subject to certain exceptions, the Company is required to make mandatory prepayments of the Term Loans with the proceeds of certain asset sales, certain ORLADEYO out-licensing or royalty monetization transactions (excluding the Royalty Sale), extraordinary receipts, debt issuances, or upon a change of control of the Company and specified other events, subject to certain exceptions. The Company may make voluntary prepayments in whole or in part. Prepayments are subject to a premium equal to, (i) with respect to any voluntary prepayment and certain mandatory prepayments paid on or prior to the second anniversary of the applicable Term Loan borrowing date, the amount, if any, by which (a) the sum of (1) 102.00% of the principal amount of the Term Loan being prepaid plus (2) the present value of all interest that would have accrued on the principal amount of the Term Loan being prepaid through and including the second anniversary of the date of the borrowing of such Term Loan, plus 0.50%, exceeds (b) the principal amount of the Term Loan being prepaid; (ii) with respect to any prepayment made between the second and third anniversaries of the applicable Term Loan borrowing date, 2.00% of the principal amount of the Term Loan being prepaid; (iii) with respect to any prepayment made between the third and fourth anniversaries of the applicable Term Loan borrowing date, 1.00% of the principal amount of the Term Loan being prepaid; and (iv) with respect to any prepayment made after the fourth anniversary of the applicable Term Loan borrowing date, 0.00% of the principal amount of the Term Loan being prepaid. Upon the prepayment or repayment, including at maturity, of all or any of the Term Loans, the Company is obligated to pay an exit fee in an amount equal to 2.00% of the principal amount of the Term Loans prepaid or repaid. In addition, each Term Loan is subject to a 1.00% commitment fee at its respective borrowing date.

The Credit Agreement also contains representations and warranties and affirmative and negative covenants customary for financings of this type, as well as customary events of default. Certain of the customary negative covenants limit the ability of the Company and certain of its subsidiaries to, among other things, grant liens, make investments, incur additional indebtedness, engage in mergers, acquisitions, and similar transactions, dispose of assets, license certain property, distribute dividends, make certain restricted payments, change the nature of the Company's business, engage in transactions with affiliates and insiders, prepay other indebtedness, or engage in sale and leaseback transactions, subject to certain exceptions. Additionally, as of the last day of each fiscal quarter (a "Test Date"), beginning with the first Test Date occurring immediately after the Term C Loan is drawn, if applicable, the Company may not permit consolidated net revenues from ORLADEYO sales in the United States for the four-fiscal quarter period ending on such Test Date to be less than the specified amounts set forth in the Credit Agreement (collectively, the "Revenue Tests"). If the Company fails to satisfy the Revenue Tests as of any Test Date, it will have a one-time right (the "Cure Right") to repay in full the entire amount of the Term C Loans outstanding at such time together with all accrued and unpaid interest thereon plus the prepayment premium, exit fee, and any other fees or amounts payable under the Credit Agreement at such time. In addition, the Credit Agreement contains a minimum liquidity covenant requiring the Company to maintain at all times, as applicable, at least $15,000 of unrestricted

cash and cash equivalents if only the Term A Loan has been drawn; at least $20,000 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 $15,000 (or, if the Cure Right has been exercised, $20,000) of unrestricted cash and cash equivalents if the Term C Loan has been drawn, subject to certain exceptions.

A failure to comply with the covenants in the Credit Agreement could permit the Lenders under the Credit Agreement to declare the outstanding principal as well as accrued interest and fees, to be immediately due and payable.

The Company's obligations under the Credit Agreement are secured by a security interest in, subject to certain exceptions, substantially all of the Company's assets.

As of December 31, 2020, the Company had borrowings of $125,000 under the Credit Agreement. The carrying amount of the debt approximates its fair value based on prevailing interest rates as of the balance sheet date.

The Credit Agreement provides for quarterly interest-only payments until the maturity date, with the unpaid principal amount of the outstanding Term Loans due and payable on the maturity date of December 7, 2025. The Company has elected the first quarterly interest payment to be a PIK Interest Payment and began accruing interest at a rate of 12.17%. As of December 31, 2020, debt fees and issuance costs totaled $7,764 and are being amortized as interest expense on an effective interest rate method over the term of the Term A Loan. Interest expense of $925, net of deferred financing amortization of $131, related to the Credit Agreement was recognized in 2020 related to the Term A Loan.

The Credit Agreement contains two provisions that, if deemed probable, would create the recognition of an embedded feature; however, at this time, the Company does not believe either provision is probable.

Note 5 — Senior Credit Facility

On February 5, 2019, the Company entered into a $100,000 Senior Credit Facility with an affiliate of MidCap Financial Services, LLC, as administrative agent (the "Second Amended and Restated Senior Credit Facility"). Borrowings under the Second Amended and Restated Senior Credit Facility were available in three tranches, with (i) the first tranche comprised of $50,000 funded at closing, which included $30,000 of proceeds that were deemed rolled over from the outstanding principal amount under the Company's prior credit agreement, (ii) the second tranche comprised of $30,000, and (iii) the third tranche comprised of $20,000, with the second and third tranches to have been funded upon the completion of certain contingencies related to the Company's development activities of its product candidates and the establishment of certain financial covenants. On September 10, 2019 the Company executed the first amendment to the Second Amended and Restated Credit Facility which extended the commitment termination date for the second tranche to November 30, 2019. On November 30, 2019, the Company's access to the second tranche expired.

The Second Amended and Restated Senior Credit Facility refinanced and replaced the Amended and Restated Senior Credit Facility dated as of July 20, 2018 (the "Amended and Restated Senior Credit Facility"). The Second Amended and Restated Senior Credit Facility had a variable interest rate of LIBOR (which was not to be less than 0.5%) plus 8%. The Second Amended and Restated Senior Credit Facility included an interest-only payment period through June 2020 and scheduled monthly principal and interest payments for the subsequent 30 months. The Company used a portion of the proceeds of the Second Amended and Restated Senior Credit Facility to pay off outstanding amounts under the Amended and Restated Senior Credit Facility and the remainder was used for general corporate purposes.

In December 2020, the Company repaid the outstanding principal of the Second Amended and Restated Senior Credit Facility of $40,000 along with exit fees and accrued interest through the payoff date that totaled $3,298. The unamortized deferred financing cost and original issue discount of $1,211 was expensed as a loss on debt extinguishment.

Note 6 — Lease Obligations and Other Contingencies

In February 2016, the FASB issued ASU 2016-02: *Leases (Topic 842)*. This ASU requires a lessee to recognize a right-of-use asset and a lease liability on its balance sheet for most operating leases. ASU 2016-02 is effective for annual and interim periods beginning after December 15, 2018, including interim periods within those fiscal years. In July 2018, the FASB issued ASU 2018-11, *Leases (Topic 842): Targeted Improvements*, which provides companies with an additional optional transition method to apply the new standard to leases in effect at the adoption date through a cumulative effect adjustment. The Company adopted the new lease standard as of January 1, 2019 using this optional transition method.

The Company elected the package of practical expedients referenced in ASU 2016-02, which permits companies to retain original lease identification and classification without reassessing initial direct costs for existing leases. The Company also elected the practical expedient that exempts leases with an initial lease term of twelve months or less, as well as the practical expedient that allows companies to select, by class of underlying asset, not to separate lease and non-lease components. Adoption of this standard resulted in the recognition of a right-of-use asset and a lease liability on the Company's January 1, 2019 Consolidated Balance Sheet of $3,621 and $4,822, respectively. There was no material impact on the Company's Consolidated Statement of Comprehensive Loss, and the cumulative transition adjustment recorded to retained earnings upon adoption was $238.

The Company leases certain assets under operating leases, which primarily consisted of real estate leases, laboratory equipment leases and office equipment leases as of December 31, 2020. Certain operating leases provide for renewal options, which can vary by lease. The right-of-use asset and lease liabilities on the Company's Consolidated Balance Sheet represent payments over the lease term, which includes renewal options for certain real estate leases that we are likely to exercise. As part of the Company's assessment of the lease term, the Company elected the hindsight practical expedient, which allows companies to use current knowledge and expectations when determining the likelihood to extend lease options. Renewal options for our leases range from 1 to 5 years in length and begin from 2023 through 2026. The weighted average lease term for the Company's operating leases was 13.1 years. The discount rate used in the calculation of the Company's right-of-use asset and lease liability was determined based on the stated rate within each contract when available, or the Company's collateralized borrowing rate from lending institutions. The weighted average discount rate for the Company's operating leases was 12.7%.

The Company has not made any residual value guarantees related to its operating leases; therefore, the Company has no corresponding liability recorded on its Consolidated Balance Sheets.

Aggregate lease expense under operating leases was $1,754 and $1,464 for the twelve-month periods ended December 31, 2020 and 2019, respectively. Certain operating leases include rent escalation provisions, which the Company recognizes as expense on a straight-line basis. Lease expense for leases with an initial term of twelve months or less was not material.

