

**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, 2022

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

BIOCRIST PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation or organization)

62-1413174
(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	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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.

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b).

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, 2022 (based upon the closing price shown on the Nasdaq Global Select Market on June 30, 2022) held by non-affiliates was \$1,949,284,603.

The number of shares of Common Stock, par value \$0.01, of the registrant outstanding as of January 31, 2023 was 188,451,137 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 2023 annual meeting of stockholders are incorporated by reference into Items 10, 11, 12, 13, and 14 under Part III hereof.

TABLE OF CONTENTS

	<u>Page No.</u>
Cautionary Note Regarding Forward-Looking Statements	1
Risk Factor Summary	2
 PART I	
ITEM 1. BUSINESS	4
ITEM 1A. RISK FACTORS	23
ITEM 1B. UNRESOLVED STAFF COMMENTS	51
ITEM 2. PROPERTIES	51
ITEM 3. LEGAL PROCEEDINGS	51
ITEM 4. MINE SAFETY DISCLOSURES	51
 PART II	
ITEM 5. MARKET FOR REGISTRANT’S COMMON EQUITY, RELATED STOCKHOLDER MATTERS, AND ISSUER PURCHASES OF EQUITY SECURITIES	52
ITEM 6. RESERVED	53
ITEM 7. MANAGEMENT’S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS	53
ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK	65
ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA	67
ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE	104
ITEM 9A. CONTROLS AND PROCEDURES	104
ITEM 9B. OTHER INFORMATION	105
ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS	105
 PART III	
ITEM 10. DIRECTORS, EXECUTIVE OFFICERS, AND CORPORATE GOVERNANCE	105
ITEM 11. EXECUTIVE COMPENSATION	105
ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS	105
ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE	105
ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES	105
 PART IV	
ITEM 15. EXHIBIT AND FINANCIAL STATEMENT SCHEDULES	106
ITEM 16. FORM 10-K SUMMARY	111
SIGNATURES	112
 EX-10.25	
EX-21	
EX-23	
EX-31.1	
EX-31.2	
EX-32.1	
EX-32.2	

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When used in this report, unless otherwise indicated, “we,” “our,” “us,” the “Company,” and “BioCryst” refer to BioCryst Pharmaceuticals, Inc. and, where appropriate, its subsidiaries.

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 (the “Exchange Act”), 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, BCX10013, BCX9250, peramivir, galidesivir, and early stage discovery programs, and our plans regarding the same;
- the timing and success of our commercialization of ORLADEYO in the United States and elsewhere and expectations regarding the commercial market for ORLADEYO;
- 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 closing out or expiration of our contracts with the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services (“BARDA/HHS”) and the National Institute of Allergy and Infectious Diseases within the HHS (“NIAID/HHS”) for the development of galidesivir;
- additional regulatory approvals, or milestones, royalties or profit from sales of our products by us or our partners;
- the implementation of our business model, strategic plans for our business, products, product candidates and technology;
- our ability to establish and maintain collaborations or out-license rights to our products and product candidates;
- plans, programs, progress and potential success of our collaborations, including with Torii Pharmaceutical Co., Ltd. (“Torii”) for ORLADEYO in Japan and Shionogi & Co., Ltd. (“Shionogi”) and Green Cross Corporation (“Green Cross”) for peramivir in their territories;
- our and our subsidiary guarantors’ ability to satisfy obligations under our Credit Agreement (as defined below) and to comply with the covenants as set forth in the agreements governing our debt obligations;
- 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 revenues, expenses, capital requirements, annual cash utilization, and our needs for additional financing;
- the timing or likelihood of regulatory filings or regulatory agreements, deferrals, approvals, and other decisions;
- 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 SEC, before making an investment decision 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 as and when needed, we may need to adjust our operations.
- Our success depends upon our ability to manage our product candidate pipeline, advance our product candidates through the various stages of development, especially through the clinical trial process, and to receive and maintain regulatory approvals for the commercial sale of our product candidates. 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, withdraw approval for our products, or take other actions that could materially impact the cost, timing, and success of our planned development and commercialization 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 establish and 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 as and when needed, 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 either were not previously identified or worse than expected, 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 have expanded, and may 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, develop our product candidates, obtain collaborators, and raise capital.
- If we fail to adequately protect or enforce our intellectual property rights, 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. If we fail to secure the rights to patents of others, this could adversely affect our business.
- We face an inherent risk of liability in the event that the use or misuse of our products or product candidates results in personal injury or death, and our product liability insurance coverage may be insufficient.
- We face risks related to our government-funded programs and are subject to various U.S. Government contract requirements, which typically contain a number of extraordinary provisions that would not typically be found in commercial contracts and which may create a disadvantage and additional risks to us as compared to competitors that do not rely on U.S. Government contracts.
- If we fail to reach milestones or to make annual minimum payments or otherwise breach our obligations under our license agreements, our licensors may terminate our agreements with them and/or seek additional remedies.
- Our Credit Agreement contains conditions and restrictions that limit our flexibility 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, legal, regulatory, political, operational, financial, and economic risks. For example, our actual or perceived failure to comply with European governmental laws and 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 or our third-party information technology systems or a cybersecurity breach could adversely affect our business.
- Our existing principal stockholders hold a substantial amount of our common stock and may be able to influence significant corporate decisions, which may conflict with the interests of other stockholders.
- Our stock price has been, and is likely to continue to be, highly volatile, which could cause the value of an investment in our common stock to decline significantly.
- Natural disasters, epidemic or pandemic disease outbreaks, trade wars, armed conflicts, 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.
- Our business, operations, clinical development or commercialization plans and timelines, and access to capital could be adversely affected by unpredictable and unstable market and economic conditions.
- We are subject to legal proceedings, which could harm our reputation or result in other losses or unexpected expenditure of time and resources.
- If we fail to retain our existing key personnel or fail to attract and retain additional key personnel, the development of our product candidates, the commercialization of our products, and the related expansion of our business will be delayed or stopped.

PART I

ITEM 1. BUSINESS

Our Business

We are a commercial-stage biotechnology company that discovers and commercializes 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 that are commercially available or that are in active development are summarized in the table below and are discussed in further detail under “Products and Product Candidates” in this “Part I—Item 1—Business” section of this report.

Drug/Drug Candidate	Drug Class	Therapeutic Area(s)	Phase	Rights*
ORLADEYO® (berotralstat)	Oral Serine Protease Inhibitor Targeting Kallikrein (once-daily treatment)	Hereditary angioedema	Approved (United States and multiple global markets)	BioCryst (worldwide, except Japan); Torii Pharmaceutical Co., Ltd. (Japan)
	Oral Serine Protease Inhibitor Targeting Kallikrein (once-daily treatment for patients who are 2 to <12 years of age)	Hereditary angioedema	Phase 3	BioCryst (worldwide, except Japan); Torii Pharmaceutical Co., Ltd. (Japan)
BCX10013	Oral Factor D Inhibitor	Complement-mediated diseases	Phase 1	BioCryst (worldwide)
RAPIVAB® (peramivir injection)	Intravenous Neuraminidase Inhibitor	Acute uncomplicated Influenza	Approved (United States, 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)

* See “Business—Collaborations and In-License Relationships” for a description of our relationships with the third parties identified in this column.

In addition to the molecules referenced in the table above, we are pursuing oral medicines directed at other targets across the classical, lectin and terminal pathways of the complement system, including C2, a critical upstream serine protease enzyme for activation of the classical and lectin pathways. See “Business—Products and Product Candidates—Complement-Mediated Diseases” below for additional details.

Business Strategy

Our business strategy is twofold: to serve patients and 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. We are unique in our 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 structural 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 progress our product candidates efficiently 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. By 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 other global markets for the commercialization of ORLADEYO, and we are continuing to build the structure and expertise to commercialize our products in additional markets where we believe we can do this efficiently and effectively. We have also established relationships with licensing, distribution and other partners in certain markets, including Japan, the pan-Latin America region, and parts of Europe and Asia, and will continue to seek such relationships where we determine this to be an effective approach.

Products and Product Candidates

ORLADEYO (Berotralstat)

ORLADEYO is an oral, once-daily therapy discovered and developed by us for the prevention of hereditary angioedema (“HAE”) attacks. 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 suppresses bradykinin production. Bradykinin is the mediator of acute swelling attacks in HAE patients.

ORLADEYO 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. Our specialty pharmacy provider for ORLADEYO in the United States began shipping ORLADEYO to patients with a prescription in the United States in December 2020. 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 supports access for each patient with comprehensive financial support tools and reimbursement support.

In 2021, we announced that ORLADEYO received approvals in the European Union, Japan, the United Arab Emirates (“UAE”) and the United Kingdom. Under our agreement with Torii, our collaborative partner commercializing ORLADEYO in Japan, we are entitled to receive tiered royalty payments, ranging from 20% to 40% of net sales of ORLADEYO in Japan during each calendar year. See “Collaborations and In-License Relationships” below for a description of our relationship with Torii.

On January 10, 2022, we announced that ORLADEYO is now covered by all major payors and national and regional pharmacy benefit managers in the United States.

On February 24, 2022, we announced new long-term efficacy and safety data from the APeX-2 clinical trial evaluating ORLADEYO for the prophylactic treatment of HAE showing sustained reductions in attack rates and improvement in quality of life among patients living with HAE, regardless of their baseline attack rates and initial responses to ORLADEYO.

On June 6, 2022, we announced that Health Canada approved ORLADEYO for the routine prevention of recurrent HAE attacks in patients 12 years and older in Canada.

On June 7, 2022, we announced that Swissmedic granted marketing authorization for ORLADEYO for the routine prevention of recurrent HAE attacks in patients 12 years and older in Switzerland.

On June 9, 2022, we announced that the Company entered into an exclusive collaboration with Pint Pharma GmbH (“Pint Pharma”) to register and promote ORLADEYO in the pan-Latin America region. Under the terms of the agreement, Pint Pharma will be responsible for obtaining and maintaining all marketing authorizations and for commercializing ORLADEYO in the region.

On July 1, 2022, we announced new long-term efficacy and safety data from the APeX-2 and APeX-S clinical trials evaluating ORLADEYO for the prophylactic treatment of HAE showing sustained reductions in attack rates and improvement in quality of life among patients living with HAE, as well as improved management of symptoms after switching to ORLADEYO from an injectable long-term prophylactic treatment.

On August 4, 2022, we announced that pricing for ORLADEYO was finalized in Germany, France, and Switzerland in the second quarter of 2022.

On August 18, 2022, we announced that the Saudi Food and Drug Authority approved ORLADEYO to prevent attacks of HAE in adults and pediatric patients 12 years of age and older in Saudi Arabia.

On November 10, 2022, we announced new real-world data demonstrating rapid, sustained reduction of patient-reported HAE attacks and consistently low attack rates among patients 12 years and older who started on ORLADEYO for the prophylactic treatment of HAE, including patients who switched from other prophylactic therapies.

On November 28, 2022, we announced that the Israeli Ministry of Health granted marketing authorization for ORLADEYO to prevent attacks of HAE in adults and pediatric patients 12 years of age and older in Israel.

On January 23, 2023, we announced that the Company entered into a collaboration with Swixx BioPharma AG (“Swixx”) to commercialize ORLADEYO in Central and Eastern Europe (“CEE”). Under the terms of the agreement, Swixx will be responsible for commercializing ORLADEYO in 15 markets within CEE.

On January 26, 2023, we announced the enrollment of the first patient in the pivotal APeX-P trial evaluating ORLADEYO in pediatric HAE patients who are 2 to <12 years of age.

On February 21, 2023, we announced that the Canadian Agency for Drugs and Technologies in Health Canadian Drug Expert Committee has recently issued a final draft positive recommendation for ORLADEYO to be reimbursed for the routine prevention of HAE attacks in adults and pediatric patients 12 years of age and older.

On each of December 7, 2020 and November 19, 2021, we entered into a Purchase and Sale 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 (the “RPI Royalty Purchase Agreements”). On November 19, 2021, we also entered into a Purchase and Sale Agreement (the “OMERS Royalty Purchase Agreement” and, collectively with the RPI Royalty Purchase Agreements, the “Royalty Purchase Agreements”) with OCM IP Healthcare Holdings Limited, an affiliate of OMERS Capital Markets (“OMERS”), pursuant to which we sold to OMERS the right to receive certain royalty payments from the Company. The transactions contemplated under the Royalty Purchase Agreements are referred to herein as the “Royalty Sales.” See “Note 8—Royalty Monetizations—ORLADEYO and Factor D Inhibitors” 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 Agreements.

We have built out our U.S. commercial infrastructure to support the launch and continued commercialization of ORLADEYO in the United States and are continuing to build our commercial infrastructure to support launches in other markets. Based on proprietary analyses of HAE prevalence and market research studies with HAE patients, physicians, and payors in the United States and Europe, and two full years of commercialization experience with ORLADEYO in the United States in 2021 and 2022, we anticipate the global commercial market for ORLADEYO has the potential to reach a global peak of \$1 billion in annual net ORLADEYO revenues. We expect at least 70 to 80 percent of our revenue at peak to come from the United States. 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 or our partners’ 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 goal of our overall complement program is to advance several compounds across multiple pathways in the complement system to treat many 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.

BCX9930

BCX9930 is a novel, oral, potent, and selective small molecule inhibitor of Factor D, discovered by us for the treatment of complement-mediated diseases. On December 15, 2022, we announced that, based on new competitive data recently presented at the American Society of Hematology annual meeting, we no longer believe that BCX9930 would be commercially competitive, and we are discontinuing the development of BCX9930. This decision allows us to focus our complement inhibitor development efforts fully on BCX10013, a potential once-daily, oral Factor D (alternative pathway) inhibitor currently in clinical development and pursue additional oral compounds for multiple targets across other complement pathways.

BCX10013

On November 1, 2022, we announced that we have begun a clinical program with BCX10013, a novel, potent, and specific Factor D inhibitor. On January 9, 2023, we announced that initial data from ongoing phase 1 single ascending dose and multiple ascending dose trials in healthy volunteers showed rapid, sustained and >97 percent

suppression of the alternative pathway of the complement system 24 hours following a single 110 mg dose, and that BCX10013 has been safe and generally well-tolerated at all doses studied to date. On February 21, 2023, we announced that recent dose-related observations in an ongoing BCX10013 nonclinical study will delay the clinical program.

Under the RPI Royalty Purchase Agreements, RPI will be entitled to receive tiered, sales-based royalties on net product sales, if any, of BCX10013, as well as tiered, profit share amounts of up to 3.0% from certain other permitted sales in certain markets. See “Note 8—Royalty Monetizations—ORLADEYO and Factor D Inhibitors” in the Notes to Consolidated Financial Statements in Part II, Item 8 of this report for additional information about our obligations under the RPI Royalty Purchase Agreements.

Additional Complement Targets

On November 1, 2022, we announced that, in addition to BCX10013, which targets the alternative pathway of complement, we are pursuing oral medicines directed at other targets across the classical, lectin and terminal pathways of the complement system, including C2, a critical upstream serine protease enzyme for activation of the classical and lectin pathways. We have developed potent, selective molecules targeting C2, which are currently in lead optimization.

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. There is no cure for this condition, and there are no approved treatments for FOP in the United States.

On November 1, 2022, we announced that we believe that patients with FOP are likely to benefit from other oral ALK-2 inhibitors that currently are substantially ahead of our ALK-2 inhibitor, BCX9250, in development. Considering the expectation that patients will be well-served by these other products, and the approximately \$100 million in additional investment that would be required to advance BCX9250 to approval, we are stopping the BCX9250 program and redirecting this investment to the other opportunities we have to serve patients with complement-mediated diseases.

Peramivir Injection (RAPIVAB, RAPIACTA, 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, 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, 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 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 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 initially delivered 20,000 doses of RAPIVAB under this contract in 2019 for a total price of approximately \$13.9 million. We further delivered 20,000 and 9,980 doses of RAPIVAB in 2022 and 2021, respectively, and recorded revenue of \$13.9 million and \$6.9 million for the years ending December 31, 2022 and December 31, 2021, respectively. As of December 31, 2022, we have delivered a total of 49,980 RAPIVAB doses of the 50,000 RAPIVAB doses available under the contract, effectively completing the contract with HHS.

Galidesivir (BCX4430)

Galidesivir is a broad-spectrum antiviral 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 has been substantially funded with federal funds under contracts with the National Institute of Allergy and Infectious Diseases within the HHS (“NIAID/HHS”) and BARDA/HHS. All of our government funding for galidesivir expired in 2022, and we have no plans to continue the galidesivir program without government funding.

Collaborations and In-License Relationships

ORLADEYO

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. We received an additional milestone payment of \$15.0 million in the second quarter of 2021 upon receipt from the Japanese National Health Insurance System (“NHI”) of a reimbursement price approval for ORLADEYO.

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 commenced 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 are responsible for supplying Torii with its required amounts of ORLADEYO. The activities of the parties pursuant to the Torii Agreement are overseen by a joint steering committee, 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.

Other Collaborations for ORLADEYO

We have entered into a number of collaborations with commercial partners to help support the global launch of ORLADEYO. In 2021, we entered into supply and distribution agreements with Neopharm Ltd. (“Neopharm”) and NewBridge Pharmaceuticals (“NewBridge”) to support commercialization efforts in Israel and the UAE, respectively. Under the terms of these agreements, Neopharm will have the exclusive rights to commercialize ORLADEYO in Israel and the Palestinian Authority, and NewBridge will support commercialization efforts in the UAE, as well as the Gulf Cooperation Council and Iraq. On June 9, 2022, we announced that we have entered into an exclusive collaboration with Pint Pharma to register and promote ORLADEYO in the pan-Latin America region. Under the terms of the agreement, Pint Pharma will be responsible for obtaining and maintaining all marketing authorizations and for commercializing ORLADEYO in the region. On January 23, 2023, we announced that we have entered into a collaboration with Swixx to commercialize ORLADEYO in CEE. Under the terms of the agreement, Swixx will be responsible for commercializing ORLADEYO in 15 markets within CEE.

Peramivir Injection (RAPIVAB, RAPIACTA, PERAMIFLU)

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. The Shionogi Agreement provided for an upfront payment in exchange for the rights to injectable formulations of peramivir in Japan, development milestone payments (which have all been paid), commercial milestone payments, and royalty payments on product sales of peramivir, in accordance with the terms of the Shionogi Agreement.

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, JPR Royalty Sub LLC, a wholly-owned subsidiary of the Company (“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.

Principal and interest on the PhaRMA Notes are payable from, and are secured by the rights to royalty and milestone payments under the Shionogi Agreement, which were transferred by us to Royalty Sub in 2011. 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.

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 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. 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. Due to the non-recourse nature of the PhaRMA Notes, 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. See “Risk Factors—Risks Relating to Our Business—Risks Relating to Contractual Arrangements—Because continuing events of default exist under the PhaRMA Notes, the holders of the PhaRMA Notes may be able to foreclose on the collateral securing the PhaRMA Notes and our equity interest in Royalty Sub. As a result, we may not realize the benefit of future royalty payments, if any, that might otherwise accrue to us following repayment of the PhaRMA Notes and we could otherwise be adversely affected” in Part I, Item 1A of this report for further discussion of the continuing events of default under the PhaRMA Notes.

As of December 31, 2022, the PhaRMA Notes remained in default. We wrote off the balance due under the PhaRMA Notes to other income as a debt extinguishment as of December 31, 2021. See “Note 8—Royalty Monetizations—RAPIACTA—Non-Recourse Notes Payable—Debt Extinguishment” in the Notes to Consolidated Financial Statements in Part II, Item 8 of this report for additional information about the write-off.

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 and we are entitled to 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.

Additional Collaborations

We have previously entered into contracts with the U.S. Government, including the procurement contract with HHS for 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 and contracts with NIAID/HHS and BARDA/HHS for the development of galidesivir, as more fully discussed above under “Products and Product Candidates” and in “Note 15—Collaborative and Other Relationships” in the Notes to Consolidated Financial Statements in Part II, Item 8 of this report. As of December 31, 2022, we have delivered a total of 49,980 RAPIVAB doses of the 50,000 RAPIVAB doses available under the procurement contract, effectively completing the contract with HHS, and all of our government funding for galidesivir has expired.

We also have non-material license agreements with certain 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 that we make certain payments related to development of the product candidates covered by these agreements, net sales on any resulting product made by us, and annual license fees. We licensed a series of potent inhibitors of Purine Nucleoside Phosphorylase from AECOM and IRL, as well as an exclusive worldwide license of galidesivir for any antiviral use, and we have agreements with UAB for influenza neuraminidase and complement inhibitors. 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.

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, 2022, we have been issued approximately 31 U.S. patents that expire between 2023 and 2039 and that relate to our kallikrein inhibitor compounds, neuraminidase inhibitor compounds, broad-spectrum

antiviral (“BSAV”) compounds, purine nucleoside phosphorylase (“PNP”) inhibitor compounds, and complement-mediated disease program 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 25 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. Our commercial potential could also be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than products that we may develop. Any of these competitive factors may impact our decisions with respect to our products, product candidates and early-stage discovery programs. See “Risk Factors—Risks Relating to Our Business—Risks Relating to Competing in our Industry” in Part I, Item 1A of this report for further discussion of these risks.

In order to compete successfully, 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.

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) and generic icatibant are indicated for the treatment of acute attacks and is administered by subcutaneous administration.
- 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:

<u>Company</u>	<u>Asset</u>	<u>Mechanism of Action</u>	<u>Route of Administration</u>	<u>Trial Phase</u>	<u>Role in Therapy</u>
KalVista	Sebetralstat	Kallikrein inhibitor	Oral	III	Acute treatment
Pharvaris	PHA121 (PHVS416/PHVS719)	B2 receptor antagonist	Oral	II/III	Acute and Prophylaxis
Attune	ATN-249	Kallikrein inhibitor	Oral	I	Prophylaxis
CSL	Garadacimab	Anti-factor XII mAb	IV/Subcutaneous	III	Prophylaxis
Ionis	Donidalorsen	Prekallikrein Antisense	Subcutaneous	III	Prophylaxis
Astria	STAR-0215	Kallikrein inhibitor	Subcutaneous	Ia	Prophylaxis
ADARx	ADX-324	siRNA	Subcutaneous	I	Prophylaxis
Intellia	NTLA-2002	Gene Therapy	IV	I/II	
BioMarin	BMN-331	Gene Therapy	IV	I/II	

Complement-Mediated Diseases

Several rare diseases are known to be mediated by defects of the complement system, including, but not limited to, paroxysmal nocturnal hemoglobinuria (“PNH”), atypical hemolytic uremic syndrome (“aHUS”), complement 3 glomerulopathy (“C3G”), Immunoglobulin A Nephropathy (“IgAN”), and myasthenia gravis. Alexion’s (part of AstraZeneca Rare Disease) Soliris® (eculizumab) is a C5 inhibitor approved for PNH, aHUS, myasthenia gravis, and neuromyelitis optica spectrum disorder. Soliris had global sales of over \$3.7 billion in 2022. Alexion also 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 over \$1.9 billion in 2022. Apellis Pharmaceuticals, Inc.’s Empaveli® is a C3 inhibitor approved for PNH in the United States and Europe in 2021.

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	Empaveli	C3 Inhibitor	Subcutaneous	Approved
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 Inhibitor	IV / Subcutaneous	BLA
	OMS906	MASP-3 Inhibitor	Subcutaneous	I
AstraZeneca	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	Tavneos (avacopan)	C5aR Inhibitor	Oral	Approved
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.

Certain diseases that are mediated by defects of the complement system, such as IgAN, may also have pathology that is mediated by other mechanisms. Products that are not inhibitors of the complement system, such as Tarpeyo (DR-budesonide) for IgAN, may change the treatment landscape and future competitive environment for our products.

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 United States and/or other countries, 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.

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.

Government Regulation

Our business is subject to extensive regulation by the FDA and foreign governments. These regulations include, among other things, regulations for the development, testing, manufacture, safety, efficacy, record-keeping, labeling, storage, approval, advertising, promotion, sale and distribution of pharmaceutical products. 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. Further, the duration of the approval process may be exacerbated by global health concerns or other considerations that could prevent regulatory authorities from conducting their inspections, reviews, or other regulatory activities that could significantly impact the ability of such authorities to timely review and process our regulatory submissions.

Even if the FDA or foreign regulatory authorities approve a product candidate, the approval may limit the indicated uses for the product candidate, impose other restrictions on the product candidate, and/or may require post-approval studies that could impair the commercial viability of the product candidate. Even upon any approval to market our potential products, whether in the United States or internationally, we will continue to be subject to extensive regulatory requirements. These requirements are wide ranging and govern, among other things:

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

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 or any foreign regulatory authority 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 policies of the FDA and foreign regulatory authorities may change, and additional government regulations may be enacted that 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 investigational 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, pharmacokinetic, 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 upon many 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 a 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. The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities.

Approved drugs that are manufactured or distributed in the United States pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion, and reporting of adverse experiences with the product. For example, 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.

After approval, most changes to the approved product, such as adding new indications or other labeling claims and some manufacturing and supplier changes, are subject to prior FDA review and approval. The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including phase 4 clinical trials, and surveillance programs to further assess and monitor the product's safety and effectiveness after commercialization.

We and all of our contract manufacturers are also required to comply with the applicable FDA current Good Manufacturing Practice ("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.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation, if sought, must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA applicant with FDA orphan drug designation for a particular active ingredient to receive FDA approval of the designated drug for the disease indication for which it has such designation is entitled to a seven-year exclusive marketing period ("orphan drug exclusivity") in the United States for that product, for that indication. During the seven-year period, the FDA may not finally approve any other applications to market the same drug for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the license holder cannot supply sufficient quantities of the product. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition, provided that the sponsor has conducted appropriate clinical trials required for approval. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee for the orphan indication.

Fast Track Designation

Under the Fast Track program, the sponsor of an IND may request the FDA to designate the drug candidate as a Fast Track drug if it is intended to treat a serious condition and fulfill an unmet medical need. The FDA must determine if the drug candidate qualifies for Fast Track designation within 60 days of receipt of the sponsor's request. Once the FDA designates a drug as a Fast Track candidate, it is required to facilitate the development and expedite the review of that drug by providing more frequent communication with, and guidance to, the sponsor.

In addition to other benefits, such as greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track drug's NDA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's review period as specified under the Prescription Drug User Fee Act for filing and reviewing an application does not begin until the last section of the NDA has been submitted. Additionally, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

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, commercial sales, and distribution of 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, some of which are discussed below, and may also include post-approval commitments.

European Union

The various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Pursuant to the Clinical Trials Directive 2001/20/EC, as amended (the “Clinical Trials Directive”), a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, approval must be obtained from the national competent authority of each EU member state in which a clinical trial is planned to be conducted. A clinical trial application (“CTA”) is submitted, which must be supported by an investigational medicinal product dossier and further supporting information prescribed by the Clinical Trials Directive and other applicable guidance documents, including, but not limited to, the clinical trial protocol. Further, a clinical trial may only be started after an independent ethics committee has issued a favorable opinion on the CTA in that country.

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014 (the “Regulation”), which is set to replace the current Clinical Trials Directive. The Regulation came into effect on January 31, 2022 with a three-year transition period in which clinical trial sponsors will be able to choose among different submission pathways. The Regulation, which is directly applicable in all EU member states, aims to simplify and streamline the approval of clinical trials in the European Union. For instance, the Regulation provides for a streamlined application procedure via a single entry point and strictly defined deadlines for the assessment of clinical trial applications.

Manufacturing and import into the European Union of investigational medicinal products for use in clinical trials is subject to the holding of appropriate authorizations and must be carried out in accordance with cGMP.

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. Under the centralized procedure, a single marketing authorization application is submitted to the Committee for Medicinal Products for Human Use of the European Medicines Agency (“EMA”), which then makes a recommendation to the European Commission (“EC”). The EC makes the final determination on whether to approve the application. 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.

United Kingdom

The United Kingdom’s exit from the European Union, 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. Since January 1, 2021, the Medicines and Healthcare products Regulatory Agency (“MHRA”) is the United Kingdom’s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules apply in Northern Ireland than in England, Wales and Scotland (together, Great Britain or “GB”). Northern Ireland continues to follow the EU regulatory regime, but its national competent authority remains the MHRA. The MHRA published a draft guidance on how various aspects of the U.K. regulatory regime for medicines will operate in GB and in Northern Ireland following the expiration of the Brexit transition period on December 31, 2020. The guidance includes clinical trials, marketing authorizations, importing, exporting and pharmacovigilance and is relevant to any business involved in the research, development or commercialization of medicines in the United Kingdom. The U.K. regulatory regime largely mirrors that of the European Union.

Japan

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 Ministry of Health, Labor and Welfare (“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 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 the 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. 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.

Fraud and Abuse and Related Regulatory Laws

We are subject to various federal and state laws pertaining to healthcare “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.

In addition, we are subject to the federal physician sunshine act and certain similar physician payment and drug pricing transparency legislation in various states. 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.

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.

Reimbursement and Healthcare Reform

In both the United States and other countries, sales and reimbursement of any approved products will depend, in part, on the extent to which the costs of such products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly challenging the prices charged for medical products and services and imposing controls to manage costs. The containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement, and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could limit our net revenue and results. In addition, there is significant uncertainty regarding the reimbursement status of newly approved healthcare products.

Adequate coverage and reimbursement in the United States and other countries is critical to the commercial success of approved products. Recently in the United States, 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, among other things, to reform government program reimbursement methodologies. In addition, 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 healthcare 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 that 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 it could take several months before a particular payor initially reviews a product and makes a decision with respect to coverage. For example, third-party payors may require cost-benefit analysis data in order to demonstrate the cost-effectiveness of a particular product.

Outside the United States, ensuring adequate coverage and payment for drug products can have challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct an active comparator clinical trial to demonstrate the relative effectiveness of our therapeutic candidates or products to other available therapies to support our pricing, which could be expensive and result in delays in our commercialization efforts. Third-party payors are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly-approved healthcare products. Recent budgetary pressures in many EU countries are also causing governments to consider or implement various cost-containment measures, including reference price grouping, price freezes, increased price cuts, and rebates. If budget pressures continue, governments may implement additional cost-containment measures. Cost-control initiatives could decrease the price we might establish for products that we may develop or sell, which would result in lower product revenues or royalties payable to us. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products.

The Patient Protection and Affordable Care Act ("PPACA") made extensive changes to the delivery of healthcare in the United States. 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 healthcare 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 United States, 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 healthcare 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 healthcare services to contain or reduce costs of healthcare could result in decreased net revenues from our pharmaceutical products and decreased 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.

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.

Data Privacy and Security Laws

Pharmaceutical companies may be subject to U.S. federal and state health information privacy, security, and data breach notification laws, which may govern the collection, use, disclosure, and protection of health-related and other personal information. State laws may be more stringent, broader in scope, or offer greater individual rights with respect to protected health information (“PHI”), than the federal Health Insurance Portability and Accountability Act of 1996, as amended, and its implementing regulations, which are collectively referred to as HIPAA, and state laws may differ from each other, which may complicate compliance efforts. Entities that are found to be in violation of HIPAA or that enter into a resolution agreement with the HHS to settle actual or potential allegations of HIPAA noncompliance may be subject to significant civil, criminal, and administrative fines and penalties and/or additional reporting and oversight obligations.

Many state laws govern the privacy of personal information in specified circumstances. For example, in California the California Consumer Privacy Act (“CCPA”) establishes a privacy framework for covered businesses by creating an expanded definition of personal information, establishing data privacy rights for consumers in the State of California, imposing special rules on the collection of consumer data from minors, and creating a potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. While clinical trial data and information governed by HIPAA are currently exempt from the CCPA, other personal information may be covered, and possible changes to the CCPA may broaden its scope. Other states, such as Virginia, Colorado and Utah, have also enacted comprehensive privacy laws, and it is possible that additional states will follow suit.

EU member states, the United Kingdom, Switzerland, and other jurisdictions have also adopted data protection laws and regulations, which impose significant compliance obligations. In the European Economic Area (“EEA”), the collection and use of personal data, including clinical trial data, is governed by the provisions of the General Data Protection Regulation (“GDPR”). The GDPR, together with national legislation, regulations, and guidelines of the states in the EEA, the United Kingdom, and Switzerland governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, analyze, and transfer personal data, including health data from clinical trials and adverse event reporting. The GDPR also imposes additional special protections for “special category data,” which includes health, biometric and genetic information of data subjects located in the EEA and, through incorporation in national legislation, the United Kingdom. Further, the 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. The GDPR and similar national legislation grant individuals the opportunity to object to the processing of their personal information, allow them to request deletion of personal information in certain circumstances, and provide 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 and similar national legislation impose strict rules on the transfer of personal data out of the EEA, the United Kingdom, Switzerland, and other countries to the United States or other regions that have not been deemed to offer “adequate” privacy protections. These obligations and regulations also concern security breach notifications, security and confidentiality of the personal data, and imposition of substantial potential fines for breaches of the data protection obligations. European data protection authorities may interpret the GDPR and national laws differently and impose additional requirements, which add to the complexity of processing personal data in or from the EEA, the United Kingdom, or Switzerland. Guidance on implementation and compliance practices are often updated or otherwise revised.

The EU Clinical Trials Regulation also imposes new obligations to make publicly available certain information generated from clinical trials. Only very limited information is exempted from disclosure, i.e. commercially confidential information (which is construed increasingly narrowly) and protected personal data. It may be possible for others to use this data (for example, competitors who may use this data in their own research and development programs) once this data is in the public domain.

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

Corporate Compliance

In order to ensure compliance with applicable laws and regulations, our Chief Financial Officer, Chief Legal Officer, and Chief People Officer oversee compliance training, education, auditing, and monitoring; enforce disciplinary guidelines for any infractions of our corporate policies; 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 European Union, the United Kingdom, and Japan. Our standard operating procedures are designed to provide a framework for corporate governance in accordance with ethical standards and best legal practices.

Human Capital Resources

As of December 31, 2022, we had approximately 531 employees, of whom approximately 217 employees were engaged in the research and development function of our operations. Our research and development staff, approximately 65 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 well-being 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. 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 report.

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 countries outside the United States is included in Notes 1 and 2 to the Consolidated Financial Statements contained in this report.

Available Information

Our website address is www.biocryst.com. We make available, free of charge, on 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 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 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 making an investment decision regarding 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 ongoing 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.

The global COVID-19 pandemic continues to affect the United States and global economies, and could cause 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, 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, including as we continue to expand internationally and bring ORLADEYO to additional global markets.

If our operations or those of third parties with whom we conduct business are impaired or curtailed as a result of these events, the development and commercialization of our products and product candidates could be stopped or delayed, or the costs of such development and commercialization activities could increase, any of which could have a material adverse impact on our business. For example, our suppliers or other vendors may be unable to meet their obligations to us or perform their services as expected as a result of the COVID-19 pandemic or other health epidemics. In such circumstances, we may not be able to enter into arrangements with alternative suppliers or vendors or do so on commercially reasonable terms or in a timely manner. Such delays could adversely impact our ability to meet our desired clinical development and any commercialization timelines. Although we carefully manage our relationships with our suppliers and vendors, there can be no assurance that we will not encounter challenges or delays in the future or that these challenges or delays 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 the startup of the inadequate C5 responder cohorts in our complement oral Factor D program and, as a result, delayed the reporting of related data in 2020. Clinical site initiation and patient enrollment may be delayed due to prioritization of hospital resources toward the COVID-19 pandemic or concerns among patients about participating in clinical trials during a pandemic. Some patients may have difficulty following certain aspects of clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Similarly, our inability to successfully recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 or experience additional restrictions by their institutions, city, or state could adversely impact our clinical trial operations.