Future lease payments for assets under operating leases as of December 31, 2020, are as follows:

Remaining Maturities of Lease Liabilities **Year Ending December 31,**	**Operating Leases**
2021	$ 1,302
2022	758
2023	619
2024	577
2025	582
Thereafter	7,327
Total lease payments	11,165
Less imputed interest	6,115
Total	$ 5,050

The Company's current lease liability at December 31, 2020 and 2019 was $1,179 and $1,377, respectively. The Company's long-term lease liability as of December 31, 2020 and 2019 was $3,871 and $3,406, respectively. The current and long-term portions of the Company's lease liability are presented within "Lease financing obligations" on the Consolidated Balance Sheets. Cash paid for amounts included in the measurement of lease liabilities was $1,696 and $1,457 for the years ended December 31, 2020 and 2019, respectively. The Company's right-of use asset balance associated with operating leases totaled $3,802 and $3,590 at December 31, 2020 and 2019, respectively. These amounts are presented within "Other assets" on the Consolidated Balance Sheets. Operating right-of-use assets are recorded net of accumulated amortization of $2,641 and $1,386 as of December 31, 2020 and 2019, respectively.

Note 7 — Stockholders' Equity

Sales of Common Stock

On November 8, 2017, the Company filed a $200,000 shelf registration statement on Form S-3 with the SEC. This shelf registration statement became effective on December 12, 2017 and allowed the Company to sell securities, including common stock, preferred stock, depository shares, stock purchase contracts, warrants and units, from time to time at prices and on terms to be determined at the time of sale.

On August 6, 2018, the Company completed an underwritten public offering of 10,455 shares of its common stock, offered at a price to the public of $5.50 per share, including shares issued pursuant to the underwriters' 30-day option to purchase additional shares, which was exercised in full. The net proceeds from this offering were approximately $53,400 after deducting underwriting discounts and commissions and estimated offering expenses.

On November 18, 2019, the Company completed an underwritten public offering of 43,621 shares of its common stock, offered at a price to the public of $1.45 per share, including shares issued pursuant to the underwriters' 30-day option to purchase additional shares, which was exercised in full. The net proceeds from this offering were approximately $58,500 after deducting underwriting discounts and commissions and estimated offering expenses.

On November 21, 2019, the Company completed an offering of pre-funded warrants to purchase up to 11,765 shares of its common stock at a price of $1.69 per warrant. Each pre-funded warrant is exercisable subject to conditions in the warrant agreement into 1 share of common stock at an exercise price of $0.01 per share. The net proceeds from this offering were $19,882, excluding any proceeds the Company may receive upon the subsequent exercise of the pre-funded warrants. All warrants issued in this offering remain outstanding at December 31, 2020.

On April 24, 2020, the Company filed a $500,000 shelf registration statement on Form S-3 with the SEC. This shelf registration statement became effective on May 14, 2020 and allows the Company to sell securities, including common stock, preferred stock, depository shares, purchase contracts, warrants, debt securities, and units, from time to time at prices and on terms to be determined at the time of sale.

On June 1, 2020, the Company issued 22,044 shares of common stock to the public at a purchase price of $4.50 per share and pre-funded warrants to purchase 3,511 shares of common stock at a purchase of $4.49 per pre-funded warrant, for total net proceeds to the Company of $108,096 million after deducting underwriting discounts and commissions and other offering expenses. Each pre-funded warrant is exercisable subject to conditions in the warrant agreement into 1 share of common stock at an exercise price of $0.01 per share. All warrants issued in this offering remain outstanding at December 31, 2020.

Note 8 — Stock-Based Compensation

As of December 31, 2020, the Company had three stock-based employee compensation plans, the Amended and Restated Stock Incentive Plan ("Incentive Plan"), the Amended and Restated Inducement Equity Incentive Plan ("Inducement Plan") and the Employee Stock Purchase Plan ("ESPP"). The Incentive Plan was amended and restated on March 19, 2020 and approved by the Company's stockholders on May 12, 2020. The Inducement Plan was adopted by the Board of Directors on April 24, 2019 and amended and restated by the Board of Directors in February 2020 and in July 2020. The ESPP was amended and restated in March 2020 and approved by the Company's stockholders on May 12, 2020. Stock-based compensation expense of $14,794 ($12,938 of expense related to the Incentive Plan, $1,494 of expense related to the Inducement Plan, $362 of expense related to the ESPP) was recognized during 2020, while $17,719 ($17,164 of expense related to the Incentive Plan, $323 of expense related to the Inducement Plan, $232 of expense related to the ESPP) was recognized during 2019 and $9,396 ($9,223 of expense related to the Incentive Plan, $173 of expense related to the ESPP) was recognized during 2018.

The Company accounts for stock-based compensation in accordance with FASB authoritative guidance regarding share-based payments. Total stock-based compensation was allocated as follows:

	Year Ended December 31,		
	2020	2019	2018
Research and development	$ 10,222	$ 13,977	$ 6,867
Selling, general and administrative	4,572	3,742	2,529
Total stock-based compensation expense	$ 14,794	$ 17,719	$ 9,396

Stock Incentive Plan

The Company grants stock option awards and restricted stock unit awards to its employees, directors, and consultants under the Incentive Plan. Under the Incentive Plan, stock option awards are granted with an exercise price equal to the market price of the Company's stock at the date of grant. Commencing March 1, 2011, stock option awards and restricted stock units granted to employees generally vest 25% each year until fully vested after four years. In August 2013, December 2014 and December 2019, the Company issued 1,032, 1,250 and 315 performance-based stock options, respectively. These awards vest upon successful completion of specific development milestones. As of December 31, 2020, 100%, 85% and 100% of the August 2013, December 2014 and December 2019 grants, respectively, have vested. During 2020, the Company recognized $1,768 and $684 of stock compensation expense related to milestones within the August 2013 and December 2019 grants for which achievement became probable. Stock option awards granted to non-employee directors of the Company generally vest over one year. All stock option awards have contractual terms of 10 years. The vesting exercise provisions of all awards granted under the Incentive Plan are subject to acceleration in the event of certain stockholder-approved transactions, or upon the occurrence of a change in control as defined in the Incentive Plan.

Related activity under the Incentive Plan is as follows:

	Awards Available	Options Outstanding	Weighted Average Exercise Price
Balance at December 31, 2017	468	14,452	$ 6.06
Plan amendment	4,400	–	–
Restricted stock awards granted	(13)	–	–
Stock option awards granted	(4,272)	4,272	7.15
Stock option awards exercised	–	(1,011)	2.92
Stock option awards cancelled	222	(222)	7.44
Balance at December 31, 2018	805	17,491	6.49
Plan amendment	4,000	–	–
Restricted stock awards granted	(27)	–	–
Stock option awards granted	(4,511)	4,511	3.91
Stock option awards exercised	–	(251)	3.75
Stock option awards cancelled	701	(701)	6.82
Balance at December 31, 2019	968	21,050	5.96
Plan amendment	8,000	–	–
Restricted stock awards granted	(31)	–	–
Stock option awards granted	(7,469)	7,469	8.06
Stock option awards exercised	–	(510)	3.56
Stock option awards cancelled	3,124	(3,124)	6.93
Balance at December 31, 2020	4,592	24,885	$ 6.52

For stock option awards granted under the Incentive Plan during 2020, 2019, and 2018, the fair value was estimated on the date of grant using a Black-Scholes option pricing model and the assumptions noted in the table below. The weighted average grant date fair value of these awards granted during 2020, 2019, and 2018 was $5.48, $2.63, and $4.92, respectively. The fair value of the stock option awards is amortized to expense over the vesting periods using a straight-line expense attribution method.

Inducement Equity Incentive Plan

The Company has the ability to grant stock option awards to newly-hired employees as inducements material to each employee entering employment with the Company. Stock option awards granted to newly hired employees generally vest 25% each year until fully vested after four years. Each stock option has a term of 10 years and is subject to the terms and conditions of the Inducement Plan. The vesting and exercise provisions of all awards granted under the Inducement Plan are subject to acceleration in the event of certain stockholder-approved transactions, or upon the occurrence of a change in control as defined in the Inducement Plan.

Related activity under the Inducement Plan is as follows:

	Awards Available	Options Outstanding	Weighted Average Exercise Price
Balance at December 31, 2019	171	1,329	$ 3.60
Plan amendment	2,900	–	–
Stock option awards granted	(3,002)	3,002	4.02
Stock option awards cancelled	160	(160)	4.15
Balance at December 31, 2020	229	4,171	$ 3.88

For stock option awards granted under the Inducement Plan during 2020 and 2019, the fair value was estimated on the date of grant using a Black-Scholes option pricing model and the assumptions noted in the table below. The weighted average grant date fair value of these awards granted during 2020 and 2019 was $2.73 and $2.41, respectively. The fair value of the stock option awards is amortized to expense over the vesting periods using a straight-line expense attribution method.

The following table summarizes the key assumptions used by the Company to value the stock option awards granted under all plans during 2020, 2019, and 2018, respectively. The expected life is based on the average of the assumption that all outstanding stock option awards will be exercised at full vesting and the assumption that all outstanding stock option awards will be exercised at the midpoint of the current date (if already vested) or at full vesting (if not yet vested) and the full contractual term. The expected volatility represents the historical volatility on the Company's publicly traded common stock. The Company has assumed no expected dividend yield, as dividends have never been paid to stock or option holders and will not be paid for the foreseeable future. The weighted average risk-free interest rate is the implied yield currently available on zero-coupon government issues with a remaining term equal to the expected term.

Weighted Average Assumptions for Stock Option Awards Granted to Employees and Directors under the Plans

	2020	2019	2018
Expected Life	5.5	5.5	5.5
Expected Volatility	84%	81%	82%
Expected Dividend Yield	0.0%	0.0%	0.0%
Risk-Free Interest Rate	0.4%	1.8%	2.7%

The total intrinsic value of stock option awards exercised under the Incentive Plan was $1,562 during 2020, $1,127 during 2019, and $4,504 during 2018. The intrinsic value represents the total proceeds (fair market value at the date of exercise, less the exercise price, times the number of stock option awards exercised) received by all individuals who exercised stock option awards during the period. No stock option awards were exercised under the Inducement Plan in 2020.

The following table summarizes, at December 31, 2020, by price range: (1) for stock option awards outstanding under the Incentive Plan, the number of stock option awards outstanding, their weighted average remaining life and their weighted average exercise price; and (2) for stock option awards exercisable under the Plan, the number of stock option awards exercisable and their weighted average exercise price:

	Outstanding			Exercisable	
Range	**Number**	**Weighted Average Remaining Life**	**Weighted Average Exercise Price**	**Number**	**Weighted Average Exercise Price**
$ 0 to 3	2,514	6.1	$ 2.19	1,414	$ 1.25
3 to 6	12,689	7.0	4.22	6,854	2.48
6 to 9	10,852	9.2	7.88	2,005	4.89
9 to 12	2,347	4.5	10.85	2,129	4.51
12 to 15	559	4.1	12.30	539	6.43
15 to 18	95	4.5	15.39	95	10.57
$ 0 to 18	29,056	7.5	$ 6.14	13,036	$ 3.27

The weighted average remaining contractual life of stock option awards exercisable under the plans at December 31, 2020 was 5.3 years.

The aggregate intrinsic value of stock option awards outstanding and exercisable under the plans at December 31, 2020 was $29,716. The aggregate intrinsic value represents the value (the period's closing market price, less the exercise price, times the number of in-the-money stock option awards) that would have been received by all stock option award holders under the plans had they exercised their stock option awards at the end of the year.

The total fair value of the stock option awards vested under the plans was $18,739 during 2020, $12,499 during 2019, and $8,952 during 2018.

As of December 31, 2020, the number of stock option awards vested and expected to vest under the plans is 26,487. The weighted average exercise price of these stock option awards is $6.13 and their weighted average remaining contractual life is 7.4 years.

The following table summarizes the changes in the number and weighted-average grant-date fair value of non-vested stock option awards during 2020:

	Non-Vested Stock Option Awards	**Weighted Average Grant-Date Fair Value**
Balance December 31, 2019	11,688	$ 3.77
Stock option awards granted	10,471	4.69
Stock option awards vested	(4,543)	4.12
Stock option awards forfeited	(1,596)	3.96
Balance December 31, 2020	16,020	$ 4.25

As of December 31, 2020, there was approximately $56,094 of total unrecognized compensation cost related to non-vested employee stock option awards granted by the Company. That cost is expected to be recognized as follows: $17,758 in 2021, $16,281 in 2022, $12,484 in 2023, and $9,571 in 2024.

Employee Stock Purchase Plan

The Company has reserved a total of 4,475 shares of common stock to be purchased under the ESPP, of which 2,873 shares remain available for purchase at December 31, 2020. Eligible employees may authorize up to 15% of their salary to purchase common stock at the lower of 85% of the beginning or 85% of the ending price during six-month purchase intervals. No more than 3 shares may be purchased by any one employee at the six-month purchase dates and no employee may purchase stock having a fair market value at the commencement date of $25 or more in any one calendar year.

There were 246, 115, and 92 shares of common stock purchased under the ESPP in 2020, 2019, and 2018, respectively, at a weighted average price per share of $2.56, $3.51, and $3.83, respectively. Expense of $362, $232, and $173 related to the ESPP was recognized during 2020, 2019, and 2018, respectively. Compensation expense for shares purchased under the ESPP related to the purchase discount and the "look-back" option were determined using a Black-Scholes option pricing model. The weighted average grant date fair values of shares granted under the ESPP during 2020, 2019, and 2018, were $1.47, $2.01, and $1.89, respectively.

Note 9 — Income Taxes

The Company has incurred net losses since inception and, consequently, has not recorded any U.S. Federal and state income tax expense or benefit.

The components of loss before provision for income taxes were as followings:

	2020
Domestic	$ (176,613)
Foreign	(6,201)
Loss before provision for income taxes	$ (182,814)

The differences between the Company's effective tax rate and the statutory tax rate in 2020, 2019, and 2018, are as follows:

	2020	2019	2018
Income tax benefit at federal statutory rate (21% for 2020, 2019 and 2018)	$ (38,391)	$ (22,868)	$ (21,263)
State and local income taxes net of federal tax benefit	(2,544)	(1,591)	(2,547)
Permanent items	774	691	503
Rate change	(82)	625	(29)
Expiration of attribute carryforwards	3,774	3,976	2,183
Research and development tax credits	(4,080)	(4,938)	(4,905)
Foreign rate differential	542	-	-
Other	1,456	281	18
Change in valuation allowance	38,551	23,824	26,040
Income tax expense	$ -	$ -	$ -

The Company recognizes the impact of a tax position in its financial statements if it is more likely than not that the position will be sustained on audit based on the technical merits of the position. The Company has concluded that it has an uncertain tax position pertaining to its research and development and orphan drug credit carryforwards. The Company has established these credits based on information and calculations it believes are appropriate and the best estimate of the underlying credit. Any changes to the Company's unrecognized tax benefits are offset by an adjustment to the valuation allowance and there would be no impact on the Company's financial statements. The Company does not expect its unrecognized tax benefits to change significantly over the next 12 months.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows:

	2020	2019
Balance at January 1,	$ 7,210	$ 5,976
Additions to current period tax positions	1,020	1,234
Additions to prior period tax positions	–	–
Reductions to prior period tax provisions	–	–
Balance at December 31,	$ 8,230	$ 7,210

The Company's ability to utilize the net operating loss and tax credit carryforwards in the future may be subject to substantial restrictions in the event of past or future ownership changes as defined in Section 382 of the Internal Revenue Code of 1986, as amended and similar state tax law.

Significant components of the Company's deferred tax assets and liabilities are as follows:

	2020	2019
Deferred tax assets:		
Net federal and state operating losses	$ 159,939	$ 155,190
Research and development credits	66,331	63,275
Royalty income	28,034	-
Stock-based compensation	10,732	9,786
Leasing obligations	1,135	1,070
Other	5,563	3,801
Total deferred tax assets	271,734	233,122
Deferred tax liabilities:		
Fixed assets	(124)	(114)
Right of use asset	(854)	(803)
Total deferred tax liabilities	(978)	(917)
Valuation allowance	(270,756)	(232,205)
Net deferred tax assets	$ –	$ –

The majority of the Company's deferred tax assets relate to net operating loss and research and development carryforwards that can only be realized if the Company is profitable in future periods. It is uncertain whether the Company will realize any tax benefit related to these carryforwards. Accordingly, the Company has provided a full valuation allowance against the net deferred tax assets due to uncertainties as to their ultimate realization. The valuation allowance will remain at the full amount of the deferred tax assets until it is more likely than not that the related tax benefits will be realized. The Company's valuation allowance increased by $38,551, $23,824, and $26,040 in 2020, 2019, and 2018, respectively.

As of December 31, 2020, the Company had U.S. federal operating loss carryforwards of $677,109, state operating loss carryforwards of $494,608, foreign net operating losses of $6,427, and U.S. research and development and orphan drug credit carryforwards of $74,561, which will expire at various dates from 2021 through 2040. Federal losses, state losses, research and development credit carryforwards began expiring in 2020. The foreign net operating losses have an indefinite carryforward period.

Tax years 2017-2020 remain open to examination by the major taxing jurisdictions to which the Company is subject. Additionally, years prior to 2017 are also open to examination to the extent of loss and credit carryforwards from those years. The Company recognizes interest and penalties accrued related to unrecognized tax benefits as components of its income tax provision. However, there were no provisions or accruals for interest and penalties in 2020, 2019 and 2018.