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

Where possible and practical, we continue to provide work-from-home flexibility for our employees, which could negatively impact productivity, disrupt our business and delay our clinical programs and timelines. In addition, we are a government contractor, and as such, we are subject to the federal COVID-19 safety protocols. We cannot accurately predict the impact on operations of any return-to-the-office plan, nor of the federal COVID-19 safety protocols on our business or on third parties with whom we conduct business. Our business may be negatively impacted in the event that large numbers of employees or key employees do not comply with these protocols. These and similar, and perhaps more severe, disruptions to our operations could negatively impact our business, operating results and financial condition.

The spread of COVID-19, which has caused a broad impact globally, could 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 further 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 could materially affect our business and the value of our common stock.

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

Financial and Liquidity Risks

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

Since our inception, we have not achieved sustained profitability. We expect to incur additional losses for the foreseeable future, and our losses could increase as our research and development efforts and commercial activities progress. We expect that such losses will fluctuate from quarter to quarter and that losses and fluctuations may be substantial. To become profitable, we, or our collaborative partners, must successfully manufacture and develop products and product candidates, receive regulatory approvals, 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 or otherwise acquire new commercially viable products, certain obligations we have to third parties, including, without limitation, our obligation to pay RPI and OMERS, as applicable, royalties on certain revenues from ORLADEYO and BCX10013 under the Royalty Purchase Agreements, 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 as and 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 2023 expenses will exceed our 2023 revenues. We expect to continue to incur operating losses and negative cash flows unless and until revenues reach a level sufficient to support ongoing operations.

In order to continue future operations, progress our drug discovery and development programs, and commercialize our current products and product candidates, we may be required to raise additional capital. In addition to seeking strategic partnerships and transactions, we may access the equity or debt markets, incur additional borrowings, pursue royalty or other monetization transactions, or seek other sources of funding to meet liquidity needs at any time, including to take advantage of attractive opportunities in the capital markets. Additional funding, whether through additional sales of securities, additional borrowings, royalty or other monetization transactions, collaborative arrangements with partners, including corporate partners such as Torii, or from other sources, may not

be available when needed or in a form 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 with Athyrium Opportunities III Co-Invest 1 LP (“Athyrium” and such agreement, as amended, the “Credit Agreement”). In addition, collaborative arrangements may require us to transfer certain material rights to our 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. See “Risks Relating to Our Business—Risks Relating to Drug Development and Commercialization—If we fail to obtain additional financing or acceptable partnership arrangements as and when needed, we may be unable to complete the development and commercialization of our products and product candidates or continue operations” in this section for further discussion of the capital requirements for our development and commercialization efforts.

Our liquidity needs will largely be determined by the success of operations in regard to the commercialization of our products, particularly ORLADEYO, 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 as discussed herein, and commercializing our approved products. See “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources” in Part II, Item 7 of this report for additional information about our liquidity needs, capital requirements, potential funding alternatives, and adequacy of available funds.

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 as and when needed, 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 manage our product candidate pipeline, advance our product candidates through the various stages of development, especially through the clinical trial process, and to receive regulatory approvals for the commercial sale of our product candidates.

The success of our business depends upon our ability to manage our product candidate pipeline, including through expanding the pipeline, as appropriate, through our internal identification and discovery of product candidates or otherwise in-licensing or acquiring products or product candidates and integrating them into our business effectively and efficiently; advancing our product candidates through the various stages of development; and receiving regulatory approvals for the commercial sale of our product candidates. Identifying, selecting, and in-licensing or acquiring products or product candidates requires substantial expense and technical and financial expertise, and if we are unable to effectively manage our pipeline and integrate viable products or product candidates into our business on acceptable terms, or at all, our business and drug development efforts would suffer.

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, failure to demonstrate adequate benefit-risk balance, failure to achieve a commercially attractive and competitive product label, failure to achieve approval in commercially attractive indications, 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, or 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, and adequate benefit-risk

profile. Failure to achieve any of these endpoints or to show adequate benefit-risk profile in any of our programs, including our complement program (inclusive of BCX10013) 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. For example, recent dose-related observations in an ongoing BCX10013 nonclinical study will delay the clinical program. 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 benefit-risk perspective. Product candidates that initially show promise in clinical or preclinical testing could later be found to be associated with or to cause undesirable or unexpected side effects that could result in substantial modifications or delays in the development plans for our product candidates, significant unexpected costs, or the termination of programs, such as we experienced with BCX9930 in 2022 prior to discontinuing its development later that year.

In addition, the development plans for our product candidates, including our clinical trials (including for BCX10013), 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 have decided in the past, and may in the future decide, to discontinue development of product candidates for various reasons, including, but not limited to, that they 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 preclinical 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 have previously, and may again in the future, pause enrollment in, suspend or terminate clinical trials at any time if we or they believe the trial participants face unacceptable health risks.

Our ability to complete the clinical development process successfully 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 pause enrollment in, 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 preclinical 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 ongoing 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 and 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 or may not receive regulatory approval for the product candidates, which in either case would adversely impact or preclude our ability to generate any revenues from product sales or licensing arrangements. In addition, 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, or at all, 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, 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 is 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 as and when needed, 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 effectively manage our product candidate pipeline; our ability to obtain regulatory approvals for our product candidates, including BCX10013; our ability to maintain regulatory approvals 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 collaboration with Torii); the commercial success of our products achieved by our partners; 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 discovery and development programs, and commercialize our current products and product candidates, we may be required to raise additional capital. Our ability to raise additional capital as and 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, clinical trial investigations, and carcinogenicity, drug-drug interaction, toxicity, or other required studies) for our complement program (including BCX10013) for diseases of the complement system 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, rising inflation or increased interest rates, may restrict our future flexibility to raise capital when such needs arise. See “Risks Relating to Our Business—Financial and Liquidity Risks—We may need to raise additional capital in the future. If we are unable to raise capital as and when needed, we may need to adjust our operations” in this section and “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources” in Part II, Item 7 of this report for additional information about our liquidity risks and capital requirements.

Furthermore, we have exposure to many different industries, financing partners and counterparties, including commercial banks, investment banks and partners (which include investors, licensing partners, distribution partners, and others), 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, rising inflation, increased interest rates, or the conflict in Ukraine. Any such instability may impact these parties’ ability to fulfill contractual obligations to us, or it might limit or place burdensome conditions upon future transactions with us. Also, it is possible that suppliers may be negatively impacted. Any such unfavorable outcomes in our current programs or unfavorable economic conditions have in the past and could again 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 regulatory approvals for our product candidates or maintain regulatory approvals 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 approvals 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 manage our product candidate pipeline, advance our product candidates through the various stages of development, especially through the clinical trial process, and to receive regulatory approvals for the commercial sale of our product candidates,” we or our partners have experienced, and may again in the future experience, any number of unfavorable outcomes during or as a result of preclinical studies and clinical trials that could delay or prevent regulatory approval of our product candidates, or negatively impact our management’s credibility, our value and our operating results.

Even if the FDA or foreign regulatory authorities approve a product candidate, the approval may limit the indicated uses for a product candidate, impose other restrictions on the product candidate, and/or may require post-approval studies that could impair the commercial viability of a product candidate. Even upon any approval to market our potential products, whether in the United States or internationally, we will continue to be subject to extensive regulatory requirements.

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. We may not be able to obtain or maintain these designations for our product candidates that receive them, and our competitors may obtain these designations for their product candidates, which could impact our ability to develop and commercialize our products and product candidates or compete with such competitors, which may adversely impact our business, financial condition or results of operations.

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

If, after obtaining regulatory approval of a product, we or others discover that the product is less effective than previously believed or causes undesirable side effects that either were not previously identified or worse than expected, 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 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 includes increasing the asset value of our product and product candidate portfolio. We believe this is best achieved by retaining full product rights or through collaborative arrangements with third parties as appropriate. As needed, potential third-party relationships could relate to preclinical development, clinical development, regulatory approval, marketing, sales, and distribution of our products and product candidates.

Currently, we have established collaborative relationships, including with Torii for the commercialization of ORLADEYO in Japan, with third-party distributors for ORLADEYO in certain other markets, and with each of Shionogi and Green Cross for the development and commercialization of peramivir. The process of establishing and implementing collaborative relationships is difficult, time-consuming and involves significant uncertainty, including:

- we or our partners may seek to renegotiate or terminate our relationships due to unsatisfactory commercial, regulatory or clinical results, including post-approval clinical commitments, a change in business strategy, a change of control or other reasons;
- our contracts for collaborative arrangements may expire;
- the possibility that expiration or termination of collaborative relationships, such as those with certain of our distribution partners, may trigger repurchase obligations of the Company for unsold product held by our partners;
- our partners may choose to pursue alternative technologies, including those of our competitors;
- we have had in the past, and in the future may have, disputes with a partner that could lead to litigation or arbitration, which could result in substantial costs and divert the attention of our management;
- we do not have day-to-day control over the activities of our partners and have limited control over their decisions;
- our ability to generate future event payments and royalties from our partners depends upon their abilities to establish the safety and efficacy of our product candidates, obtain regulatory approvals and achieve market acceptance of products developed from our product candidates;
- we or our partners may fail to properly initiate, maintain or defend our intellectual property rights, where applicable, or a party may utilize our proprietary information in such a way as to invite litigation that could jeopardize or potentially invalidate our proprietary information or expose us to potential liability;
- we or our partners may not devote sufficient capital or resources toward our products and product candidates; and
- we or our partners may not comply with applicable government regulatory requirements.

If we or our partners fail to fulfill our responsibilities in a timely manner, or at all, our development and commercialization efforts related to that collaboration could be reduced, delayed or terminated, or it may be necessary for us to assume responsibility for activities that would otherwise have been the responsibility of our partner. If we are unable to establish and maintain collaborative relationships on acceptable terms, we may have to delay or discontinue further development or commercialization of one or more of our products or product candidates, undertake commercialization activities at our own expense or find alternative sources of funding. Any delay in the development or commercialization of our products and product candidates would severely affect our business, because if our product candidates do not progress through the development process or reach the market in a timely manner, or at all, or if our products do not achieve market success, we may not receive any revenues from product sales or licensing arrangements.

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

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

The Torii Agreement provides that we are 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 currently remain responsible for regulatory activities with respect to ORLADEYO in Japan, and we continue to use third parties to satisfy many of our obligations under the Torii Agreement, including, but not limited to, our regulatory and other responsibilities in Japan. If our interactions, or those of our third-party agents, are unsuccessful, we could fail to meet our obligations under the Torii Agreement, which could negatively impact the commercial success and the partnership, impact the economic benefit expected or require additional development of ORLADEYO.

Torii may terminate the Torii Agreement under certain limited circumstances, including upon one year's written notice after the sixth anniversary of the first commercial sale of ORLADEYO in Japan. If the Torii Agreement is terminated in connection with these provisions, or at all, 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 has sole control over, and decision-making authority with respect to, commercialization activities for ORLADEYO for the prevention of HAE attacks in Japan, subject to oversight from a joint steering committee. Therefore, our receipt, and the amounts, of any royalty payments under the Torii Agreement are dependent upon Torii's successful performance of such commercialization activities. In addition, competitive products and variations in patient demand, prescription levels, reimbursement determinations or other factors may limit the commercial potential of ORLADEYO in Japan, which could materially reduce the amount of any royalties we are entitled to receive under the Torii Agreement.

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

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

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.

There can be no assurance that our or our partners' commercialization efforts, methods and strategies will succeed. 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 complete clinical trials successfully, or satisfy post-marketing commitments, sufficient to obtain and maintain regulatory agency marketing approval;
- many competitors are more experienced and have significantly more resources, and their products could reach the market faster, be more cost effective or have a better efficacy or tolerability profile than our products and product candidates;
- we may fail to employ a comprehensive and effective intellectual property strategy, which could result in decreased commercial value of our Company, our products and product candidates, or royalties associated with such products (e.g., the loss of the peramivir patent in Korea, which may result in a reduced royalty from Green Cross);
- we may fail to employ a comprehensive and effective regulatory strategy, which could result in a delay or failure in commercialization of our products;

- our and our partners' ability to successfully commercialize our products is affected by the competitive landscape, which cannot be fully known at this time;
- revenue from product sales depends 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 will depend on our ability to successfully complete clinical studies, obtain regulatory approvals, and manufacture, market, distribute and commercialize our approved drugs; and
- the impact of the COVID-19 pandemic on us or our partners.

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

Even if we are able to successfully commercialize our existing products, or to develop new commercially viable products, certain obligations we have to third parties, including, without limitation, our obligations to pay royalties on certain revenues from ORLADEYO and BCX10013 under the Royalty Purchase Agreements, may reduce the profitability of such products.

We have expanded, and may 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 have experienced, and may continue to experience, significant growth in the number of our employees and the scope of our operations in the United States and internationally, particularly in the areas of drug development, regulatory affairs, sales, marketing, and distribution. To manage our growth, we must continue to implement and improve our managerial, operational and financial systems and processes, expand our facilities and continue to recruit and train qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such growth, we may not be able to effectively manage the expansion of our operations, implement appropriate systems and processes in a timely manner or at all, or recruit, train, and retain 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 products and product candidates. If we cannot rely on existing third-party vendors, we will be required to incur significant costs and potential delays in finding new third-party vendors, which could adversely impact the development and commercialization timeframes for our products and product candidates.

We depend on third-party vendors, including third-party manufacturers, distributors, and specialty pharmacies, in the manufacture and distribution of our products, product candidates, and the materials for our products and 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, each of which may be the only vendor we have engaged for a particular product, product candidate, or service or in a particular region, may encounter difficulties with meeting our requirements, including, but not limited to, problems involving, as applicable:

- insufficient resources being devoted in the manner necessary to satisfy our requirements within expected timeframes;
- inconsistent production yields;
- product liability claims or recalls of commercial product;

- difficulties in scaling production to commercial and validation sizes;
- interruption of the delivery of materials required for the manufacturing process;
- failure to distribute commercial supplies of our products to commercial vendors or end users in a timely manner;
- scheduling of plant time with other vendors or unexpected equipment failure;
- potential catastrophes that could strike their facilities or have an effect on infrastructure;
- potential impurities in our drug substance or products that could affect availability of product for our clinical trials or future commercialization;
- poor quality control and assurance or inadequate process controls;
- failure to provide us with accurate or timely information regarding inventories, the number of patients who are using our products, or serious adverse events and/or product complaints regarding our products;
- inability of third parties to satisfy their financial obligations to us or to others;
- potential breach of the manufacturing or distribution agreement by the third party;
- possible termination or nonrenewal of a critical agreement by the third party at a time that is costly or inconvenient to us; and
- lack of compliance or cooperation with regulations and specifications or requests set forth by the FDA or other foreign regulatory agencies or local customs, particularly associated with ORLADEYO, BCX10013, 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 or shortages, acts of terrorism or war, equipment malfunctions, raw material shortages or supply chain issues. 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 with respect to inventories and sales, serious adverse events, and/or product complaints, our business, including our commercialization efforts for 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, are not effectively managed, the continuance of our commercialization efforts for and sales of ORLADEYO, may be delayed or compromised.

In addition, our contract manufacturers may not be able to manufacture the materials required for our products or product candidates at a cost or in quantities necessary to make them commercially viable. Our raw materials, drug substances, products, and product candidates are manufactured by a limited group of suppliers, including some at a single facility. If any of these suppliers were unable to produce these items, this could significantly impact our supply of products and product candidate material for further preclinical testing and clinical trials. Our third-party manufacturers also may not meet our manufacturing requirements. 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.

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

- our products may not prove to be adequately safe and effective for market approval in markets other than the markets in which they are currently approved;
- necessary funding for post-marketing commitments and further development of our products may not be available timely, at all, or in sufficient amounts;
- advances in competing products could substantially replace potential demand for our products;
- government and third-party payors may not provide sufficient coverage or reimbursement, which would negatively impact the demand for our products;
- we may not be able to supply commercial material to our partners and our partners may not be able to maintain or establish sufficient and acceptable commercial manufacturing, either directly or through third-party manufacturers;
- the commercial demand and acceptance for our products by healthcare providers and by patients may not be sufficient to result in substantial product revenues to us or to our partners and may result in little to no revenue, milestone payments, or royalties to us;
- effectiveness of marketing and commercialization efforts for our products by us or our partners;
- market satisfaction with existing alternative therapies;
- perceived efficacy relative to other available therapies;
- disease prevalence;
- cost of treatment;
- our pricing and reimbursement strategy may not be effective;
- pricing and availability of imports or 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 for products that compete with our products. Companies that complete clinical trials, obtain required regulatory approvals, and commence commercial sale of their drugs before we do may achieve a significant competitive advantage, including patent and FDA exclusivity rights that would delay our ability to market products. We face, and will continue to face, competition in the commercialization of our products, licensing of potential product candidates for desirable disease targets, licensing of desirable product candidates, and development and marketing of our product candidates from academic institutions, government agencies, research institutions and biotechnology and pharmaceutical companies. Competition may also arise from, among other things:

- other drug development technologies;

- methods of preventing or reducing the incidence of disease, including vaccines; and
- new small molecule or other classes of therapeutic agents.

Developments by others may render our products, product candidates, or technologies obsolete or noncompetitive.

We received FDA approval of ORLADEYO, an oral, once-daily therapy for the prevention of HAE attacks in adults and pediatric patients aged 12 years and older, in December 2020. We subsequently received regulatory approvals for ORLADEYO in multiple markets. In addition, we are performing research on or developing products for the treatment of several other rare diseases, including diseases of the complement system. 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. In addition, various government entities throughout the world may offer incentives, grants and contracts to encourage additional investment into certain preventative and therapeutic agents, 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 and our partners’ activities related to approved products or, following their regulatory approval (if applicable), any of our product candidates under development, such as BCX10013, are subject to regulatory and law enforcement authorities in the United States (including the FDA, the Federal Trade Commission, the Department of Justice (“DOJ”), and state and local governments) and their foreign equivalents (including the EMA, MHLW, MHRA, and others).