Note 10 — Employee 401(k) Plan

In January 1991, the Company adopted an employee retirement plan ("401(k) Plan") under Section 401(k) of the Internal Revenue Code covering all employees. Employee contributions may be made to the 401(k) Plan up to limits established by the Internal Revenue Service. Company matching contributions may be made at the discretion of the Board of Directors. The Company made matching contributions of $1,569, $926, and $724 in 2020, 2019, and 2018, respectively.

Note 11 — Collaborative and Other Research and Development Contracts

National Institute of Allergy and Infectious Diseases ("NIAID/HHS"). In September 2013, NIAID/HHS contracted with the Company for the development of galidesivir as a treatment for Marburg virus disease and subsequently, Yellow Fever and Ebola virus disease. As of December 31, 2020, all options under this contract have been awarded, and the total value of the contract, as amended, is $45,931, inclusive of the $2,897 added to the contract in August 2020 to support the development of galidesivir. In August 2020, NIAID/HHS awarded the Company a new contract, with potential aggregate funding up of to $43,908 if all contract options are exercised, to manufacture and evaluate the safety, efficacy and tolerability of galidesivir. NIAID/HHS made an initial award of $6,326 to the Company under this new contract.

Biomedical Advanced Research and Development Authority ("BARDA/HHS"). In March 2015, BARDA/HHS awarded the Company a contract for the continued development of galidesivir as a potential treatment for diseases caused by RNA pathogens, including filoviruses. This BARDA/HHS contract includes a base contract of $16,265 to support galidesivir

drug manufacturing, as well as $22,855 in additional development options that can be exercised by the government, bringing the potential value of the contract to $39,120. As of December 31, 2020, a total of $20,574 has been awarded under exercised options within this contract.

The contracts with NIAID/HHS and BARDA/HHS are cost-plus-fixed-fee contracts. That is, the Company is entitled to receive reimbursement for all costs incurred in accordance with the contract provisions that are related to the development of galidesivir plus a fixed fee, or profit. BARDA/HHS and NIAID/HHS will make periodic assessments of progress, and the continuation of the contract is based on the Company's performance, the timeliness and quality of deliverables, and other factors. The government has rights under certain contract clauses to terminate these contracts. These contracts are terminable by the government at any time for breach or without cause.

U.S. Department of Health and Human Services ("HHS"). In September 2018, HHS awarded the Company a $34,660 contract for the procurement of up to 50,000 doses of RAPIVAB (peramivir injection) over a five-year period, including an initial base order of 10,000 doses. In September 2019, HHS exercised its option to purchase an additional 10,000 doses of RAPIVAB. The Company delivered a total of 20,000 doses of RAPIVAB and approximately $13,864 of product sales in 2019. On September 3, 2020, the Company announced that HHS had exercised an option under this contract to purchase an additional 10,000 doses of RAPIVAB for $6,932, which the Company expects to deliver in 2021. No shipments were delivered in 2020 under this additional 10,000 dose option.

Torii Pharmaceutical Co., Ltd. ("Torii"). On November 5, 2019, the Company entered into a Commercialization and License Agreement with Torii (the "Torii Agreement"), granting Torii the exclusive right to commercialize ORLADEYO™ for the prevention of hereditary angioedema ("HAE") attacks in Japan.

Under the Torii Agreement, the Company received an upfront, non-refundable payment of $22,000 and is eligible to receive an additional milestone payment of $15,000 upon receipt from Japan's National Health Insurance System of a reimbursement price approval for ORLADEYO in excess of the threshold specified in the Torii Agreement.

In addition, under the Torii Agreement, the Company is entitled to receive tiered royalty payments, ranging from 20% to 40% of annual net sales of ORLADEYO in Japan during each calendar year. Torii's royalty payment obligations are subject to customary reductions in certain circumstances, but may not be reduced by more than 50% of the amount that otherwise would have been payable to the Company in the applicable calendar quarter. Torii's royalty payment obligations commence upon the first commercial sale of ORLADEYO in Japan and expire upon the later of (i) the tenth anniversary of the date of first commercial sale of ORLADEYO in Japan, (ii) the expiration of the Company's patents covering ORLADEYO, and (iii) the expiration of regulatory exclusivity for ORLADEYO in Japan. The Company will be responsible for supplying Torii with its required amounts of ORLADEYO. The activities of the parties pursuant to the Torii Agreement will be overseen by a joint steering committee, to be composed of an equal number of representatives from each party to coordinate the development and commercialization of ORLADEYO in Japan.

Under the Torii Agreement, the Company has granted Torii a right of first negotiation ("ROFN") to commercialize ORLADEYO in Japan for the acute treatment of HAE attacks if the Company develops ORLADEYO for such indication and to commercialize any additional kallikrein inhibitor that the Company may develop in the future for use in HAE in Japan. Under both ROFNs, if the parties do not agree to terms with respect to a definitive amendment to the Torii Agreement or new agreement, as applicable, the terms of the amendment or agreement would be set by a third-party arbitrator.

The Company identified performance obligations related to (i) the license to develop and commercialize ORLADEYO, (ii) regulatory approval support and (iii) reimbursement pricing approval support. These were each determined to be distinct from the other performance obligations. The Company allocated the $22,000 upfront consideration to the identified performance obligations using estimation approaches to determine the standalone selling prices under ASC 606. Specifically, in determining the value related to the license, a valuation approach utilizing risk adjusted discounted cash flow projections was used and an expected cost plus margin approach was utilized for the other performance obligations. The Company recognized $20,101 in revenue in 2019 including $19,344 associated with the license which was transferred to Torii at the execution of the Agreement and $757 related to the 2020 services provided in the performance of the two approvals. The remaining $1,899 of the $22,000 upfront payment was recognized as revenue in 2020 as the services were delivered.

Seqirus UK Limited ("SUL"). On June 16, 2015, the Company and SUL, a limited company organized under the laws of the United Kingdom and a subsidiary of CSL Limited, a company organized under the laws of Australia,entered into a License Agreement (the "SUL Agreement") granting SUL and its affiliates worldwide rights to develop, manufacture and commercialize RAPIVAB (peramivir injection) for the treatment of influenza except for the rights to conduct such activities in Israel, Japan, Korea and Taiwan (the permitted geographies together constituting the "Territory"). Under the terms of the

SUL Agreement, the Company received an upfront payment of $33,740 and has achieved all development milestones under the contract totaling $12,000.

On March 4, 2020, the International Court of Arbitration of the International Chamber of Commerce ("ICC Tribunal") delivered a Partial Arbitration Award (the "Partial Arbitration Award") in an arbitration matter between the Company and SUL with respect to the SUL Agreement. In the Partial Arbitration Award, the ICC Tribunal found that, during the term, SUL materially breached and abandoned its core duties to the Company under the Diligent Efforts (as defined in the SUL Agreement) requirements of the SUL Agreement as applicable in the U.S. The ICC Tribunal granted a declaratory judgment in favor of the Company terminating the SUL Agreement and restoring all rights to peramivir to the Company. The parties agreed on a transition process for the product, with a full transition of commercialization of the product in the U.S. and Australia returned to the Company as of August 1, 2020 and November 1, 2020, respectively. The ICC Tribunal also awarded the Company its attorneys' fees and expenses incurred in securing the declaratory judgment as well as the costs incurred by the Company in the arbitration. Finally, the ICC Tribunal found that SUL breached the SUL Agreement by failing to pay the milestone payment due to the Company within 30 days of the approval of peramivir for adult use in the European Union and awarded the Company $5,000 (plus interest) for this claim. The ICC Tribunal retained jurisdiction for further proceedings relating to the award of attorneys' fees and for any dispute relating to the return to the Company of all rights to peramivir in the Territory. The Company recorded the settlement gain of $8,893 in other income and legal fees and other expenses of $5,026 in selling, general and administrative expenses for the year ended December 31, 2020.

Shionogi & Co., Ltd. ("Shionogi"). In February 2007, the Company entered into an exclusive license agreement with Shionogi to develop and commercialize peramivir in Japan for the treatment of seasonal and potentially life-threatening human influenza. Under the terms of the agreement, Shionogi obtained rights to injectable formulations of peramivir in Japan. The Company developed peramivir under a license from UAB and will owe sublicense payments to UAB on any future milestone payments and/or royalties received by the Company from Shionogi. In October 2008, the Company and Shionogi amended the license agreement to expand the territory covered by the agreement to include Taiwan. Shionogi has commercially launched peramivir under the commercial name RAPIACTA in Japan and Taiwan.

In December 2017, the Company, on behalf of Royalty Sub, instituted arbitration proceedings against Shionogi in order to resolve a dispute with Shionogi under the Shionogi Agreement regarding the achievement of sales milestones and escalating royalties. The arbitration proceedings have concluded, with the decision that no sale milestones had been achieved and that royalties would remain the same. The costs associated with the arbitration proceedings are recoverable from the assets of Royalty Sub in accordance with the terms of the indenture and servicing agreement relating to the PhaRMA Notes.

Green Cross Corporation ("Green Cross"). In June 2006, the Company entered into an agreement with Green Cross to develop and commercialize peramivir in Korea. Under the terms of the agreement, Green Cross will be responsible for all development, regulatory, and commercialization costs in Korea. The Company received a one-time license fee of $250. The license also provides that the Company will share in profits resulting from the sale of peramivir in Korea, including the sale of peramivir to the Korean government for stockpiling purposes. Furthermore, Green Cross will pay the Company a premium over its cost to supply peramivir for development and any future marketing of peramivir products in Korea.

Mundipharma International Holdings Limited ("Mundipharma"). In February 2006, the Company entered into an exclusive, royalty bearing right and license agreement with Mundipharma for the development and commercialization of Mundesine, a Purine Nucleoside Phosphorylase ("PNP") inhibitor, for use in oncology. The agreement, as amended and restated, provides for the possibility of future event payments totaling $15,000 for achieving specified regulatory events for certain indications and tiered royalties ranging from mid to high single-digit percentages of net product sales in each country where Mundesine is sold by Mundipharma. The Company licensed forodesine and other PNP inhibitors from AECOM/IRL (as defined below) and will owe sublicense payments to AECOM/IRL on all milestone payments and royalties received from Mundipharma.

Albert Einstein College of Medicine of Yeshiva University and Industrial Research, Ltd. ("AECOM" and "IRL" respectively). In June 2000, the Company licensed a series of potent inhibitors of PNP from AECOM and IRL,(together, the "Licensors"). The lead product candidates from this collaboration is forodesine. The Company has obtained worldwide exclusive rights to develop and ultimately distribute these, or any other, product candidates that might arise from research on these inhibitors. The Company has the option to expand the agreement to include other inventions in the field made by the investigators or employees of the Licensors. Under this agreement, as amended and restated, the Company has agreed to use commercially reasonable efforts to develop these drugs and to pay certain milestone payments for each licensed product (which range in the aggregate from $1,400 to almost $4,000 per indication) for future development, single digit royalties on net sales of any resulting product made by the Company, and to share a portion of future payments received from other third-party partners, if any. In addition, the Company has agreed to pay annual license fees, which can range from $150 to $500,

that are creditable against actual royalties and other payments due to the Licensors. The Licensors have also granted the Company an exclusive worldwide license of galidesivir for any antiviral use.

The University of Alabama at Birmingham ("UAB"). The Company currently has agreements with UAB for influenza neuraminidase and complement inhibitors. Under the terms of these agreements, UAB performed specific research for the Company in return for research payments and license fees. UAB has granted the Company certain rights to any discoveries in these areas resulting from research developed by UAB or jointly developed by UAB with the Company. The Company has agreed to pay single digit royalties on sales of any resulting product and to share in future payments received from other third-party partners. The Company has completed the research under the UAB agreements. These two agreements each have an initial 25-year term, are automatically renewable for five-year terms throughout the life of the last patent and are terminable by the Company upon three months' notice and by UAB under certain circumstances. Upon termination both parties shall cease using the other parties' proprietary and confidential information and materials, the parties shall jointly own joint inventions and UAB shall resume full ownership of all UAB licensed products. There is currently no activity between the Company and UAB on these agreements, but when the Company licenses this technology, such as in the case of the Shionogi and Green Cross, or commercializes products related to these programs, the Company will owe sublicense fees or royalties on amounts received.

Note 12 — Quarterly Financial Information (Unaudited)

	First	Second	Third	Fourth
2020 Quarters				
Revenues	$ 4,823	$ 2,871	$ 6,102	$ 4,016
Net Loss	(37,599)	(38,607)	(46,115)	(60,493)
Basic and diluted net loss per share	(0.24)	(0.24)	(0.26)	(0.34)
2019 Quarters				
Revenues	$ 5,887	$ 1,448	$ 1,775	$ 39,725
Net Loss	(31,054)	(37,629)	(37,592)	(2,622)
Basic and diluted net loss per share	(0.28)	(0.34)	(0.34)	(0.02)

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors of BioCryst Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of BioCryst Pharmaceuticals, Inc. (the Company) as of December 31, 2020 and 2019, the related consolidated statements of comprehensive loss, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2020, and the related notes(collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2020, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework),and our report dated March 1, 2021 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Accrued Clinical Trial and Manufacturing Activities

Description of the Matter

As discussed in Note 1 to the consolidated financial statements, the Company has recorded $33.9 million of accrued expenses, which includes costs for clinical trial and manufacturing activities (together, clinical related activities) based upon estimates of expenses incurred through the balance sheet date that have yet to be invoiced by the contract research organizations (CROs), clinical study sites, contract manufacturing organizations, or other vendors (together, clinical vendors). This accrual process involves identifying services that have been performed and estimating the level of service performed and the associated cost when the Company has not yet been invoiced or otherwise notified of actual cost.

Auditing the Company's accruals for costs associated with in-process clinical related activities may include judgment because the timing and pattern of vendor invoicing may not correspond to the level of services provided and the estimate can incorporate significant assumptions such as expected patient enrollment, site activation, and estimated project duration.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of internal controls that addressed the information used in and the identified risks related to the Company's process for recording accrued costs for clinical related activities.

To evaluate the accrual for clinical related expenses, our audit procedures included, among others, inspecting the Company's contracts with clinical vendors (including pending change orders), testing the completeness and accuracy of the underlying data used in the estimate of the level of service provided including evaluating the significant assumptions as discussed above for the applicable in process contracts with clinical vendors. To assess the significant assumptions, we corroborated the progress of clinical related activities through inquiry with the Company's clinical team and with information obtained directly from third party clinical vendors, as well as tested invoices received from clinical vendors subsequent to the balance sheet date.

Valuation of Royalty Financing Obligation

Description of the Matter

As described in Note 3 to the consolidated financial statements, the Company entered into a Royalty Purchase Agreement ("RPA") in December 2020 with a third party. Pursuant to the RPA, the Company received proceeds of $125.0 million in exchange for the right to receive royalty payments based on future net revenues of the Company's drug, Orladeyo.

The Company recorded the financing as a non-current liability instrument (royalty financing obligation) on the balance sheet at its carrying value of $124.7 million as of December 31, 2020 and imputed interest expense associated with this liability using the effective interest rate method. The effective interest rate is calculated based on the rate that would enable the liability to be repaid in full over the anticipated life of the arrangement. The interest rate on this liability may vary during the term of the agreement depending on a number of factors, including the level and timing of forecasted net revenues which affects the repayment timing and ultimate amount of repayment. The Company evaluates the interest rate quarterly based on its current revenue forecasts utilizing the prospective method.

Auditing the royalty financing obligation was complex and highly judgmental due to the estimation uncertainty in determining the effective interest rate. The Company's effective interest rate model includes revenue projections for which royalties will be paid, which are sensitive to significant assumptions (including population, penetration and sales price) that are affected by expectations about future market conditions.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the Company's processes to account for the royalty financing obligation, including controls over management's review of the revenue projections within the model.

To evaluate the royalty financing obligation, our audit procedures included, among others, assessing the underlying data and assumptions used by the Company in its effective interest rate model. We compared the significant assumptions in the revenue projections to current industry, market and economic trends. We recalculated the current year interest expense based on the amortization schedule and estimate of royalties using the effective interest method, and performed sensitivity analyses to evaluate the changes in the effective interest rate, and associated interest expense, that would result from changes in the assumptions.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 1993.

Raleigh, North Carolina

March 1, 2021

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors of BioCryst Pharmaceuticals, Inc.

Opinion on Internal Control Over Financial Reporting

We have audited BioCryst Pharmaceuticals Inc.'s internal control over financial reporting as of December 31, 2020, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework)(the COSO criteria). In our opinion, BioCryst Pharmaceuticals Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2020, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of BioCryst Pharmaceuticals, Inc. as of December 31, 2020 and 2019, the related consolidated statements of comprehensive loss, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2020, and the related notes and our report dated March 1, 2021 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Raleigh, North Carolina

March 1, 2021

ITEM 9. *CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE*

None.

ITEM 9A. *CONTROLS AND PROCEDURES*

Evaluation of Disclosure Controls and Procedures

We maintain a set of disclosure controls and procedures that are designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Our disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to management, including our principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. We carried out an evaluation as required by paragraph (b) of Rule 13a-15 or Rule 15d-15 under the Exchange Act, under the supervision and with the participation of management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rule 13a-15(e) or Rule 15d-15(e) under the Exchange Act). Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2020, our disclosure controls and procedures are effective.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting and for the assessment of the effectiveness of internal control over financial reporting. As defined in Rule 13a-15(f) or Rule 15d-15(f) under the Exchange Act, internal control over financial reporting is a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our Board of Directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of the financial statements in accordance with U.S. GAAP. Internal control over financial reporting includes policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect our transactions and the dispositions of our assets; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In connection with the preparation of our annual financial statements, management has undertaken an assessment of the effectiveness of our internal control over financial reporting as of December 31, 2020, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) (the COSO Framework). Management's assessment included an evaluation of the design of our internal control over financial reporting and testing of the operational effectiveness of those controls.