We are responsible for reporting adverse drug experiences, have responsibility for certain post-approval studies, and may have responsibilities and costs related to a recall or withdrawal of our products from sale in the jurisdictions in which they are approved. We may also incur liability associated with product manufacturing contracted by us or in support of any of our partners. We are required to maintain records and provide data and reports to regulatory agencies related to our products (e.g. risk evaluation and mitigation strategies, track and trace requirements, and adverse events), and we may incur certain promotional regulatory and government pricing risks, all of which could have a material adverse impact on our operations and financial condition. Similar responsibilities would apply upon regulatory approval of any of our other product candidates currently under development.

In addition, we are subject to the federal physician sunshine act and certain similar physician payment and drug pricing transparency legislation in various states. We are also subject to various federal and state laws pertaining to healthcare “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 and our partners’ operations, sales and marketing practices, price reporting, and relationships with physicians and other customers and third-party payors. Although we seek to comply

with these statutes, it is possible that our practices, or those of our partners, might be challenged under healthcare 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.

The FDA and foreign regulatory authorities may also impose post-approval commitments on us for approved products, which we may not complete successfully or on time for any number of reasons, including but not limited to lack of funds to complete the studies and insufficient interest by appropriate sites, investigators or study subjects. We are currently subject to certain post-approval commitments. If we fail to comply with post-approval legal and regulatory requirements, we could be subject to penalties, and our products could be subject to continual recordkeeping and reporting requirements, review and periodic inspections by the FDA and other regulatory bodies. Regulatory approval of a product may be subject to limitations on the indicated uses for which the product may be marketed or to the other restrictive conditions of approval that limit our ability to promote, sell or distribute a product. Furthermore, the approval of our products and any other future product candidates may be subject to requirements for costly post-approval testing and surveillance to monitor their 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. 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 HHS, the DOJ and individual U.S. Attorney offices within the DOJ, 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 in “Business—Government Regulation” in Part I, Item 1 of this report 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, consultants and partners 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, consultants and partners, including intentional or unintentional failures to comply with FDA regulations or similar regulations of comparable other regulatory authorities, provide accurate information to the FDA or comparable other 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 other regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee and consultant misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee and consultant misconduct, whether intentional, reckless, negligent, or unintentional, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

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

We are subject to new legislation, regulatory, and healthcare payor initiatives, including the PPACA, which made extensive changes to the delivery of healthcare in the United States, as discussed in “Business—Government Regulation” in Part I, Item 1 of this report. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare 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 applicable 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 United States and other markets is critical to the commercial success of our approved products. Recently in the United States, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. For example, the Inflation Reduction Act of 2022 (“IRA”) implements a number of drug pricing measures intended to lower the cost of prescription drugs and related healthcare reforms, including limits on price increases and subjecting an escalating number of drugs to annual price negotiations with the Centers for Medicare and Medicaid Services. We cannot be sure whether additional legislation or rulemaking related to the IRA will be issued or enacted, or what impact, if any, such changes will have on the profitability of our products or any of our product candidates, if approved for commercial use, in the future. The effect of the IRA on our business and the healthcare industry in general is not yet known. In addition, regional healthcare 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 a 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 may be 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 also may be subject to the GDPR in the EEA and similar legislation in the United Kingdom and Switzerland. See “Business—Government Regulation—Data Privacy and Security Laws” in Part I, Item 1 of this report and “Risks Relating to Our Business—Risks Relating to International Operations—Our actual or perceived failure to comply with European governmental laws and regulations and other legal obligations related to privacy, data protection and information security could harm our business” in this section for additional discussion of 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, the value of those rights would diminish, and if we fail to secure the rights to patents of others, it could adversely affect our business.

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, time-consuming and unsuccessful. An adverse result in any legal proceeding could put one or more of our patents at risk. Our success depends in part on avoiding the infringement of other parties' patents and other intellectual property rights as well as avoiding the breach of any licenses relating to our technologies and products. In the United States, patent applications filed in recent years are confidential for 18 months, while older applications are not published until the patent issues. As a result, avoiding patent infringement may be difficult and we may inadvertently infringe third-party patents or proprietary rights. These third parties could bring claims against us, our partners or our licensors that even if resolved in our favor, could cause us to incur substantial expenses and, if resolved against us, could additionally cause us to pay substantial damages. Further, if a patent infringement suit were brought against us, our partners or our licensors, we or they could be forced to stop or delay research, development, manufacturing or sales of any infringing product in the country or countries covered by the patent we infringe, unless we can obtain a license from the patent holder. Such a license may not be available on acceptable terms, or at all, particularly if the third party is developing or marketing a product competitive with the infringing product. Even if we, our partners or our licensors were able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property.

If we or our partners are unable or fail to adequately initiate, protect, defend or enforce our intellectual property rights in any area of commercial interest or in any part of the world where we wish to seek regulatory approval for our products, methods, processes and other technologies, the value of our products and product candidates to produce revenue would diminish. Additionally, if our products, methods, processes, and other technologies or our commercial use of such products, processes, and other technologies, including, but not limited to, any trade name, trademark or commercial strategy infringe the proprietary rights of other parties, we could incur substantial costs. The USPTO and the patent offices of other jurisdictions have issued to us a number of patents for our various inventions, and we have in-licensed several patents from various institutions. We have filed additional patent applications and provisional patent applications with the USPTO. We have filed a number of corresponding foreign patent applications and intend to file additional foreign and U.S. patent applications, as appropriate. We have also filed certain trademark and trade name applications worldwide. We cannot assure you as to:

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

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

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

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

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

Product Liability Risks

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

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and face even greater risks upon commercialization by us of our products or product candidates. We have product liability insurance covering our clinical trials. Clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance or increase our existing coverage at a reasonable cost to protect us against losses that could have a material adverse effect on our business. An individual may bring a product liability claim against us if one of our products or product candidates causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any product liability claim brought against us, with or without merit, could result in:

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

Risks Relating to Contractual Arrangements

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

We have contracts with BARDA/HHS and NIAID/HHS for the development of galidesivir as a treatment for diseases caused by RNA pathogens, including Marburg virus disease, Yellow Fever and Ebola virus disease. In contracting with these government agencies, we are subject to various U.S. Government contract requirements, including general clauses for a cost-reimbursement research and development contract, which may limit our reimbursement. While all government funding for galidesivir expired in 2022, we still face risks related to our U.S. Government contracts.

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.

Upon termination or 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.

In addition, 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, including a final financial audit. 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 BARDA/HHS and NIAID/HHS galidesivir contracts may occur at the election of the U.S. Government and have been concluded through fiscal 2019; 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. 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 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.

There can be no assurance that we or our manufacturers will be able to fully meet the demand for our antivirals with respect to any 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. 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/or 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 and/or seek other available remedies. As a result, our development of the respective product candidate or commercialization of the product would cease.

Because continuing events of default exist under the PhaRMA Notes, the holders of the PhaRMA Notes may be able to foreclose on the collateral securing the PhaRMA Notes and our equity interest in Royalty Sub. As a result, we may not realize the benefit of future royalty payments, if any, that might otherwise accrue to us following repayment of the PhaRMA Notes and we could otherwise be adversely affected.

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, if any, 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. In addition, 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 these amounts at the maturity date constituted an additional event of default under the PhaRMA Notes. 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, if any, that might otherwise accrue to us following repayment of the PhaRMA Notes, we may incur legal costs, and we might otherwise be adversely affected.

We 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. 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, if any, 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, we cannot assure you 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 or the failure by Royalty Sub to repay the PhaRMA Notes at maturity.

We wrote off the balance due under the PhaRMA Notes to other income as a debt extinguishment as of December 31, 2021. See “Note 8—Royalty Monetizations—RAPIACTA—Non-Recourse Notes Payable—Debt Extinguishment” in the Notes to Consolidated Financial Statements in Part II, Item 8 of this report for additional information about the write-off.

We have incurred significant indebtedness, which could adversely affect our business. Additionally, our Credit Agreement contains conditions and restrictions that limit our flexibility 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, 2022, we had an outstanding principal balance under our Credit Agreement of \$240.5 million, inclusive of the quarterly PIK Interest Payments. We will be required to pay to Athyrium, for the account of the lenders, a make-whole premium plus certain fees set forth in the Credit Agreement in the event that we prepay or repay, or are required to prepay or repay, voluntarily or pursuant to a mandatory prepayment obligation under the Credit Agreement (e.g., with the proceeds of certain asset sales, certain ORLADEYO out-licensing or royalty monetization transactions (excluding the Royalty Sales), extraordinary receipts, debt issuances, or upon a change of control of the Company and specified other events, subject to certain exceptions), all of the then-outstanding Term Loans under the Credit Agreement, in each case, subject to certain exceptions set forth in the Credit Agreement.

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; 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 at least \$15.0 million (or, in certain circumstances, \$20.0 million) of unrestricted cash and cash equivalents, subject to certain exceptions. In addition, we are required to achieve certain minimum targets for consolidated net revenues from ORLADEYO sales in the United States.

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 Agreements. 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, legal, regulatory, political, operational, financial, and economic risks.

Our business strategy includes international expansion, including the commercialization of products outside of the United States. In addition, 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 and maintaining protection for, and enforcing, our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits on our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations, which have been increasingly prevalent alongside a fluctuating U.S. dollar;
- natural disasters and political and economic instability, including wars (e.g., the conflict in Ukraine), terrorism, political unrest, results of certain elections and votes, actual or threatened public health emergencies and outbreak of disease (e.g., the ongoing COVID-19 pandemic), 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, 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 international expansion of operations and adversely affect our business and results of operations.

Additionally, in some countries, such as Japan and the countries of the European Union, 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.

Foreign currency exchange rate fluctuations could have an adverse impact on our results of operations, financial position, and cash flows.

We conduct operations in many countries outside of the United States involving transactions in a variety of currencies other than the U.S. dollar. These transactions include, without limitation, commercial sales, contract manufacturing, and clinical trial activities. Although most of our revenues and expenses are denominated in U.S. dollars, our commercial sales in Europe are primarily denominated in Euros and British Pounds. In addition, our royalties from Torii are derived from Torii's sales of ORLADEYO in Japan, which sales are denominated in Japanese yen and converted into U.S. dollars for purposes of determining the royalty owed to us. We also have foreign currency exposure to fluctuations in other foreign currencies, such as the Swiss Franc, Danish Krone, Swedish Krona, and the Canadian Dollar. Changes in the value of these currencies relative to the U.S. dollar may impact our consolidated operating results, including our revenues and expenses, causing fluctuations in our operating results from period to period and/or resulting in foreign currency transaction losses that adversely impact our results of operations, financial position, and cash flows. As we continue to expand our operations internationally, our exposure to foreign currency transaction gains or losses may become more significant. See "Quantitative and Qualitative Disclosures about Market Risk—Foreign Currency Risk" in Part II, Item 7A of this report for additional information about our foreign currency risk.

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

EU member states, the United Kingdom, Switzerland and other countries have adopted data protection laws and regulations, which impose significant compliance obligations. These laws include the GDPR and similar national legislation, the EU Clinical Trials Regulation, and the e-Privacy Directive (2002/58/EC), and are discussed in more detail in "Business—Government Regulation—Data Privacy and Security Laws" in Part I, Item 1 of this report. Failure to comply with the requirements of the GDPR or related national data protection laws, which may deviate 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 or similar national legislation 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 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, requires 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 European Union, 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 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. Compliance with the requirements imposed by the GDPR and other such laws can be time-consuming, expensive and difficult, and may increase our cost of doing business or require us to change our business practices, and despite our efforts we may not be successful in achieving compliance if our personnel, collaborators, partners or vendors do not comply with applicable data protection obligations.

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

The United Kingdom's decision to withdraw from the 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.

The United Kingdom's exit from the European Union, 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 European Union, 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 European Union take effect in practice. Changes in U.K. 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 European Union 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 European Union 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 European Union. 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 European Union will have and how such withdrawal will affect us, and the full extent to which our business could be adversely affected.

Risks Relating to Technology

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

We and our third-party vendors store commercial product, clinical and stability samples at our facilities that could be damaged if the facilities incur physical damage or in the event of an extended power failure. We have backup power systems in addition to backup generators to maintain power to all critical functions, but any loss of these products or samples could result in significant delays in our commercialization or drug development process.

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

A significant disruption in our or our third-party 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 facilities. 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 facilities incur damage, or if our vendor data systems fail, suffer damage or are destroyed. In addition, we have outsourced significant parts of our information technology and business infrastructure to third-party providers, and we currently use these providers to perform business critical information technology and business services for us. We are therefore vulnerable to cybersecurity attacks and incidents on the associated networks and systems, whether they are managed by us directly or by the third parties with whom we contract, and we have experienced and may in the future experience such cybersecurity threats and attacks.

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. These risks have increased as we have experienced significant growth in the number of our employees and the scope of our operations and as virtual and remote working have become more widely used, and sensitive data is accessed by employees working in less secure, home-based environments. 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.

Some of our stockholders own greater than 5% of our outstanding common stock. Our top ten stockholders own approximately 50% of our common stock 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, 2022, the 52-week range of the market price of our stock was from \$7.61 to \$19.99 per share. The following factors, in addition to other risk factors described in this section, may have, and in some cases have had, 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;
- us 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 and the comparison of such estimates to our actual results;
- changes in our public guidance;
- 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, capital commitments or other monetization transactions;
- 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.

This volatility could cause the value of an investment in our common stock to decline significantly. In addition, companies that have experienced volatility in the market price of their stock in the past have been subject to securities class action litigation. Securities litigation, and any other type of litigation, brought against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business and adversely affect our results of operations.

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, 2023, there were 188,451,137 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, 2023, there were 34,992,042 stock options and restricted stock units outstanding and 4,254,957 shares available for issuance under our Amended and Restated Stock Incentive Plan, 6,150,129 stock options and restricted stock units outstanding and 607,208 shares available for issuance under our Amended and Restated Inducement Equity Incentive Plan, and 5,616,817 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 of 1933, as amended (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, of which warrants to purchase 11,511,472 shares of our common stock remain outstanding. In addition, on June 1, 2020, we issued to certain of the Baker Entities pre-funded warrants to purchase 3,511,111 shares of our common stock at a price of \$4.49 per warrant. Each warrant has an exercise price of \$0.01 per share. If the Baker Entities, by exercising their registration 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 Amended and Restated 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 or the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction.

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

General Risk Factors

Natural disasters, epidemic or pandemic disease outbreaks, trade wars, armed conflicts, 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, such as natural disasters (including as a result of climate change), epidemic or pandemic disease outbreaks (such as the ongoing COVID-19 pandemic), trade wars, armed conflict, 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 conduct 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, for example, "Risk Factors—General Risk Factors—Our business, operations, clinical development or commercialization plans and timelines, and access to capital could be adversely affected by unpredictable and unstable market and economic conditions." In addition, other events, such as the armed conflict between Russia and Ukraine, could adversely impact our business. For example, the conflict could lead to sanctions, embargoes, supply shortages, regional instability, geopolitical shifts, cyber-attacks, other retaliatory actions, and adverse effects on macroeconomic conditions, currency exchange rates, and financial markets, which could adversely impact our operations and financial results, as well as those of third parties with whom we conduct business.

Our business, operations, clinical development or commercialization plans and timelines, and access to capital could be adversely affected by unpredictable and unstable market and economic conditions.

Our business, operations, clinical development or commercialization plans and timelines, and access to capital could be adversely affected by unpredictable and unstable market and economic conditions, including as a result of rising inflation, increased interest rates, the effects of the ongoing COVID-19 pandemic, foreign exchange rate fluctuations, and the conflict in Ukraine. The magnitude, duration and long-term effect of each of these factors, as well as the effects of actions taken by governments to address them, are unknown at this time, but they could result in further significant disruption of the global economy and financial markets. Our business may be adversely affected by any related economic downturn, volatile geopolitical and business environment, or continued market instability.

Unstable market and economic conditions could materially affect 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 could materially affect our business and the value of our common stock.

Market and economic conditions continue to evolve, with the ultimate impacts being uncertain and subject to change. These effects could be material, and we will continue to monitor the economic climate, COVID-19 pandemic, and the conflict in Ukraine closely. We do not yet know the full extent and magnitude of the impacts that these developments will have on our business, on the healthcare system, or on the global economy. In addition, unstable market conditions could have the effect of heightening many of the other risks described in this “Risk Factors” section.

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

From time to time, we may be involved in disputes, including, without limitation, disputes with our employees, collaborative partners, and third-party vendors. We may be called upon to initiate legal proceedings or to defend ourselves in such legal proceedings relating to our relationships with these parties, our decisions and actions or omissions with respect thereto, and our business. In addition, if our stock price is volatile, we may become involved in securities class action lawsuits in the future. Due to the inherent uncertainties in legal proceedings, we cannot accurately predict the ultimate outcome of any such proceedings. An unfavorable outcome in any such proceedings could have an adverse impact on our business, financial condition and results of operations. Any current or future dispute resolution or legal proceeding, regardless of the merits of any such proceeding, could harm our reputation and result in substantial costs and a diversion of management’s attention and resources that are needed to successfully run our business.

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

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

If we fail to retain our existing key personnel or fail to attract and retain additional key personnel, the development of our product candidates, the commercialization of our products, and the related expansion of our business will be delayed or stopped.

We are highly dependent upon our senior management and scientific team, the unexpected loss of whose services might impede the achievement of our development and commercial objectives. 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 would 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 24,500 square feet in Durham through leases expiring December 31, 2023 and June 30, 2024, and we lease approximately 34,000 square feet in Birmingham through October 31, 2026. We recently entered into an amendment to our lease in Birmingham to add additional space in 2023 and to extend the term of the lease at that time, with options for additional extensions. We also contract for smaller offices in a number of other countries. 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.

Holder

As of January 31, 2023, there were approximately 155 holders of record of our common stock.