Based on this assessment, management has concluded that, as of December 31, 2020, our internal control over financial reporting was effective. Management believes our internal control over financial reporting will provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. GAAP.

Ernst & Young LLP, the independent registered public accounting firm that audited our financial statements included in this report, has issued an attestation report on the Company's internal control over financial reporting, a copy of which appears on page 89 of this annual report.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. *OTHER INFORMATION*

None.

PART III

ITEM 10. *DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE*

The information required by this item is set forth under the captions *"Items to be Voted upon — 1. Election of Directors," "Executive Officers,"* and *"Corporate Governance"* in our definitive Proxy Statement for the 2021 Annual Meeting of Stockholders and incorporated herein by reference.

ITEM 11. *EXECUTIVE COMPENSATION*

The information required by this item is set forth under the captions *"Compensation Discussion and Analysis," "Summary Compensation Table," "Grants of Plan-Based Awards in 2020," "Outstanding Equity Awards at December 31, 2020," "2020 Option Exercises and Stock Vested," "Potential Payments Upon Termination or Change in Control," "2020 Director Compensation," "Compensation Committee Interlocks and Insider Participation," "Compensation Committee Report,"* and *"Delinquent Section 16(a) Reports"* in our definitive Proxy Statement for the 2021 Annual Meeting of Stockholders and incorporated herein by reference.

ITEM 12. *SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS*

The information required by this item is set forth under the captions *"Equity Compensation Plan Information"* and *"Security Ownership of Certain Beneficial Owners and Management"* in our definitive Proxy Statement for the 2021 Annual Meeting of Stockholders and incorporated herein by reference.

ITEM 13. *CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE*

The information required by this item is set forth under the captions *"Certain Relationships and Related Transactions"* and *"Corporate Governance"* in our definitive Proxy Statement for the 2021 Annual Meeting of Stockholders and incorporated herein by reference.

ITEM 14. *PRINCIPAL ACCOUNTING FEES AND SERVICES*

The information required by this item is set forth under the caption *"Items to be Voted upon — 2. Ratification of Appointment of Independent Registered Public Accountants"* in our definitive Proxy Statement for the 2021 Annual Meeting of Stockholders and incorporated herein by reference.

PART IV

ITEM 15. *EXHIBITS, FINANCIAL STATEMENT SCHEDULES*

(a) Financial Statements

The following financial statements appear in Item 8 of this Form 10-K:

	Page in Form 10-K
Consolidated Balance Sheets at December 31, 2020 and 2019	60
Consolidated Statements of Comprehensive Loss for the years ended December 31, 2020, 2019, and 2018	61
Consolidated Statements of Cash Flows for the years ended December 31, 2020, 2019, and 2018	62
Consolidated Statements of Stockholders' Equity for the years ended December 31, 2020, 2019, and 2018	63
Notes to Consolidated Financial Statements	64
Report of Independent Registered Public Accounting Firm on Consolidated Financial Statements	87
Report of Independent Registered Public Accounting Firm on Internal Control	89

No financial statement schedules are included because the information is either provided in the consolidated financial statements or is not required under the related instructions or is inapplicable and such schedules therefore have been omitted.

(b) Exhibits

Number	**Description**
3.1	Third Restated Certificate of Incorporation of BioCryst Pharmaceuticals, Inc. Incorporated by reference to Exhibit 3.1 to the Company's Form 8-K filed December 22, 2006.
3.2	Certificate of Amendment to the Third Restated Certificate of Incorporation of BioCryst Pharmaceuticals, Inc. Incorporated by reference to Exhibit 3.1 to the Company's Form 8-K filed July 24, 2007.
3.3	Certificate of Amendment to the Third Restated Certificate of Incorporation of BioCryst Pharmaceuticals, Inc. Incorporated by reference to Exhibit 3.1 to the Company's Form 8-K filed May 7, 2014.
3.4	Certificate of Increase of Authorized Number of Shares of Series B Junior Participating Preferred Stock. Incorporated by reference to Exhibit 3.1 to the Company's Form 8-K filed November 4, 2008.
3.5	Certificate of Increase of Authorized Number of Shares of Series B Junior Participating Preferred Stock. Incorporated by reference to Exhibit 3.2 to the Company's Form 8-K filed May 7, 2014.
3.6	Certificate of Elimination of the Series B Junior Participating Preferred Stock. Incorporated by reference to Exhibit 3.1 to the Company's Form 8-K filed May 13, 2020.
3.7	Certificate of Amendment to the Third Restated Certificate of Incorporation of BioCryst Pharmaceuticals, Inc. Incorporated by reference to Exhibit 3.2 to the Company's Form 8-K filed May 13, 2020.
3.8	Amended and Restated Bylaws of BioCryst Pharmaceuticals, Inc., effective October 29, 2008. Incorporated by reference to Exhibit 3.2 to the Company's Form 8-K filed November 4, 2008.
3.9	Amendment to Amended and Restated By-Laws of BioCryst Pharmaceuticals, Inc., effective January 21, 2018. Incorporated by reference to Exhibit 3.1 to the Company's Form 8-K filed January 22, 2018.
(4.1)	Description of Securities
4.2	Indenture, dated as of March 9, 2011 by and between JPR Royalty Sub LLC and U.S. Bank National Association, as trustee. Incorporated by reference to Exhibit 4.3 to the Company's Form 10-Q filed May 6, 2011.
4.3	Form of Pre-Funded Warrant to Purchase Common Stock, dated November 21, 2019. Incorporated by reference to Exhibit 4.1 to the Company's Form 8-K filed November 21, 2019.
4.4	Form of Pre-Funded Warrant to Purchase Common Stock, dated June 1, 2020. Incorporated by reference to Exhibit 4.1 to the Company's Form 8-K filed June 1, 2020.
10.1&	BioCryst Pharmaceuticals, Inc. Stock Incentive Plan (as amended and restated March 29, 2012). Incorporated by reference to Exhibit 10.1 of the Company's Form 8-K filed May 25, 2012.
10.2&	BioCryst Pharmaceuticals, Inc. Stock Incentive Plan (as amended and restated March 8, 2014). Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed May 5, 2014.
10.3&	BioCryst Pharmaceuticals, Inc. Stock Incentive Plan (as amended and restated May 23, 2016). Incorporated by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-8, filed May 23, 2016.
10.4&	BioCryst Pharmaceuticals, Inc. Stock Incentive Plan (as amended and restated April 3, 2017). Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed May 30, 2017.

10.5& BioCryst Pharmaceuticals, Inc. Stock Incentive Plan (as amended and restated September 17, 2018). Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed October 31, 2018.

10.6& BioCryst Pharmaceuticals, Inc. Stock Incentive Plan (as amended and restated as of April 12, 2019). Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed June 4, 2019.

10.7& BioCryst Pharmaceuticals, Inc. Amended and Restated Stock Incentive Plan (as amended and restated as of March 19, 2020). Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed May 13, 2020.

10.8& Form of Notice of Grant of Non-Employee Director Automatic Stock Option and Stock Option Agreement under the BioCryst Pharmaceuticals, Inc. Stock Incentive Plan. Incorporated by reference to Exhibit 10.4 to the Company's Form 10-K filed March 4, 2008.

10.9& Form of Notice of Grant of Stock Option and Stock Option Agreement under the BioCryst Pharmaceuticals, Inc. Stock Incentive Plan. Incorporated by reference to Exhibit 10.5 to the Company's Form 10-K filed March 4, 2008.

10.10& Standard Stock Option Agreement under the BioCryst Pharmaceuticals, Inc. Stock Incentive Plan. Incorporated by reference to Exhibit 10.7 to the Company's Form 10-K filed March 2, 2015.

10.11& Form of Notice of Grant of Restricted Stock Unit Award and Restricted Stock Unit Agreement under the BioCryst Pharmaceuticals, Inc. Stock Incentive Plan. Incorporated by reference to Exhibit 10.8 of the Company's Form 10-K filed March 2, 2015.

10.12& BioCryst Pharmaceuticals, Inc. Employee Stock Purchase Plan (as amended and restated as of March 19, 2020). Incorporated by reference to Exhibit 10.2 to the Company's Form 8-K filed May 13, 2020.

10.13& BioCryst Pharmaceuticals, Inc. Inducement Equity Incentive Plan (effective as of April 24, 2019). Incorporated by reference to Exhibit 99.1 to the Company's Form S-8 (File No. 333-231108) filed April 29, 2019.

10.14& BioCryst Pharmaceuticals, Inc. Inducement Equity Incentive Plan (as amended and restated February 7, 2020). Incorporated by reference to Exhibit 10.2 of the Company's Form 10-Q filed May 11, 2020.

10.15& BioCryst Pharmaceuticals, Inc. Inducement Equity Incentive Plan (as amended and restated July 17, 2020). Incorporated by reference to Exhibit 99.1 to the Company's Form S-8 (File No. 333-245024) filed August 12, 2020.

(10.16)& Form of Notice of Grant of Stock Option and Standard Stock Option Agreement under the BioCryst Pharmaceuticals, Inc. Inducement Equity Incentive Plan.

10.17& BioCryst Pharmaceuticals, Inc. Annual Incentive Plan (effective as of December 16, 2020). Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed December 17, 2020.

10.18& Executive Relocation Policy. Incorporated by reference to Exhibit 10.2 to the Company's Form 10-K filed March 4, 2008.

10.19& Amended and Restated Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and Jon P. Stonehouse, dated February 14, 2007. Incorporated by reference to Exhibit 10.12 to the Company's Form 10-K filed March 14, 2007.

10.20& Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and Thomas R. Staab II, dated May 23, 2011. Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed May 25, 2011.

10.21& Separation Agreement between BioCryst Pharmaceuticals, Inc. and Thomas R. Staab II, dated November 7, 2019. Incorporated by reference to Exhibit 10.18 to the Company's Form 10-K filed March 13, 2020.

10.22& Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and William P. Sheridan, dated June 12, 2008. Incorporated by reference to Exhibit 10.27 to the Company's Form 10-Q filed August 8, 2008.

10.23& Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and Yarlagadda S. Babu, dated April 27, 2012. Incorporated by reference to Exhibit 10.10 to the Company's Form 10-K filed March 10, 2014.

10.24& Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and Alane P. Barnes, dated August 8, 2013. Incorporated by reference to Exhibit 10.11 to the Company's Form 10-K filed March 10, 2014.

10.25& Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and Megan Sniecinski, dated May 31, 2019. Incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed August 8, 2019.

(10.26)& Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and Charles Gayer, dated January 14, 2020.

10.27& Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and Anthony Doyle, dated March 29, 2020. Incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed May 11, 2020.

(10.28)†* License, Development and Commercialization Agreement dated as of February 28, 2007, by and between the Company and Shionogi & Co., Ltd. Incorporated by reference to Exhibit 10.4 to the Company's Form 10-Q filed May 10, 2007.

(10.29)†* First Amendment to License, Development and Commercialization Agreement, effective as of September 30, 2008, between the Company and Shionogi & Co., Ltd. Incorporated by reference to Exhibit 10.19 to the Company's Form 10-K filed March 6, 2009.

10.30 Stock and Warrant Purchase Agreement dated as of August 6, 2007, by and among BioCryst Pharmaceuticals, Inc. and each of the Investors identified on the signature pages thereto. Incorporated by reference to Exhibit 4.1 of the Company's Form 8-K filed August 7, 2007.

10.31 Stock Purchase Agreement, dated as of February 17, 2005, by and among BioCryst Pharmaceuticals, Inc., Baker Bros. Investments, L.P., Baker Biotech Fund II, L.P., Baker Bros. Investments II, L.P., Baker Biotech Fund II (Z), L.P., Baker/Tisch Investments, L.P., Baker Biotech Fund III, L.P., Baker Biotech Fund I, L.P., Baker Biotech Fund III (Z), L.P. and 14159, L.P. Incorporated by reference to Exhibit 4.1 to the Company's Form 8-K filed February 17, 2005.

(10.32)†* License Agreement dated as of June 27, 2000, by and among Albert Einstein College of Medicine, Industrial Research, Ltd. and BioCryst Pharmaceuticals, Inc., as amended by the First Amendment Agreement dated as of July 26, 2002 and the Second Amendment Agreement dated as of April 15, 2005.

(10.33)†* Third Amendment Agreement by and among Albert Einstein College of Medicine, Industrial Research, Ltd. and BioCryst Pharmaceuticals, Inc., dated as of December 11, 2009.

10.34# Fourth Amendment Agreement by and among Albert Einstein College of Medicine, Industrial Research, Ltd. and BioCryst Pharmaceuticals, Inc., dated as of May 5, 2010. Incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed August 6, 2010. (Portions omitted pursuant to request for confidential treatment.)

(10.35)†* Fifth Amendment Agreement by and among Albert Einstein College of Medicine, Industrial Research, Ltd. and BioCryst Pharmaceuticals, Inc., dated as of November 17, 2011.

(10.36)†* Sixth Amendment Agreement by and among Albert Einstein College of Medicine, Industrial Research, Ltd. and BioCryst Pharmaceuticals, Inc., dated as of June 19, 2012.

10.37 Novation Agreement among Albert Einstein College of Medicine of Yeshiva University, BioCryst Pharmaceuticals, Inc., Mundipharma International Corporation Limited, Callaghan Innovation Research Limited, and Victoria Link Limited, dated May 18, 2015. Incorporated by reference to Exhibit 10.6 to the Company's Form 10-Q filed August 7, 2015.

10.38 Novation Agreement among Albert Einstein College of Medicine of Yeshiva University, BioCryst Pharmaceuticals, Inc., Callaghan Innovation Research Limited, and Victoria Link Limited, dated June 24, 2015. Incorporated by reference to Exhibit 10.7 to the Company's Form 10-Q filed August 7, 2015.

10.39 Purchase and Sale Agreement, dated as of March 9, 2011 between BioCryst Pharmaceuticals, Inc. and JPR Royalty Sub LLC. Incorporated by reference to Exhibit 10.1 of the Company's Form 10-Q filed May 6, 2011.

10.40 Pledge and Security Agreement, dated as of March 9, 2011 between BioCryst Pharmaceuticals, Inc. and U.S. Bank National Association, as trustee. Incorporated by reference to Exhibit 10.2 of the Company's Form 10-Q filed May 6, 2011.

10.41 Confirmation of terms and conditions of ISDA Master Agreement, dated as of March 7, 2011, between Morgan Stanley Capital Services Inc. and BioCryst Pharmaceuticals, Inc. dated as of March 9, 2011. Incorporated by reference to Exhibit 10.3 of the Company's Form 10-Q filed May 6, 2011.

10.42# Agreement, dated as of September 12, 2013, between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases. Incorporated by reference to Exhibit 10.2 of the Company's Form 10-Q filed November 8, 2013. (Portions omitted pursuant to request for confidential treatment.)

10.43# Amendment #1 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated December 26, 2013. Incorporated by reference to Exhibit 10.51 to the Company's Form 10-K filed on March 10, 2014. (Portions omitted pursuant to request for confidential treatment.)

10.44# Amendment #2 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated January 24, 2014. Incorporated by reference to Exhibit 10.52 to the Company's Form 10-K filed on March 10, 2014. (Portions omitted pursuant to request for confidential treatment.)

10.45# Amendment #3 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated June 17, 2014. Incorporated by reference to Exhibit 10.5 to the Company's Form 10-Q filed on August 8, 2014. (Portions omitted pursuant to request for confidential treatment.)

10.46# Amendment #4 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated June 17, 2014. Incorporated by reference to Exhibit 10.6 to the Company's Form 10-Q filed on August 8, 2014. (Portions omitted pursuant to request for confidential treatment.)

10.47# Amendment #5 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated August 11, 2014. Incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 7, 2014. (Portions omitted pursuant to request for confidential treatment.)

10.48# Amendment #6 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated August 27, 2014. Incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on November 7, 2014. (Portions omitted pursuant to request for confidential treatment.)

10.49# Amendment #8 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated September 17, 2014. Incorporated by reference to Exhibit 10.3 to the Company's Form 10-Q filed on November 7, 2014. (Portions omitted pursuant to request for confidential treatment.)

10.50# Amendment #9 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated October 29, 2014. Incorporated by reference to Exhibit 10.4 to the Company's Form 10-Q filed on November 7, 2014. (Portions omitted pursuant to request for confidential treatment.)

10.51# Amendment #10 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated February 13, 2015. Incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on August 7, 2015. (Portions omitted pursuant to request for confidential treatment.)

10.52# Amendment #11 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated March 19, 2015. Incorporated by reference to Exhibit 10.3 to the Company's Form 10-Q filed on August 7, 2015. (Portions omitted pursuant to request for confidential treatment.)

10.53# Amendment #12 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated June 12, 2015. Incorporated by reference to Exhibit 10.4 to the Company's Form 10-Q filed on August 7, 2015. (Portions omitted pursuant to request for confidential treatment.)

10.54# Amendment #13 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated June 17, 2015. Incorporated by reference to Exhibit 10.5 to the Company's Form 10-Q filed on August 7, 2015. (Portions omitted pursuant to request for confidential treatment.)

10.55# Amendment #14 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated September 16, 2015. Incorporated by reference to Exhibit 10.3 to the Company's Form 10-Q filed on November 6, 2015. (Portions omitted pursuant to request for confidential treatment.)

10.56 Amendment #15 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated November 16, 2015. Incorporated by reference to Exhibit 10.70 to the Company's Form 10-K filed on February 26, 2016.