Dividends

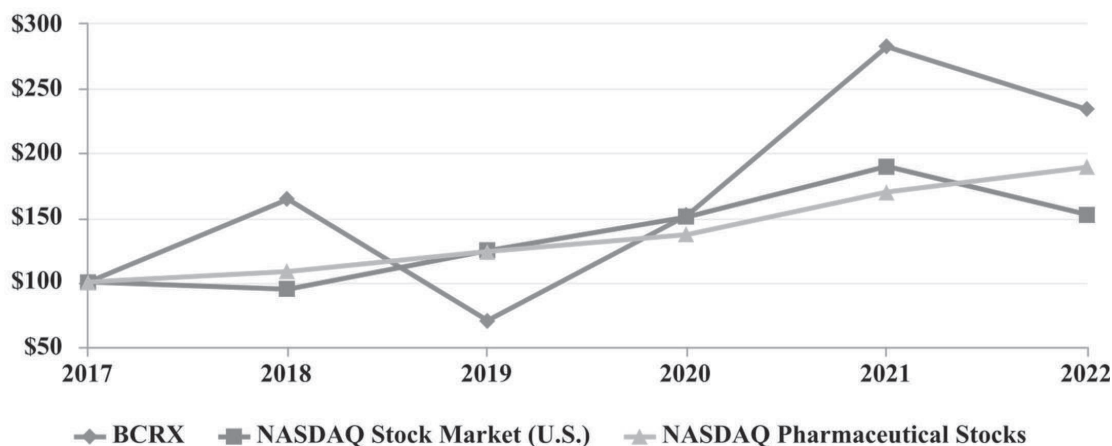
We have never paid cash dividends and do not anticipate paying cash dividends in the foreseeable future.

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 2017



	Beginning Investment at 12/31/17	Investment at 12/31/18	Investment at 12/31/19	Investment at 12/31/20	Investment at 12/31/21	Investment at 12/31/22
BioCryst Pharmaceuticals, Inc.	\$100.00	\$164.36	\$ 70.26	\$151.73	\$282.08	\$233.81
Nasdaq Stock Market (United States) . . .	100.00	94.56	124.03	150.41	189.36	152.00
Nasdaq Pharmaceutical Stocks.	100.00	107.95	123.62	136.62	169.94	189.23

The above graph measures the change in a \$100 investment in our common stock based on its closing price of \$4.91 on December 29, 2017 (the last trading day of the year) and its year-end closing price thereafter. Our relative performance is then compared with the CRSP Total Return Indexes for the Nasdaq Stock Market (United States) and Nasdaq Pharmaceutical Stocks.

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

There were no repurchases of our common stock during the fourth quarter of 2022.

ITEM 6. *RESERVED*

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 and commercializes 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 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.

Products and Product Candidates

ORLADEYO® (berotralstat). ORLADEYO is an oral, once-daily therapy discovered and developed by us for the prevention of hereditary angioedema ("HAE") attacks. ORLADEYO is approved in the United States and multiple global markets for the prevention of HAE attacks in adults and pediatric patients 12 years and older.

We have built out our U.S. commercial infrastructure to support the launch and continued commercialization of ORLADEYO in the United States and are continuing to build our commercial infrastructure to support launches in other markets. Based on proprietary analyses of HAE prevalence and market research studies with HAE patients, physicians, and payors in the United States and Europe, and two full years of commercialization experience with ORLADEYO in 2021 and 2022, we anticipate the global commercial market for ORLADEYO has the potential to reach a global peak of \$1 billion in annual net ORLADEYO revenues. We expect at least 70 to 80 percent of our revenue at peak to come from the United States. 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 or our partners' 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.

Revenue from sales of ORLADEYO in 2022, which was our second full year of ORLADEYO sales, is discussed under "Results of Operations" in this MD&A. Revenue from sales of ORLADEYO in future periods is subject to uncertainties and will depend on several factors, including the success of our and our partners' commercialization efforts in the United States and elsewhere, the number of new patients switching to ORLADEYO, patient retention and demand, the number of physicians prescribing ORLADEYO, the rate of monthly prescriptions, reimbursement from third-party and government payors, the conversion of patients from our clinical trials and early access programs to commercial customers, our pricing strategy, and market trends. We are continuing to monitor and analyze this data as we continue to commercialize ORLADEYO. In addition, because of typical first quarter requirements from payors

for prescription reauthorization of specialty products, like ORLADEYO, that can temporarily move patients from paid drug to free product, copayment assistance and Medicare D cost sharing dynamics, we expect ORLADEYO net revenue in the first quarter of 2023 to be similar to, or slightly less than, the fourth quarter of 2022.

Complement Program. The goal of our overall complement program is to advance several compounds across multiple pathways in the complement system to treat many complement-mediated diseases. These compounds include BCX10013, which targets the alternative pathway of complement. In addition, we are pursuing oral medicines directed at other targets across the classical, lectin, and terminal pathways of the complement system, including C2, a critical upstream serine protease enzyme for activation of the classical and lectin pathways. We have developed potent, selective molecules targeting C2, which are currently in lead optimization.

RAPIVAB®/RAPIACTA®/PERAMIFLU® (peramivir injection). RAPIVAB (peramivir injection) is approved in the United States for the treatment of acute uncomplicated influenza for patients six months and older. Peramivir injection is also approved in Canada (RAPIVAB), Australia (RAPIVAB), Japan (RAPIACTA), Taiwan (RAPIACTA), and Korea (PERAMIFLU).

Revenues and Expenses

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, and the resources dedicated to our products and product candidates by us and our collaborative partners, 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, drug manufacturing, clinical research activities, the ongoing requirements of our development programs, the costs of commercialization, 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 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 accounting principles generally accepted in the United States (“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 Estimates” at the end of this MD&A 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 Developments

ORLADEYO (berotralstat)

On November 10, 2022, we announced new real-world data demonstrating rapid, sustained reduction of patient-reported HAE attacks and consistently low attack rates among patients 12 years and older who started on ORLADEYO for the prophylactic treatment of HAE, including patients who switched from other prophylactic therapies.

On November 28, 2022, we announced that the Israeli Ministry of Health granted marketing authorization for ORLADEYO to prevent attacks of HAE in adults and pediatric patients 12 years of age and older in Israel.

On January 23, 2023, we announced that the Company entered into a collaboration with Swixx BioPharma AG (“Swixx”) to commercialize ORLADEYO in Central and Eastern Europe (“CEE”). Under the terms of the agreement, Swixx will be responsible for commercializing ORLADEYO in 15 markets within CEE.

On January 26, 2023, we announced the enrollment of the first patient in the pivotal APeX-P trial evaluating ORLADEYO in pediatric HAE patients who are 2 to <12 years of age.

On February 21, 2023, we announced that the Canadian Agency for Drugs and Technologies in Health Canadian Drug Expert Committee has recently issued a final draft positive recommendation for ORLADEYO to be reimbursed for the routine prevention of HAE attacks in adults and pediatric patients 12 years of age and older.

Complement-Mediated Diseases

BCX9930. On December 15, 2022, we announced that, based on new competitive data recently presented at the American Society of Hematology annual meeting, we no longer believe that BCX9930 would be commercially competitive, and we are discontinuing the development of BCX9930. This decision allows us to fully focus our complement inhibitor development efforts on BCX10013 and pursue additional oral compounds for multiple targets across other complement pathways.

BCX10013. On November 1, 2022, we announced that we have begun a clinical program with BCX10013, a novel, potent, and specific Factor D inhibitor. On January 9, 2023, we announced that initial data from ongoing phase 1 single ascending dose and multiple ascending dose trials in healthy volunteers showed rapid, sustained and >97 percent suppression of the alternative pathway of the complement system 24 hours following a single 110 mg dose, and that BCX10013 has been safe and generally well-tolerated at all doses studied to date. On February 21, 2023, we announced that recent dose-related observations in an ongoing BCX10013 nonclinical study will delay the clinical program.

Additional Complement Targets. On November 1, 2022, we announced that, in addition to BCX10013, which targets the alternative pathway of complement, we are pursuing oral medicines directed at other targets across the classical, lectin and terminal pathways of the complement system, including C2, a critical upstream serine protease enzyme for activation of the classical and lectin pathways. We have developed potent, selective molecules targeting C2, which are currently in lead optimization.

Fibrodysplasia Ossificans Progressiva (“FOP”)

On November 1, 2022, we announced that we believe that patients with FOP are likely to benefit from other oral ALK-2 inhibitors that currently are substantially ahead of our ALK-2 inhibitor, BCX9250, in development. Considering the expectation that patients will be well-served by these other products, and the approximately \$100 million in additional investment that would be required to advance BCX9250 to approval, we are stopping the BCX9250 program and redirecting this investment to the other opportunities we have to serve patients with complement-mediated diseases.

Results of Operations

The discussion below presents a summary of our results of operations for fiscal years 2022 and 2021. 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, 2021, filed with the SEC on February 28, 2022, for a summary of our results of operations for the fiscal year ended December 31, 2020.

Year Ended December 31, 2022 Compared to 2021

For the year ended December 31, 2022, total revenues were \$270.8 million as compared to \$157.2 million for the year ended December 31, 2021. This increase of \$113.6 million was primarily due to an increase of \$129.1 million of ORLADEYO net revenue, including royalties from sales in Japan through our partner Torii. Additionally, RAPIVAB revenues, primarily from the stockpiling sales to HHS, increased by \$7.9 million, and other royalty revenue, primarily from Green Cross, increased by \$1.7 million. These increases in revenue were partially offset by a reduction in milestone revenue of \$15.0 million related to the NHI approval of ORLADEYO in Japan in 2021 and lower peramivir product revenue from inventory sales to our partners, which decreased by \$4.4 million. Additionally, there was a reduction in contract revenue of \$5.7 million in 2022 as a result of closing out our contracts with NIAID/HHS and BARDA/HHS for the development of galidesivir.

Cost of product sales for the years ended December 31, 2022 and 2021 was \$6.4 million and \$7.2 million, respectively. The decrease in cost of product sales for the year ended December 31, 2022 was primarily associated with the decrease in sales of peramivir to our partners resulting in a decrease in cost of product sales of \$3.0 million. This decrease was partially offset by increases in cost of product sales relative to the overall increase in ORLADEYO sales and the increase in RAPIVAB stockpiling sales to HHS for the year ended December 31, 2022. Additionally, for the year ended December 31, 2022, an inventory valuation reserve of \$0.9 million was recorded for inventory, primarily ORLADEYO, that was determined to be short-dated or at risk of expiration prior to usage.

Research and development (“R&D”) expenses increased to \$253.3 million for the year ended December 31, 2022 from \$208.8 million for the year ended December 31, 2021, primarily due to increased investment in the development of our Factor D program, including BCX9930 and BCX10013, as well as the BCX9250 / FOP program and other research, preclinical and development costs. In December 2022, we announced the discontinuation of the development of the BCX9930 program as well as the BCX9250 program. Accordingly, certain costs necessary to discontinue and close out these development programs were expensed in the fourth quarter ended December 31, 2022.

The following table summarizes our R&D expenses for the periods indicated (amounts are in thousands). Certain prior period amounts have been reclassified for consistency with the current year presentation. These reclassifications had no effect on the total R&D expenses.

	<u>2022</u>	<u>2021</u>	<u>2020</u>
R&D expenses by program:			
Factor D Program	\$146,912	\$132,267	\$ 35,265
Berotrastat	28,230	30,559	44,329
FOP	19,857	2,840	2,583
Galidesivir	1,077	5,740	9,705
Peramivir	788	1,245	1,613
Other research, preclinical and development costs	<u>56,433</u>	<u>36,157</u>	<u>29,469</u>
Total R&D expenses	<u>\$253,297</u>	<u>\$208,808</u>	<u>\$122,964</u>

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, and conduct and manage clinical trials, as well as other costs related to our clinical and preclinical studies. Additionally, direct expenses consist of those costs necessary to discontinue and close out a development program, including termination fees and other commitments. 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 for the year ended December 31, 2022 were \$159.4 million compared to \$118.8 million in the year ended December 31, 2021. The increase was primarily due

to increased investment to support the U.S. commercial launch of ORLADEYO and the expansion of international operations. SG&A expenses for the year ended December 31, 2021 included non-cash compensation charges on the accelerated vesting of certain outstanding stock options of \$8.9 million.

Interest expense for the year ended December 31, 2022 was \$99.1 million as compared to \$59.3 million for the year ended December 31, 2021. The increase in interest expense was primarily associated with the sale of certain royalty payments under the 2021 RPI Royalty Purchase Agreement and the OMERS Royalty Purchase Agreement, which were entered into in November 2021, as well as the additional aggregate borrowing of \$75.0 million of Term B and Term C Loans under the Credit Agreement (as defined below), which were funded on July 29, 2022. The nature of the royalty sales requires that we recognize a liability (the “Royalty Financing Obligations”) for the future sale of royalties under these agreements. These liabilities are amortized using the effective interest rate method, resulting in the recognition of non-cash interest expense over the estimated term of the Royalty Purchase Agreements (as defined in “Note 8—Royalty Monetizations—ORLADEYO and Factor D Inhibitors” in the Notes to Consolidated Financial Statements in Part II, Item 8 of this report). These increases were partially offset by the discontinuation of interest expense associated with the PhaRMA Notes, which were written-off at the end of 2021.

Interest expense for the year ended December 31, 2022 consisted of \$76.5 million of non-cash interest expense due to the amortization of interest associated with the Royalty Financing Obligations and \$22.5 million of interest expense, net of deferred financing amortization, associated with the borrowings under the Credit Agreement. Interest expense for the year ended December 31, 2021 consisted of \$37.7 million of non-cash interest expense due to the amortization of interest associated with the Royalty Financing Obligations and \$15.5 million of interest expense, net of deferred financing amortization, associated with the Term A Loan under the Credit Agreement. Additionally, we recognized \$6.1 million in interest expense on the non-recourse PhaRMA Notes issued in March 2011.

For the year ended December 31, 2022, interest and other income was \$3.1 million compared to interest and other income of \$55.2 million for the year ended December 31, 2021. For the year ended December 31, 2022, interest income earned on investments of \$5.1 million was partially offset by foreign currency losses of \$2.0 million. For the year ended December 31, 2021, a gain of \$55.8 million on extinguishment of debt was recognized related to the write-off of the non-recourse PhaRMA Notes and related accrued interest payable. See “Note 8—Royalty Monetizations—RAPIACTA—Non-Recourse Notes Payable—Debt Extinguishment” in the Notes to Consolidated Financial Statements in Part II, Item 8 of this report for additional information. This gain, as well as interest income of \$0.1 million, was partially offset by foreign currency losses of \$0.7 million for the year ended December 31, 2021.

For the year ended December 31, 2022, we incurred a tax expense of \$2.7 million as compared to tax expense of \$2.3 million for the year ended December 31, 2021. The tax expense for 2022 was primarily the result of amendments to Section 174 of the Internal Revenue Code of 1986, as amended (“IRC”), which no longer permits an immediate deduction for research and development expenditures in the tax year that such costs are incurred. Instead, these IRC Section 174 research and development costs are capitalized and amortized over either a five or fifteen year period, depending on the location of the activities performed. The new amortization period begins with the midpoint of any taxable year that IRC Section 174 research and development costs are first incurred, regardless of whether the expenditures were made prior to or after July 1, and runs until the midpoint of year five for activities conducted in the United States or year fifteen for research and development activities conducted outside of the United States. Tax expense in 2021 was primarily the result of the recognition as upfront taxable income of \$300.0 million received from the RPI Royalty Purchase Agreement and the OMERS Royalty Purchase Agreement. For both 2022 and 2021, increased sales of ORLADEYO and increased nexus in multiple states and foreign jurisdictions, where historically we had none, contributed to increased tax expense.

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; our credit facilities; and the Royalty Sales. In addition, we have previously received funding from other sources, including other collaborative and other research and development agreements, government grants, the PhaRMA Notes financing, equipment lease financing, facility leases, research grants, and interest income on our investments.

In 2020 and 2021, we entered into the Royalty Purchase Agreements with RPI and OMERS. Under the Royalty Purchase Agreements, RPI and OMERS are entitled to receive tiered, sales-based royalties on net product sales of ORLADEYO in the United States and certain key European markets (collectively, the “Key Territories”), and other

markets where we sell ORLADEYO directly or through distributors. In addition, RPI and OMERS are 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. We will be required to make payments to OMERS commencing with the calendar quarter beginning October 1, 2023. See “Note 8—Royalty Monetizations—ORLADEYO and Factor D Inhibitors” in the Notes to Consolidated Financial Statements in Part II, Item 8 of this report for additional information about these financing transactions.

In 2020, we entered into our Credit Agreement with Athyrium Opportunities III Co-Invest 1 LP (“Athyrium” and such agreement, as subsequently amended, the “Credit Agreement”). Our Credit Agreement with Athyrium provides for three term loans. We received the proceeds from the \$125.0 million Term A Loan in December 2020. The Term B Loan and the Term C Loan were both funded in the respective principal amounts of \$25.0 million and \$50.0 million on July 29, 2022. The maturity date of the Credit Agreement is December 7, 2025. For each of the first eight full fiscal quarters following December 7, 2020, we had 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 quarter ended December 31, 2022 was the last PIK eligible period. Accordingly, we are obligated to make quarterly interest payments on the outstanding principal of the Term Loans as of December 31, 2022. See “Note 9—Debt—Credit Agreement” in the Notes to Consolidated Financial Statements in Part II, Item 8 of this report for additional information about the Credit Agreement.

As of December 31, 2022, we had net working capital of \$411.0 million, a decrease of approximately \$51.4 million from \$462.4 million at December 31, 2021. The decrease in working capital was primarily the result of general operations, partially offset by the \$75.0 million proceeds received from the funding of the Term B Loan and Term C Loan in July 2022. Our principal sources of liquidity at December 31, 2022 were approximately \$304.8 million in cash and cash equivalents and approximately \$119.5 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, commercialize ORLADEYO, and hire additional personnel. 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 to maintain 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;
- public or private equity and/or debt financing;
- our existing capital resources and interest earned on that capital;
- revenues from product sales; 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 of funding or assistance, if any, we receive from 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, the success of our commercialization efforts for, 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 revenues, expenses, and cash utilization rate.

Based on our expectations for revenue and operating expenses, we believe our financial resources will be sufficient to fund our operations for at least the next 12 months. However, we have sustained operating losses for the majority of our corporate history and expect that our 2023 expenses will exceed our 2023 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 regularly evaluate other opportunities to fund future operations, including: (1) out-licensing rights to certain of our products or product candidates, pursuant to which we would receive cash milestone payments; (2) raising additional capital through equity or debt financings or from other sources, including royalty or other monetization transactions; (3) obtaining additional product candidate regulatory approvals, which would generate revenue, milestone payments and cash flow; (4) reducing spending on one or more research and development programs, including by discontinuing development; (5) restructuring operations to change our overhead structure and/or (6) securing or increasing U.S. Government funding of our programs, including obtaining procurement contracts. 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 our 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 research and development and commercial expenses; and key developments 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 of such products by either us or our partners;
- our ability to receive reimbursement and stockpiling procurement contracts;
- the progress and magnitude of our research, drug discovery and development programs;
- changes in existing collaborative relationships;
- 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 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 may 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, including to take advantage

of favorable opportunities in the capital markets. Additional funding may not be available when needed or in the form or on terms acceptable to us. Our future working capital requirements, including the need for additional working capital, will largely be determined by the advancement of our portfolio of product candidates and the commercialization of ORLADEYO, as well as any future decisions regarding the future of the RAPIVAB program, 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. See “Risk Factors—Risks Relating to Our Business—Financial and Liquidity Risks” and “Risk Factors—Risks Relating to Our Business—Risks Relating to Drug Development and Commercialization—If we fail to obtain additional financing or acceptable partnership arrangements as and when needed, we may be unable to complete the development and commercialization of our products and product candidates or continue operations” in Part I, Item 1A of this report for further discussion of the risks related to obtaining additional capital.

The restrictive covenants contained in our Credit Agreement 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; 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, 2022, we were in compliance with the covenants under the Credit Agreement.

Critical Accounting Estimates

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” in the Notes to 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.

Revenue Recognition

Pursuant to Accounting Standards Codification (“ASC”) Topic 606, we recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To achieve this core principle, Topic 606 includes provisions within a five step model that includes (i) identifying the contract with a customer, (ii) identifying the performance obligations in the contract, (iii) determining the transaction price, (iv) allocating the transaction price to the performance obligations, and (v) recognizing revenue when, or as, an entity satisfies a performance obligation.

At contract inception, we identify the goods or services promised within each contract, assess whether each promised good or service is distinct, and determine those that are performance obligations. We recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when the performance obligation is satisfied.

Product Sales, Net

Our principal sources of product sales are sales of ORLADEYO, which we began shipping to patients in December 2020, sales of peramivir to our licensing partners and sales of RAPIVAB to the HHS under our procurement contract. In the United States, we ship ORLADEYO directly to patients through a single specialty pharmacy, which is considered our customer. In the European Union, United Kingdom and elsewhere, we sell ORLADEYO to specialty distributors as well as hospitals and pharmacies, which collectively are considered our customers.

We recognize revenue for sales when our customers obtain control of the product, which generally occurs upon delivery. For ORLADEYO, we classify payments to our specialty pharmacy customer for certain services provided by our customer as selling, general and administrative expenses to the extent such services provided are determined to be distinct from the sale of our product.

Net revenue from sales of ORLADEYO is recorded at net selling price (transaction price), which includes estimates of variable consideration for which reserves are established for (i) estimated government rebates, such as Medicaid and Medicare Part D reimbursements, and estimated managed care rebates, (ii) estimated chargebacks, (iii) estimated costs of co-payment assistance programs and (iv) product returns. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable or as a current liability. Overall, these reserves reflect our best estimates of the amount of consideration to which the Company is entitled based on the terms of the applicable contract. The amount of variable consideration included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from estimates, we adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Government and Managed Care Rebates. We contract with government agencies and managed care organizations or, collectively, third-party payors, so that ORLADEYO will be eligible for purchase by, or partial or full reimbursement from, such third-party payors. We estimate the rebates we will provide to third-party payors and deduct these estimated amounts from total gross product revenues at the time the revenues are recognized. These reserves are recorded in the same period in which the revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability. We estimate the rebates that we will provide to third-party payors based upon (i) our contracts with these third-party payors, (ii) the government mandated discounts applicable to government-funded programs, (iii) a range of possible outcomes that are probability-weighted for the estimated payor mix, and (iv) product distribution information obtained from our specialty pharmacy.

Chargebacks. Chargebacks are discounts that occur when certain contracted customers, pharmacy benefit managers, insurance companies, and government programs purchase directly from our specialty pharmacy. These customers purchase our products under contracts negotiated between them and our specialty pharmacy. The specialty pharmacy, in turn, charges back to us the difference between the price the specialty pharmacy paid and the negotiated price paid by the contracted customers, which may be higher or lower than the specialty pharmacy purchase price with us. We estimate chargebacks and adjust gross product revenues and accounts receivable based on the estimates at the time revenues are recognized.

Co-payment assistance and patient assistance programs. Patients who have commercial insurance and meet certain eligibility requirements may receive co-payment assistance. Based upon the terms of the program and co-payment assistance utilization reports received from the specialty pharmacy, we are able to estimate the co-payment assistance amounts, which are recorded in the same period in which the related revenue is recognized, resulting in a reduction of product revenue. We also offer a patient assistance program that provides free drug product, for a limited period of time, to allow a patient's insurance coverage to be established. Based on patient assistance program utilization reports provided by the specialty pharmacy, we record gross revenue of the product provided and a full reduction of the revenue amount for the free drug discount.

Product returns. We do not provide contractual return rights to our customers, except in instances where the product is damaged or defective. Non-acceptance by the patient of shipped drug product by the specialty pharmacy

is reflected as a reversal of sales in the period in which the sales were originally recorded. Reserves for estimated non-acceptances by patients are recorded as a reduction of revenue in the period that the related revenue is recognized, as well as a reduction to accounts receivable. Estimates of non-acceptance are based on quantitative information provided by the specialty pharmacy.

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 from these collaborative and other research and development arrangements are license, service and royalty revenues.

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. For performance obligations based on services performed, we measure progress using an input method based on the effort we expend or costs we incur toward the satisfaction of the performance obligation in relation to the total estimated effort or 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 we separately sell the products or services. If a standalone selling price is not directly observable, then we estimate the standalone selling price using either an adjusted market assessment approach or an expected cost plus margin approach, representing the amount that we believe 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) 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.

Inventory

Our inventories primarily relate to ORLADEYO. Additionally, our inventory includes RAPIVAB and peramivir.

We value our inventories at the lower of cost or estimated net realizable value. We determine the cost of our inventories, which includes amounts related to materials, labor, manufacturing overhead and shipping and handling costs on a first-in, first-out (FIFO) basis. Raw materials and work-in-process includes all inventory costs prior to packaging and labeling, including raw material, active product ingredient, and drug product. Finished goods include packaged and labeled products.

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. During the quarter ended December 31, 2022, we evaluated our inventory levels and associated expiration dating relative to the latest sales forecasts for ORLADEYO and RAPIVAB and estimated those inventories at risk of obsolescence. Accordingly, we recorded an increase to the inventory valuation reserve of \$0.9 million for a total reserve of \$1.2 million as of December 31, 2022.

We expense 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 upon receipt of regulatory approval. Upon regulatory approval, we capitalize subsequent costs related to the production of inventories.

Accrued Expenses

We enter 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. We record liabilities under these contractual commitments when we determine 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 (i) fees paid to clinical research organizations (“CROs”) in connection with preclinical and toxicology studies and clinical trials; (ii) fees paid to investigative sites in connection with clinical trials; (iii) fees paid to contract manufacturers in connection with the production of our raw materials, drug substance, drug products, and product candidates; and (iv) 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.

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, as well as termination fees and other commitments associated with discontinued programs. 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 ongoing review of the level of services actually performed.

Additionally, we have 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 (“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 sublicense 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. Additionally, direct expenses consist of those costs necessary to discontinue and close out a development program, including termination fees and other commitments. 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 stock option 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 and restricted stock units 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 Obligations

The royalty financing obligations are eligible to be repaid based on royalties from net sales of ORLADEYO and BCX10013. Interest expense is accrued using the effective interest rate method over the estimated period each of the related liabilities 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 each of the royalty financing obligations and record interest expense using an imputed effective interest rate. We 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 each of the liabilities, as well as the periods over which associated issuance costs will be amortized. A significant increase or decrease in forecasted net sales could materially impact each of the liability balances, interest expense and the time periods 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. 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 and therefore mark-to-market adjustments were recognized in our Consolidated Statements of Comprehensive Loss.

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 substantially 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.

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 Loans under the Credit Agreement bear interest each quarter at a rate equal to the three-month London Interbank Offered Rate (“LIBOR”), which is capped to be no less than 1.75% and no more than 3.50%, plus 8.25% or, for each quarterly interest period in which a PIK Interest Payment is made, the three-month 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. For the year ended December 31, 2022, interest was accrued at an effective interest rate of 12.87% on the \$200.0 million borrowings under the Credit Agreement.

The quarter ended December 31, 2022 was the last PIK eligible period. Accordingly, we are obligated to make quarterly interest payments on the outstanding principal of the Term Loans as of December 31, 2022. The three-month LIBOR was 4.73% as of December 28, 2022, the LIBOR measurement date for the three-month interest period beginning January 1, 2023. As the three-month LIBOR rate exceeds the LIBOR cap of 3.50%, the 3.50% cap plus 8.25% will be used to record interest expense for the three-month interest period beginning January 1, 2023.

In June 2023, LIBOR will be discontinued as a reference rate. The Credit Agreement contains language allowing for the substitution, through an amendment, of a new benchmark rate, which may be the Secured Overnight Financing Rate (“SOFR”), in the event that LIBOR is no longer available. This transition is not expected to have a material impact on our financial statements.

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

Most of our revenues and expenses are denominated in U.S. dollars. Our commercial sales in Europe are primarily denominated in Euros and the British Pound. We also had other transactions denominated in foreign currencies during the year ended December 31, 2022, primarily related to operations in Europe, contract manufacturing and ex-U.S. clinical trial activities, and we expect to continue to do so. Our royalties from Torii are derived from Torii's sales of ORLADEYO in Japan. Those sales are denominated in Japanese yen and converted into U.S. dollars for purposes of determining the royalty owed to us. Our limited foreign currency exposure relative to our European operations is to fluctuations in the Euro, British Pound, Swiss Franc, Danish Krone, and Swedish Krona. Additionally, we have initiated operations in Canada and have foreign currency exposure relative to the Canadian Dollar.

We do not anticipate that foreign currency transaction gains or losses will be significant at our current level of operations. However, transaction gains or losses may become significant in the future as we continue to expand our operations internationally. We have not engaged in foreign currency hedging during 2022; however, we may do so in the future.

Inflation Risk

Inflation generally impacts us by potentially increasing our operating expenses, including clinical trial costs and selling activities. We do not believe that inflation has had a material impact on our business or results of operations during the periods for which the condensed consolidated financial statements are presented in this report. Significant adverse changes in inflation could negatively impact our future results of operations.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

**BIOCRIST PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except per share amounts)**

	<u>December 31,</u>	
	<u>2022</u>	<u>2021</u>
ASSETS		
Cash and cash equivalents	\$ 304,767	\$ 504,389
Restricted cash	1,472	3,345
Investments	119,543	3,212
Trade receivables	50,599	29,413
Inventory, net	27,533	15,791
Prepaid expenses and other current assets	<u>12,586</u>	<u>9,986</u>
Total current assets	516,500	566,136
Property and equipment, net	8,617	8,714
Long-term investments	18,077	6,829
Other assets	<u>6,806</u>	<u>6,472</u>
Total assets	<u>\$ 550,000</u>	<u>\$ 588,151</u>
LIABILITIES AND STOCKHOLDERS' DEFICIT		
Accounts payable	\$ 14,356	\$ 27,808
Accrued expenses	87,565	72,670
Deferred revenue	1,224	1,421
Lease financing obligation	<u>2,369</u>	<u>1,819</u>
Total current liabilities	105,514	103,718
Lease financing obligation	5,804	5,962
Royalty financing obligations	501,655	449,375
Secured term loan	231,624	136,082
Stockholders' deficit:		
Preferred stock, \$0.01 par value; shares authorized — 5,000; no shares outstanding	—	—
Common stock, \$0.01 par value; shares authorized — 450,000; Issued and outstanding — 187,906 and 184,350 at December 31, 2022 and 2021, respectively	1,879	1,843
Additional paid-in capital	1,158,118	1,098,498
Accumulated other comprehensive income	26	177
Accumulated deficit	<u>(1,454,620)</u>	<u>(1,207,504)</u>
Total stockholders' deficit	<u>(294,597)</u>	<u>(106,986)</u>
Total liabilities and stockholders' deficit	<u>\$ 550,000</u>	<u>\$ 588,151</u>

See accompanying notes to consolidated financial statements.

BIOCRIST PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(In thousands, except per share amounts)

	Years Ended December 31,		
	2022	2021	2020
Revenues			
Product sales, net	\$ 267,710	\$ 136,350	\$ 3,301
Royalty revenue	2,903	(100)	3,381
Milestone revenue	—	15,000	—
Collaborative and other research and development	214	5,920	11,130
Total revenues	270,827	157,170	17,812
Expenses			
Cost of products sold	6,408	7,229	1,550
Research and development	253,297	208,808	122,964
Selling, general and administrative	159,371	118,818	67,929
Royalty	186	35	126
Total operating expenses	419,262	334,890	192,569
Loss from operations	(148,435)	(177,720)	(174,757)
Interest and other income	5,127	62	9,420
Interest expense	(99,092)	(59,294)	(14,501)
Gain (loss) on extinguishment of debt	—	55,838	(2,011)
Foreign currency losses, net	(1,983)	(695)	(965)
Loss before income taxes	\$(244,383)	\$(181,809)	\$(182,814)
Income tax expense	2,733	2,253	—
Net loss	\$(247,116)	\$(184,062)	\$(182,814)
Foreign currency translation adjustment	890	189	—
Unrealized loss on available for sale investments	(1,041)	(15)	(36)
Net comprehensive loss	\$(247,267)	\$(183,888)	\$(182,850)
Basic and diluted net loss per common share	\$ (1.33)	\$ (1.03)	\$ (1.09)
Weighted average shares outstanding	185,908	179,117	167,267

See accompanying notes to consolidated financial statements.

BIOCRIST PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands, except per share amounts)

	Years Ended December 31,		
	2022	2021	2020
Cash flows from operating activities:			
Net loss	\$(247,116)	\$(184,062)	\$(182,814)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,437	777	748
Inventory obsolescence expense	932	—	—
Stock-based compensation expense	44,701	34,640	14,794
Non-cash interest expense on royalty financing obligations and secured term loan and amortization of debt issuance costs	98,918	54,204	3,325
Amortization of premium/discount on investments	(1,777)	(2)	121
Change in fair value of foreign currency derivative	—	—	632
(Gain) loss on extinguishment of debt	—	(55,838)	1,211
Changes in operating assets and liabilities:			
Receivables	(21,470)	(20,817)	13,903
Inventory	(12,423)	(8,767)	(7,039)
Prepaid expenses and other assets	(2,583)	(7,155)	(2,140)
Accounts payable and accrued expenses	(22,360)	39,412	17,355
Interest payable	—	4,168	6,766
Deferred revenue	(109)	1,283	(1,970)
Net cash used in operating activities	(161,850)	(142,157)	(135,108)
Cash flows from investing activities:			
Acquisition of property and equipment	(1,351)	(2,385)	(514)
Purchases of investments	(244,283)	(10,012)	(49,818)
Sales and maturities of investments	117,396	28,201	43,476
Net cash (used in) provided by investing activities	(128,238)	15,804	(6,856)
Cash flows from financing activities:			
Sale of common stock, net	—	50,000	93,279
Sale of pre-funded warrants	—	—	14,817
Net proceeds from common stock issued under stock-based compensation plans	14,955	15,794	2,446
Proceeds from additional credit facility	73,072	—	—
Payment of senior credit facility	—	—	(52,420)
Net proceeds from secured term loan	—	—	119,867
Net proceeds from royalty financing obligations	—	293,874	122,600
Net cash provided by financing activities	88,027	359,668	300,589
Effects of exchange rates on cash, cash equivalents and restricted cash	566	71	—
(Decrease) increase in cash, cash equivalents and restricted cash	(201,495)	233,386	158,625
Cash, cash equivalents and restricted cash at beginning of year	507,734	274,348	115,723
Cash, cash equivalents and restricted cash at end of year	<u>\$ 306,239</u>	<u>\$ 507,734</u>	<u>\$ 274,348</u>

See accompanying notes to consolidated financial statements.