10.57# Amendment #16 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated December 18, 2015. Incorporated by reference to Exhibit 10.71 to the Company's Form 10-K filed on February 26, 2016. (Portions omitted pursuant to request for confidential treatment.)

10.58 Amendment #17 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated April 18, 2016. Incorporated by reference to Exhibit 10.74 to the Company's Form 10-K filed on February 27, 2017.

10.59# Amendment #18 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated June 30, 2016. Incorporated by reference to Exhibit 10.3 to the Company's Form 10-Q filed on August 8, 2016. (Portions omitted pursuant to request for confidential treatment.)

10.60# Amendment #19 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated August 10, 2016. Incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 8, 2016. (Portions omitted pursuant to request for confidential treatment.)

10.61# Amendment #20 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated January 9, 2017. Incorporated by reference to Exhibit 10.77 to the Company's Form 10-K filed on February 27, 2017. (Portions omitted pursuant to request for confidential treatment.)

10.62# Amendment #21 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated March 21, 2018. Incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on May 9, 2018. (Portions omitted pursuant to request for confidential treatment.)

10.63 Amendment #22 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated September 10, 2018. Incorporated by reference to Exhibit 10.3 to the Company's Form 10-Q filed November 8, 2018.

10.64 Amendment #23 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated August 21, 2020. Incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed November 6, 2020.

10.65 Amendment #23 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated September 14, 2020. Incorporated by reference to Exhibit 10.3 to the Company's Form 10-Q filed November 6, 2020.

10.66†* Agreement, dated September 1, 2020, between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases. Incorporated by reference to Exhibit 10.4 to the Company's Form 10-Q filed November 6, 2020.

10.67†* Amendment #1 to the Agreement between BioCryst Pharmaceuticals, Inc. and the National Institute of Allergy and Infectious Diseases, dated October 14, 2020. Incorporated by reference to the Company's Form 10-Q filed November 6, 2020.

10.68# Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response, dated March 27, 2015. Incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on May 8, 2015. (Portions omitted pursuant to request for confidential treatment.)

10.69# Amendment #1 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response, dated June 2, 2015. Incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on August 7, 2015. (Portions omitted pursuant to request for confidential treatment.)

10.70# Amendment #2 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response, dated July 8, 2015. Incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 6, 2015. (Portions omitted pursuant to request for confidential treatment.)

10.71# Amendment #3 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response, dated August 25, 2015. Incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on November 6, 2015. (Portions omitted pursuant to request for confidential treatment.)

10.72# Amendment #4 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response, dated February 25, 2016. Incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on May 9, 2016. (Portions omitted pursuant to request for confidential treatment.)

10.73# Amendment #5 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response, dated April 11, 2016. Incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on August 8, 2016. (Portions omitted pursuant to request for confidential treatment.)

10.74# Amendment #6 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response, dated May 20, 2016. Incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on August 8, 2016. (Portions omitted pursuant to request for confidential treatment.)

10.75# Amendment #7 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response, dated September 26, 2016. Incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on November 8, 2016. (Portions omitted pursuant to request for confidential treatment.)

10.76 Amendment #8 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the

Assistant Secretary for Preparedness and Response, dated September 20, 2017. Incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 8, 2017.

10.77# Amendment #9 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response, dated December 1, 2017. Incorporated by reference to Exhibit 10.88 to the Company's Form 10-K filed on March 12, 2018.

10.78 Amendment #10 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response, dated March 19, 2018. Incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 8, 2018.

10.79 Amendment #11 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response, dated September 20, 2018. Incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on November 8, 2018. (Portions omitted pursuant to request for confidential treatment.)

10.80†* Amendment #12 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness Response, dated April 17, 2020. Incorporated by reference to Exhibit 10.3 to the Company's Form 10-Q filed August 7, 2020.

10.81 Amendment #13 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness Response, dated September 29, 2020. Incorporated by reference to Exhibit 10.8 to the Company's Form 10-Q filed November 6, 2020.

(10.82) Amendment #14 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness Response, dated November 24, 2020.

10.83 Registration Rights Agreement, dated March 15, 2017, by and between BioCryst Pharmaceuticals, Inc. 667, L.P., and Baker Brothers Life Sciences, L.P. Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed March 17, 2017.

10.84 Amendment to the Registration Rights Agreement, dated January 21, 2018, by and among BioCryst Pharmaceuticals, Inc., 667, L.P. and Baker Brothers Life Sciences, L.P. Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed January 22, 2018.

10.85 Securities Purchase Agreement, dated November 19, 2019, among BioCryst Pharmaceuticals, Inc., Baker Brothers Life Sciences, L.P. and 667, L.P. Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed on November 20, 2019.

10.86 Agreement dated as of September 1, 2018 between BioCryst Pharmaceuticals, Inc. and the Centers for Disease Control and Prevention. Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed on September 6, 2018.

(10.87) Amendment #1 to Agreement between BioCryst Pharmaceuticals, Inc. and the Centers for Disease Control and Prevention, dated October 1, 2018, assigning contract administration to ASPR-BARDA within the U.S. Department of Health and Human Services.

10.88 Amendment #2 to Agreement between BioCryst Pharmaceuticals, Inc. and the U.S. Department of Health and Human Services, dated September 23, 2019. Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed on September 26, 2019.

10.89	Amendment #3, dated August 31, 2020, to the Contract dated September 1, 2018 between BioCryst Pharmaceuticals, Inc. and the U.S. Department of Health and Human Services. Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed September 3, 2020.
10.90†*	Commercialization and License Agreement dated as of November 5, 2019 between BioCryst Pharmaceuticals, Inc. and Torii Pharmaceutical Co., Ltd. Incorporated by reference to Exhibit 10.83 to the Company's Form 10-K filed March 13, 2020.
(10.91)†*	Purchase and Sale Agreement, dated as of December 7, 2020, between BioCryst Pharmaceuticals, Inc. and RPI 2019 Intermediate Finance Trust.
(10.92)†*	Credit Agreement, dated as of December 7, 2020, among BioCryst Pharmaceuticals, Inc., as borrower, BioCryst Ireland Limited, as a guarantor, the other guarantors from time to time party thereto, the lenders from time to time party thereto, and Athyrium Opportunities III Co-Invest 1 LP, as lender and as administrative agent for the lenders.
(21)	Subsidiaries of the Registrant.
(23)	Consent of Ernst & Young, LLP, Independent Registered Public Accounting Firm.
(31.1)	Certification of the Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
(31.2)	Certification of the Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
(32.1)	Certification of the Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
(32.2)	Certification of the Chief Financial Officer pursuant to 18.U.S.C. Section 1350, as adopted pursuant to section 906 of the Sarbanes-Oxley Act of 2002.
(101)	Financial statements from the Annual Report on Form 10-K of BioCryst Pharmaceuticals, Inc. for the fiscal year ended December 31, 2020, formatted in Inline XBRL: (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Comprehensive Loss, (iii) Consolidated Statements of Cash Flows, (iv) Consolidated Statements of Stockholders' Equity and (v) Notes to Consolidated Financial Statements.
(104)	Cover Page Interactive Data File – The cover page from this annual report on Form 10-K for the fiscal year ended December 31, 2020 is formatted in Inline XBRL (contained in Exhibit 101).

#	Confidential treatment granted.
†	Portions of this exhibit have been omitted pursuant to Item 601(b)(10) of Regulation S-K. The Company agrees to furnish to the Securities and Exchange Commission a copy of any omitted portions of the exhibit upon request.
*	Certain identified information has been excluded from this exhibit because it is both not material and would likely cause competitive harm to the Company if publicly disclosed.
&	Management contracts.
( )	Filed herewith.

ITEM 16. ***FORM 10-K SUMMARY.***

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized on March 1, 2021.

BIOCRYST PHARMACEUTICALS, INC.

By: /s/ Jon P. Stonehouse
Jon P. Stonehouse
Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities indicated on March 1, 2021:

Signature	**Title(s)**
/s/ Jon P. Stonehouse Jon P. Stonehouse	President, Chief Executive Officer and Director (Principal Executive Officer)
/s/ Anthony Doyle Anthony Doyle	Senior Vice President and Chief Financial Officer (Principal Financial Officer)
/s/ Michael L. Jones Michael L. Jones	Executive Director, Finance and Principal Accounting Officer (Principal Accounting Officer)
/s/ George B. Abercrombie George B. Abercrombie	Director
/s/ Stephen Aselage Stephen Aselage	Director
/s/ Theresa Heggie Theresa Heggie	Director
/s/ Nancy Hutson Nancy Hutson, Ph.D.	Director
/s/ Robert A. Ingram Robert A. Ingram	Director
/s/ Kenneth B. Lee, Jr. Kenneth B. Lee, Jr.	Director
/s/ Alan G. Levin Alan G. Levin	Director
/s/ Helen Thackray Helen Thackray, M.D.	Director