BIOCRIST PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' DEFICIT
(In thousands, except per share amounts)

	<u>Common Stock</u>	<u>Additional Paid-In Capital</u>	<u>Accumulated Other Comprehensive (Loss) Income</u>	<u>Accumulated Deficit</u>	<u>Total Stockholders' Equity (Deficit)</u>
Balance at December 31, 2019	<u>\$1,541</u>	<u>\$ 877,300</u>	<u>\$ 39</u>	<u>\$ (840,628)</u>	<u>\$ 38,252</u>
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	<u>\$1,769</u>	<u>\$1,002,408</u>	<u>\$ 3</u>	<u>\$(1,023,442)</u>	<u>\$ (19,262)</u>
Net loss	—	—	—	(184,062)	(184,062)
Other comprehensive income	—	—	174	—	174
Exercise of stock options, 3,299 shares, net	33	13,772	—	—	13,805
Employee stock purchase plan sales, 321 shares, net	3	1,986	—	—	1,989
Issuance of common stock associated with royalty financing agreement, 3,846 shares, net	38	45,692	—	—	45,730
Stock-based compensation expense	—	34,640	—	—	34,640
Balance at December 31, 2021	<u>\$1,843</u>	<u>\$1,098,498</u>	<u>\$ 177</u>	<u>\$(1,207,504)</u>	<u>\$(106,986)</u>
Net loss	—	—	—	(247,116)	(247,116)
Other comprehensive loss	—	—	(151)	—	(151)
Exercise of stock options, 3,044 shares, net	30	12,060	—	—	12,090
Employee stock purchase plan sales, 260 shares, net	3	2,859	—	—	2,862
Exercise of warrants, 253 shares	3	—	—	—	3
Stock-based compensation expense	—	44,701	—	—	44,701
Balance at December 31, 2022	<u>\$1,879</u>	<u>\$1,158,118</u>	<u>\$ 26</u>	<u>\$(1,454,620)</u>	<u>\$(294,597)</u>

See accompanying notes to consolidated financial statements.

BIOCRIST PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(In thousands, except per share amounts)

Note 1— Significant Accounting Policies and Concentrations of Risk

The Company

BioCryst Pharmaceuticals, Inc. (the “Company”) is a commercial-stage biotechnology company that discovers and commercializes novel, oral, small-molecule medicines. The Company focuses 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. 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’s marketed products include oral, once-daily ORLADEYO® for the prevention of hereditary angioedema (“HAE”) attacks and RAPIVAB® (peramivir injection) for the treatment of acute uncomplicated influenza in the United States. ORLADEYO received regulatory approval in the United States in December 2020. ORLADEYO has also received regulatory approvals in multiple global markets. The Company is commercializing ORLADEYO in each of these territories directly or through distributors, except in Japan where Torii Pharmaceutical Co., Ltd. (“Torii”), the Company’s collaborative partner, has the exclusive right to commercialize ORLADEYO for the prevention of HAE attacks in exchange for certain milestone and royalty payments to the Company. In addition to its approval in the United States, peramivir injection has received regulatory approvals in Canada, Australia, Japan, Taiwan and Korea.

Based on the Company’s expectations for revenue and operating expenses, the Company believes its financial resources available at December 31, 2022 will be sufficient to fund its operations for at least the next 12 months. The Company has sustained operating losses for the majority of its corporate history and expects that its 2023 expenses will exceed its 2023 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 regularly evaluates other opportunities to fund future operations, including: (1) out-licensing rights to certain of its products or product candidates, pursuant to which the Company would receive cash milestone payments; (2) raising additional capital through equity or debt financings or from other sources, including royalty or other monetization transactions; (3) obtaining additional product candidate regulatory approvals, which would generate revenue, milestone payments and cash flow; (4) reducing spending on one or more research and development programs, including by discontinuing development; (5) restructuring operations to change its overhead structure; and/or (6) securing or increasing U.S. Government funding of its programs, including obtaining procurement contracts. 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; the timing, scope and magnitude of its research and development and commercial expenses; and key developments 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.

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 ORLADEYO and Factor D inhibitors royalty financing obligations 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.

Revenue Recognition

Pursuant to Accounting Standards Codification ("ASC") Topic 606, the Company recognizes revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To achieve this core principle, Topic 606 includes provisions within a five step model that includes (i) identifying the contract with a customer, (ii) identifying the performance obligations in the contract, (iii) determining the transaction price, (iv) allocating the transaction price to the performance obligations, and (v) recognizing revenue when, or as, an entity satisfies a performance obligation.

At contract inception, the Company identifies the goods or services promised within each contract, assesses whether each promised good or service is distinct and determines those that are performance obligations. The Company recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when the performance obligation is satisfied.

Product Sales, Net

The Company's principal sources of product sales are sales of ORLADEYO, which the Company began shipping to patients in December 2020, sales of peramivir to the Company's licensing partners and sales of RAPIVAB to the U.S. Department of Health and Human Services ("HHS") under the Company's procurement contract. In the United States, the Company ships ORLADEYO directly to patients through a single specialty pharmacy, which is considered its customer. In the European Union, United Kingdom and elsewhere, the Company sells ORLADEYO to specialty distributors as well as hospitals and pharmacies, which collectively are considered its customers.

The Company recognizes revenue for sales when its customers obtain control of the product, which generally occurs upon delivery. For ORLADEYO, the Company classifies payments to its specialty pharmacy customer for certain services provided by its customer as selling, general and administrative expenses to the extent such services provided are determined to be distinct from the sale of its product.

Net revenue from sales of ORLADEYO is recorded at net selling price (transaction price), which includes estimates of variable consideration for which reserves are established for (i) estimated government rebates, such as Medicaid and Medicare Part D reimbursements, and estimated managed care rebates, (ii) estimated chargebacks, (iii) estimated costs of co-payment assistance programs and (iv) product returns. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable or as a current liability. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which it is entitled based on the terms of the applicable contract. The amount of variable consideration included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from estimates, the Company adjusts these estimates, which would affect net product revenue and earnings in the period such variances become known.

Government and Managed Care Rebates. The Company contracts with government agencies and managed care organizations or, collectively, third-party payors, so that ORLADEYO will be eligible for purchase by, or partial or full reimbursement from, such third-party payors. The Company estimates the rebates it will provide to third-party payors and deducts these estimated amounts from total gross product revenues at the time the revenues are recognized. These reserves are recorded in the same period in which the revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability. The Company estimates the rebates that it

will provide to third-party payors based upon (i) the Company's contracts with these third-party payors, (ii) the government mandated discounts applicable to government-funded programs, (iii) a range of possible outcomes that are probability-weighted for the estimated payor mix, and (iv) product distribution information obtained from the Company's specialty pharmacy.

Chargebacks. Chargebacks are discounts that occur when certain contracted customers, pharmacy benefit managers, insurance companies, and government programs purchase directly from the Company's specialty pharmacy. These customers purchase the Company's product under contracts negotiated between them and the Company's specialty pharmacy. The specialty pharmacy, in turn, charges back to the Company the difference between the price the specialty pharmacy paid and the negotiated price paid by the contracted customers, which may be higher or lower than the specialty pharmacy's purchase price from the Company. The Company estimates chargebacks and adjusts gross product revenues and accounts receivable based on the estimates at the time revenues are recognized.

Co-payment assistance and patient assistance programs. Patients who have commercial insurance and meet certain eligibility requirements may receive co-payment assistance. Based upon the terms of the program and co-payment assistance utilization reports received from the specialty pharmacy, the Company is able to estimate the co-payment assistance amounts, which are recorded in the same period in which the related revenue is recognized, resulting in a reduction of product revenue. The Company also offers a patient assistance program that provides free drug product, for a limited period of time, to allow a patient's insurance coverage to be established. Based on patient assistance program utilization reports provided by the specialty pharmacy, the Company records gross revenue of the product provided and a full reduction of the revenue amount for the free drug discount.

Product returns. The Company does not provide contractual return rights to its customers, except in instances where the product is damaged or defective. Non-acceptance by the patient of shipped drug product by the specialty pharmacy is reflected as a reversal of sales in the period in which the sales were originally recorded. Reserves for estimated non-acceptances by patients are recorded as a reduction of revenue in the period that the related revenue is recognized, as well as a reduction to accounts receivable. Estimates of non-acceptance are based on quantitative information provided by the specialty pharmacy.

Collaborative and Other Research and Development Arrangements and Royalties

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 from these collaborative and other research and development arrangements are license, service and royalty revenues.

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 it expends or costs it incurs toward the satisfaction of the performance obligation in relation to the total estimated effort or 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 HHS ("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.

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 of \$23 and \$1,924 as of December 31, 2022 and 2021, respectively, reflects royalty revenue paid by Shionogi & Co., Ltd. ("Shionogi") designated for interest on the PharMA Notes (defined in Note 8). Additionally, restricted cash of \$1,449 and \$1,421, respectively, reflects collateral for a letter of credit the Company is required to maintain associated with the lease execution and build-out of its 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, certificates of deposits, municipal and corporate notes and bonds, and commercial paper, 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 12 months. Some of the securities in which the Company invests 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, 2022, the Company believes that the cost of its investments is recoverable in all material respects.

Trade Receivables

The majority of the Company's trade receivables arise from product sales and primarily represent amounts due from its specialty pharmacy customer in the United States and other third-party distributors, hospitals and pharmacies in the European Union, United Kingdom and elsewhere and have standard payment terms that generally require payment within 30 to 90 days.

Receivables from collaborations are recorded for amounts due to the Company related to reimbursable research and development costs from the HHS, and royalty receivables from the Company's partners, including Shionogi, Green Cross, and Torii.

Invoices are submitted to the HHS 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.

The Company does not adjust its receivables for the effects of a significant financing component at contract inception if it expects to collect the receivables in one year or less from the time of sale.

The Company provides reserves against trade receivables for estimated losses that may result from a customer's inability to pay. Receivables 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, specific circumstances and the Company's own historical collection experience. Amounts determined to be uncollectible are charged or written-off against the reserve.

Inventory

The Company values its inventories at the lower of cost or estimated net realizable value. The Company determines the cost of its inventories, which includes amounts related to materials, labor, manufacturing overhead, and shipping and handling costs on a first-in, first-out (FIFO) basis. Raw materials and work-in-process include all inventory costs prior to packaging and labelling, including raw material, active product ingredient, and the drug product. Finished goods include packaged and labelled products.

The Company's inventories are subject to expiration dating. The Company regularly evaluates the carrying value of its inventories and provides valuation reserves for any estimated obsolete, short-dated or unmarketable inventories. In addition, the Company may experience spoilage of its raw materials and supplies. The Company's determination that a valuation reserve might be required, in addition to the quantification of such reserve, requires it to utilize significant judgment. During the quarter ended December 31, 2022, the Company evaluated its inventory levels and associated expiration dating relative to the latest sales forecasts for ORLADEYO and RAPIVAB and estimated those inventories at risk of obsolescence. Accordingly, the Company recorded an increase to the inventory valuation reserve of \$932 for a total reserve of \$1,177 as of December 31, 2022.

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.

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 which can include assumptions such as expected patient enrollment, site activation and estimated project duration. The Company periodically confirms the accuracy of its estimates with the service providers and makes adjustments if necessary. Examples of estimated accrued expenses include (i) fees paid to clinical research organizations (“CROs”) in connection with preclinical and toxicology studies and clinical trials; (ii) fees paid to investigative sites in connection with clinical trials; (iii) fees paid to contract manufacturers in connection with the production of the Company’s raw materials, drug substance, drug products, and product candidates; and (iv) 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, 2022 and December 31, 2021, the carrying value of accrued expenses approximates their fair value due to their short-term settlement.

Cost of Product Sales

Cost of product sales includes the cost of producing and distributing inventories that are related to product revenue during the respective period, including freight. In addition, shipping and handling costs for product shipments are recorded as incurred. Finally, cost of product sales may also include costs related to excess or obsolete inventory adjustment charges.

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, as well as termination fees and commitments associated with discontinued programs. 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 ongoing 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 sublicense 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.

Selling, General and Administrative Expenses

Selling, general and administrative expense is primarily comprised of compensation and benefits associated with sales and marketing, finance, human resources, legal, information technology and other administrative personnel. Additionally, selling, general and administrative expenses are comprised of market research, marketing, advertising and legal expenses, including patent costs, licenses and other general and administrative costs.

Advertising expenses related to ORLADEYO were \$14,891, \$5,705 and \$6,567 for the years ended December 31, 2022, 2021 and 2020 respectively.

All patent related costs are expensed to selling, general and administrative expenses when incurred as recoverability of such expenditures is uncertain.

Leases

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, 2022. The Company accounts for lease obligations in accordance with ASU 2016-02: *Leases (Topic 842)*, which requires a lessee to recognize a right-of-use asset and a lease liability on its balance sheet for most operating leases.

Certain of the Company’s 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 Sheets represent payments over the lease term, which includes renewal options for certain real estate leases that the Company is 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. 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.

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 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.

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, the Company has outstanding performance-based stock options and restricted stock units for which no compensation expense is recognized until “performance” is deemed to have occurred.

Interest Expense and Deferred Financing Costs

Interest expense for the years ended December 31, 2022, 2021 and 2020 was \$99,092, \$59,294 and \$14,501, respectively, and primarily relates to the royalty financing obligations and PhaRMA Notes (Note 8), the secured term loan borrowing from the Credit Agreement and the senior credit facility (Note 9). Costs directly associated with the borrowings have been capitalized and are netted against the corresponding debt liabilities on the Consolidated Balance Sheets. These costs are being amortized to interest expense over the terms of the corresponding borrowings using the effective interest rate method. Amortization of deferred financing costs included in interest expense was \$(916), \$(531) and \$1,217 for the years ended December 31, 2022, 2021 and 2020, respectively.

In December 2021, the PhaRMA Notes and associated accrued interest payable was written-off into other income as a debt extinguishment (Refer to “Note 8—Royalty Monetizations—RAPIACTA—Non-Recourse Notes Payable—Debt Extinguishment” for additional information regarding the debt extinguishment). 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.

Interest Expense and Royalty Financing Obligations

The royalty financing obligations are eligible to be repaid based on royalties from net sales of ORLADEYO and BCX10013. Interest expense is accrued using the effective interest rate method over the estimated period each of the related liabilities 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 each of the royalty financing obligations and records interest expense using an imputed effective interest rate. The Company reassesses the expected royalty payments each reporting period and accounts 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 require that the Company make estimates that could impact the carrying value of each of the liabilities, as well as the periods over which associated issuance costs will be amortized. A significant increase or decrease in forecasted net sales could materially impact each of the liability balances, interest expense and the time periods for repayment.

Currency Hedge Agreement

In connection with the issuance by JPR Royalty Sub LLC 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 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 year ended December 31, 2020 resulted in a loss of \$632. In addition, realized currency exchange gains of \$662 were recognized in 2020 related to the exercise of a U.S. dollar/Japanese yen currency option under the Company’s foreign currency hedge.

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.

Beginning in fiscal year 2021, the Company began accruing for U.S. state taxes and foreign income taxes as a result of increased nexus in both U.S. state and foreign jurisdictions where historically the Company had no presence.

In addition, starting in 2022, amendments to Section 174 of the Internal Revenue Code of 1986, as amended (“IRC”), will no longer permit an immediate deduction for research and development expenditures in the tax year that such costs are incurred. Instead, these IRC Section 174 development costs must now be capitalized and amortized over either a five- or 15-year period, depending on the location of the activities performed. The new amortization period begins with the midpoint of any taxable year that IRC Section 174 costs are first incurred, regardless of

whether the expenditures were made prior to or after July 1, and runs until the midpoint of year five for activities conducted in the United States or year fifteen in the case of development conducted on foreign soil. As a result of this tax law change, the Company has recorded an increased U.S. state tax provision for the year ended December 31, 2022.

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, warrants and common shares expected to be issued under the Company's equity compensation plans were anti-dilutive. The calculation of diluted earnings per share for the years ended December 31, 2022, 2021, and 2020 does not include 25,596, 26,034, and 14,957, respectively, of potential common shares as their impact would be anti-dilutive.

Accumulated Other Comprehensive Income

Accumulated other comprehensive income is comprised of cumulative foreign currency translation adjustments and unrealized gains and losses on available-for-sale investments and is disclosed as a separate component of stockholders' equity. Realized gain and loss amounts on available-for-sale investments are reclassified from accumulated other comprehensive loss and recorded as interest and other income on the Consolidated Statements of Comprehensive Loss. For the year ended December 31, 2021, realized gains of \$1 were reclassified out of accumulated other comprehensive income.

Significant Customers and Other Risks

Significant Customers

The Company's primary sources of revenue and cash flow are the sales of ORLADEYO in the United States and other global markets and, for 2022, sales of RAPIVAB (peramivir injection) under the Company's procurement contract with the Assistant Secretary for Preparedness and Response within HHS. Additionally, the Company received reimbursement of galidesivir (formerly BCX4430) development expenses earned under cost-plus-fixed-fee contracts with BARDA/HHS and NIAID/HHS.

ORLADEYO is distributed through an arrangement with a single specialty pharmacy in the United States which represents the substantial majority of the ORLADEYO net product sales. The specialty pharmacy subsequently sells ORLADEYO to its customers (pharmacy benefit managers, insurance companies, government programs and group purchasing organizations) and dispenses product to patients. The specialty pharmacy's inability or unwillingness to continue these distribution activities could adversely impact the Company's business, results of operations and financial condition.

The Company is distributing ORLADEYO in other global markets directly or through distributors, except in Japan where Torii, the Company's collaborative partner, has the exclusive right to commercialize ORLADEYO.

The Company relied on BARDA/HHS and NIAID/HHS to reimburse predominantly all of the development costs for its galidesivir program and stockpiling sales of RAPIVAB to HHS. Accordingly, reimbursement of these expenses has represented a significant portion of the Company's collaborative and other research and development revenues. All government funding for galidesivir expired in 2022.

Additionally, HHS is the primary customer for RAPIVAB, and it exercised the remaining options for the purchase of RAPIVAB under the procurement contract with the Company during 2022.

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 its 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 a single source manufacturer for active pharmaceutical ingredient and finished drug product manufacturing of product candidates in development and on a single specialty pharmacy for distribution of approved drug product in the United States. Delays or disruption in the manufacture or distribution of any product could adversely impact the future procurement stockpiling of the Company's commercial product, commercial revenue and product candidates.

Credit Risk

Cash equivalents and investments are financial instruments that 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 12 months or less.

The Company's receivables from sales of ORLADEYO are primarily due from one customer, resulting in a concentration of credit risk. Sales of ORLADEYO from the Company to the specialty pharmacy only occur once an order of product has been received by the specialty pharmacy from one of its customers, which include pharmacy benefit managers, insurance companies, government programs and group purchasing organizations.

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

Recently Adopted Accounting Pronouncements

In December 2020, the FASB issued ASU No. 2019-12 (ASC Topic 740), *Simplifying the Accounting for Income Taxes*. ASU 2019-12 simplifies accounting for income taxes by removing certain exceptions to the general principles and clarifying existing guidance. This standard is effective for fiscal years, and interim periods within those years, beginning after December 15, 2020. The adoption of this standard did not have a material impact to the Company's financial position, results of operations or cash flows.

New Accounting Pronouncements Not Yet Adopted

In December 2022, the FASB issued ASU No. 2022-06 Reference Rate Reform (ASC Topic 848), *Deferral of the Sunset Date of Topic 848*, to provide optional guidance to temporarily ease the potential burden in accounting for (or recognizing the effects of) reference rate reform on financial reporting. Preceding the issuance of ASU 2020-04, which established ASC Topic 848, the United Kingdom's Financial Conduct Authority ("FCA") announced that it would no longer need to persuade or compel banks to submit to LIBOR after December 31, 2021. In response, the FASB established December 31, 2022 as the expiration date for ASC Topic 848. In March 2021, the FCA announced the intended cessation date of the overnight 1-month, 3-month, 6-month, and 12-month USD LIBOR would be June 30, 2023. Because the current relief in ASC Topic 848 may not cover a period of time during which a significant number of modifications may take place, this update deferred the sunset date in ASC Topic 848 from December 31, 2022 to December 31, 2024, after which entities will no longer be permitted to apply the relief in ASC Topic 848. The FASB guidance provides temporary optional expedients and exceptions for applying generally accepted accounting principles to contracts, hedging relationships and other transactions affected by reference rate reform. The provisions of the FASB guidance may impact the Company as contract modifications and other changes occur during the LIBOR transition period. The Company's Credit Agreement (as defined in Note 9 herein) references the 3-month LIBOR for quarterly interest rate determinations. The Credit Agreement contains language allowing for the substitution, through an amendment, of a new benchmark rate, which may be the Secured Overnight Financing Rate ("SOFR") in the event that LIBOR is no longer available. This transition is not expected to have a material impact on the Company's financial statements.

The Company has reviewed other new accounting pronouncements that were issued as of December 31, 2022 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— Revenue

The Company recorded the following revenues for the years ended December 31 (in thousands):

	<u>2022</u>	<u>2021</u>	<u>2020</u>
Product sales, net:			
ORLADEYO	\$249,689	\$121,865	\$ 133
RAPIVAB	15,156	7,231	483
Peramivir	<u>2,865</u>	<u>7,254</u>	<u>2,685</u>
Total product sales, net	267,710	136,350	3,301
Royalty revenue	2,903	(100)	3,381
Milestone revenue	—	15,000	—
Collaborative and other research and development revenues:			
U.S. Department of Health and Human Services	190	5,920	9,231
Other Collaborations	24	—	—
Torii Pharmaceutical Co., Ltd.	<u>—</u>	<u>—</u>	<u>1,899</u>
Total collaborative and other research and development revenues	<u>214</u>	<u>5,920</u>	<u>11,130</u>
Total revenues	<u>\$270,827</u>	<u>\$157,170</u>	<u>\$17,812</u>

Royalty revenue from sales of ORLADEYO in Japan by our collaborative partner, Torii, were \$1,944 and \$690 for the years ended December 31, 2022 and 2021, respectively.

Note 3— Investments

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.

	<u>December 31, 2022</u>				
	<u>Amortized Cost</u>	<u>Accrued Interest</u>	<u>Gross Unrealized Gains</u>	<u>Gross Unrealized Losses</u>	<u>Estimated Fair Value</u>
Obligations of U.S. Government and its agencies	\$129,940	\$427	\$—	\$ (996)	\$129,371
Corporate debt securities	6,093	37	—	(38)	6,092
Certificates of deposit	<u>2,163</u>	<u>23</u>	<u>—</u>	<u>(29)</u>	<u>2,157</u>
Total Investments	<u>\$138,196</u>	<u>\$487</u>	<u>\$—</u>	<u>\$(1,063)</u>	<u>\$137,620</u>

	<u>December 31, 2021</u>				
	<u>Amortized Cost</u>	<u>Accrued Interest</u>	<u>Gross Unrealized Gains</u>	<u>Gross Unrealized Losses</u>	<u>Estimated Fair Value</u>
Obligations of U.S. Government and its agencies	\$4,043	\$17	\$—	\$ (7)	\$ 4,053
Corporate debt securities	4,294	40	—	(5)	4,329
Certificates of deposit	<u>1,652</u>	<u>8</u>	<u>—</u>	<u>(1)</u>	<u>1,659</u>
Total Investments	<u>\$9,989</u>	<u>\$65</u>	<u>\$—</u>	<u>\$(13)</u>	<u>\$10,041</u>

The following table summarizes the scheduled maturity for the Company's investments at December 31, 2022 and 2021.

	<u>2022</u>	<u>2021</u>
Maturing in one year or less	\$119,543	\$ 3,212
Maturing after one year through two years	<u>18,077</u>	<u>6,829</u>
Total investments	<u>\$137,620</u>	<u>\$10,041</u>

Note 4— Trade Receivables

Product Sales

Receivables from product sales are recorded for amounts due to the Company related to sales of ORLADEYO® and RAPIVAB®. At December 31, 2022 and 2021, receivables related to sales of ORLADEYO were \$41,508 and \$27,384, respectively. At December 31, 2022 and 2021, receivables related to sales of RAPIVAB were \$823 and \$49, respectively. No bad debt reserve or allowance amounts were recorded as of December 31, 2022 and December 31, 2021, respectively.

Collaborations

Receivables from collaborations were as follows (in thousands):

	December 31, 2022		
	Billed	Unbilled	Total
U.S. Department of Health and Human Services, net	\$7,218	\$284	\$7,502
Royalty receivables from partners	741	—	741
Other collaborations	—	25	25
Total receivables from collaborators	<u>\$7,959</u>	<u>\$309</u>	<u>\$8,268</u>

	December 31, 2021		
	Billed	Unbilled	Total
U.S. Department of Health and Human Services, net	\$ 5	\$1,670	\$1,675
Royalty receivables from partners	305	—	305
Total receivables from collaborators	<u>\$310</u>	<u>\$1,670</u>	<u>\$1,980</u>

As of December 31, 2022 and 2021, the Company maintained a reserve of \$437 and \$701, respectively, related to royalties associated with Green Cross.

Note 5— Inventory

At December 31, 2022 and 2021, the Company's inventory primarily related to ORLADEYO. Additionally, inventory included RAPIVAB and peramivir, which is manufactured for the Company's partners.

The Company's inventories consisted of the following (in thousands):

	December 31,	
	2022	2021
Raw materials	\$ 8,906	\$ 5,658
Work-in-process	14,990	9,669
Finished goods	4,814	709
Total inventory	<u>\$28,710</u>	<u>\$16,036</u>
Reserves	<u>(1,177)</u>	<u>(245)</u>
Total inventory, net	<u>\$27,533</u>	<u>\$15,791</u>

Note 6— Property and Equipment

Property and equipment consisted of the following (in thousands):

	December 31,	
	2022	2021
Furniture and fixtures	\$ 1,308	\$ 1,122
Office equipment	633	467
Software	1,501	1,159
Laboratory equipment	4,588	4,247
Leasehold improvements	10,137	9,832
Total property and equipment	<u>\$18,167</u>	<u>\$16,827</u>
Less accumulated depreciation and amortization	<u>(9,550)</u>	<u>(8,113)</u>
Property and equipment, net	<u>\$ 8,617</u>	<u>\$ 8,714</u>

Depreciation and amortization expense for the years ended December 31, 2022, 2021, and 2020 was \$1,437, \$777, and \$748, respectively.

Note 7— Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2022	2021
Development costs	\$30,360	\$30,215
Compensation and benefits	22,125	20,674
Revenue-related reserves for discounts and allowances	14,332	5,957
Royalties payable	7,700	4,426
Inventory	4,193	3,793
Professional fees	1,128	1,305
Duties and taxes	410	2,622
Other	<u>7,317</u>	<u>3,678</u>
Total accrued expenses	<u>\$87,565</u>	<u>\$72,670</u>

Note 8— Royalty Monetizations

RAPIACTA

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 JPR Royalty Sub LLC, a wholly-owned subsidiary of the Company (“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 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/U.S. 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 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, if any, from Shionogi and legal costs associated with retiring the PhaRMA Notes. 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.

Non-Recourse Notes Payable – Debt Extinguishment

During 2021, the royalty-bearing patents associated with RAPIACTA in Japan expired. Accordingly, the Company evaluated the current circumstances of the PhaRMA Notes, including (i) their non-recourse nature relative to the Company, (ii) the current state of default since September 1, 2014 and the legal maturity on December 1, 2020 and (iii) the loss of patent protection relative to RAPIACTA in Japan, upon which any significant repayment of the PhaRMA Notes is predicated. As a result, the Company determined that it was no longer the financial obligor, and as a result, the principal balance of \$30,000 and associated accrued interest payable balance of \$25,838 were written off, resulting in a gain on extinguishment recorded in other income (expense) for the year ended December 31, 2021.

ORLADEYO and Factor D Inhibitors

On December 7, 2020, the Company and RPI 2019 Intermediate Finance Trust (“RPI”) entered into a Purchase and Sale Agreement (the “2020 RPI 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 “2020 RPI Royalty Sale”). Under the 2020 RPI Royalty Purchase Agreement, RPI is entitled to receive tiered, sales-based royalties on net product sales of ORLADEYO in the United States and certain key European markets (collectively, the “Key Territories”), and other markets where the Company sells ORLADEYO directly or through distributors (collectively, the “Direct Sales”) in an amount equal to: (i) 8.75% of aggregate annual net sales of ORLADEYO for annual net sales up to \$350,000 and (ii) 2.75% of annual net sales for annual net sales between \$350,000 and \$550,000. No royalty payments are payable on annual Direct Sales over \$550,000. In addition, RPI will be entitled to receive 1.0% of global net sales, if any, of BCX9930. On December 15, 2022, the Company announced that it was discontinuing the development of BCX9930.

Under the 2020 RPI 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.

On November 19, 2021, the Company and RPI entered into (i) a Purchase and Sale Agreement (the “2021 RPI Royalty Purchase Agreement” and together with the 2020 RPI Royalty Purchase Agreement, the “RPI Royalty Purchase Agreements”), pursuant to which the Company sold to RPI the right to receive certain royalty payments from the Company for a purchase price of \$150,000 in cash, and (ii) a Purchase and Sale Agreement with OCM IP Healthcare Holdings Limited, an affiliate of OMERS Capital Markets (“OMERS”) (the “OMERS Royalty Purchase Agreement” and collectively with the RPI Royalty Purchase Agreements, the “Royalty Purchase Agreements”), pursuant to which the Company sold to OMERS the right to receive certain royalty payments from the Company for a purchase price of an additional \$150,000 in cash.

Under the 2021 RPI Royalty Purchase Agreement, RPI is entitled to receive tiered, sales-based royalties on Direct Sales in an amount equal to: (i) 0.75% of aggregate annual net sales of ORLADEYO for annual net sales up to \$350,000 and (ii) 1.75% of annual net sales of ORLADEYO for annual net sales between \$350,000 and \$550,000. No royalty payments are payable on Direct Sales over \$550,000. RPI is also entitled to receive a tiered revenue share on ORLADEYO sublicense revenue or net sales by licensees in the Other Markets in an amount equal to 3.0% of proceeds received by the Company on annual net sales of up to \$150,000 in the Other Markets, and (iii) 2.0% 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.

Under the 2021 RPI Royalty Purchase Agreement, RPI is also entitled to receive tiered, sales-based royalties on net product sales of BCX10013 in an amount equal to: (i) 3.0% of worldwide aggregate annual net sales up to \$1,500,000 and (ii) 2.0% of worldwide aggregate annual net sales between \$1,500,000 and \$3,000,000. No royalty payments are payable on annual net sales above \$3,000,000. RPI is also entitled to receive tiered profit share amounts of up to 3.0% from certain other permitted sales in certain other markets.

The royalties payable under the 2021 RPI Royalty Purchase Agreement are in addition to the royalties payable to RPI under the 2020 RPI Royalty Purchase Agreement.

Under the OMERS Royalty Purchase Agreement, commencing with the calendar quarter beginning October 1, 2023, OMERS will be entitled to receive tiered, sales-based royalties on Direct Sales in an amount equal to: (i) 7.5% of aggregate annual net sales of ORLADEYO for annual net sales up to \$350,000 and (ii) 6.0% of annual net sales of ORLADEYO for annual net sales between \$350,000 and \$550,000 (with no royalty payments payable on annual Direct Sales over \$550,000) (the “Regime A Royalty Rate”). If annual Direct Sales for calendar year 2023 reach a specified amount set forth in the OMERS Royalty Purchase Agreement, then for each calendar quarter beginning on or after January 1, 2024, OMERS will be entitled to receive the Regime A Royalty Rate. If annual Direct Sales for calendar year 2023 are less than the specified amount, OMERS will be entitled to receive tiered, sales-based royalties on Direct Sales in an amount equal to: (i) 10.0% of aggregate annual net sales of ORLADEYO for annual net sales up to \$350,000 and (ii) 3.0% of annual net sales of ORLADEYO for annual net sales between \$350,000 and \$550,000 (with no royalty payments payable on annual Direct Sales over \$550,000) (the “Regime B Royalty Rate”).

Under the OMERS Royalty Purchase Agreement, OMERS is also entitled to receive a tiered revenue share on ORLADEYO sublicense revenue or net sales by licensees in the Other Markets in an amount equal to: (i) 20.0% of the proceeds received by the Company for upfront license fees and development milestones for ORLADEYO in the Other Markets, (ii) 20.0% of proceeds received by the Company on annual net sales of up to \$150,000 in the Other Markets, and (iii) 10.0% 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. OMERS is also entitled to receive profit share amounts of up to 10% from certain other permitted sales in certain other markets.

Under the 2020 RPI Royalty Purchase Agreement, the Company is 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 2021 RPI Royalty Purchase Agreement, the Company is required to make payments to RPI in respect of net sales or sublicense revenue in each calendar quarter from and after October 1, 2021. Under the OMERS Royalty Purchase Agreement, the Company will be required to make payments to OMERS in respect of net sales or sublicense revenue in each calendar quarter from and after October 1, 2023. OMERS will no longer be entitled to receive any payments on the date in which aggregate payments actually received by OMERS equals either 142.5% or 155.0% of the \$150,000 purchase price, depending on sales levels in calendar year 2023.

The transactions contemplated by each of the Royalty Purchase Agreements are referred to herein as the “Royalty Sales.”

Under the Royalty Purchase Agreements, the Company has agreed to specified affirmative and negative covenants, including covenants regarding periodic reporting of information by the Company to RPI and OMERS, third-party audits of royalties paid under the Royalty Purchase Agreements, 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 9 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 Agreements.

The cash consideration obtained pursuant to the Royalty Purchase Agreements is recorded in “Royalty financing obligations” on the Company’s Consolidated Balance Sheets. The fair value for the royalty financing obligations at the time of the transactions was based on the Company’s estimates of future royalties expected to be paid to the counterparty over the life of the arrangement. The Company subsequently records the obligations at its carrying value using the effective interest method. In order to amortize the royalty financing obligations, the Company utilizes the prospective method to estimate the future royalties to be paid by the Company to the counterparty over the life of the arrangement. Under the prospective method, a new effective interest rate is determined based on the revised estimate of remaining cash flows. The new rate is the discount rate that equates the present value of the revised estimate of remaining cash flows with the carrying amount of the debt, and it will be used to recognize interest expense for the remaining periods. The Company periodically assesses the amount and timing of expected royalty payments using a combination of internal projections and forecasts from external sources. The estimates of future net product sales (and resulting royalty payments) are based on key assumptions including population, penetration, probability of success, and sales price, among others. To the extent such payments are greater or less than the Company’s initial estimates or the timing of such payments is materially different than its original estimates, the Company will prospectively adjust the amortization of the royalty financing obligations and the effective interest rate.

In 2022, the Company adjusted its forecasts related to its R&D programs and ORLADEYO sales. Accordingly, this impacted the amount and timing of expected royalties to be made under the RPI Royalty Purchase Agreements. As a result, the effective interest rate related to the 2020 RPI Royalty Purchase Agreement decreased from 27.3% to 22.4%, and the effective interest rate related to the 2021 RPI Royalty Purchase Agreement decreased from 16.5% to 13.1%. Additionally, the effective interest rate related to the OMERS Agreement increased from 8.5% to 10.6%.

The following table shows the activity within the Royalty financing obligations account (in thousands) as well as the effective interest rate as of December 31, 2022:

	<u>2020 RPI Royalty Agreement</u>	<u>2021 RPI Royalty Agreement</u>	<u>OMERS Royalty Agreement</u>	<u>Total</u>
2020 Royalty sale: Royalty financing obligation, net of issuance costs.....	\$122,609	\$ —	\$ —	\$122,609
Non-cash Interest expense on Royalty financing obligation.....	<u>2,108</u>	<u>—</u>	<u>—</u>	<u>2,108</u>
Balance as of December 31, 2020.....	<u>\$124,717</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$124,717</u>
2021 Royalty sale: Royalty financing obligations, net of issuance costs.....	—	150,833	147,309	298,142
Non-cash Interest expense on Royalty financing obligations.....	33,308	2,897	1,465	37,670
Royalty revenues paid and payable.....	<u>(10,801)</u>	<u>(353)</u>	<u>—</u>	<u>(11,154)</u>
Balance as of December 31, 2021.....	<u>\$147,224</u>	<u>\$153,377</u>	<u>\$148,774</u>	<u>\$449,375</u>
Deferred financing costs.....	—	(34)	—	(34)
Non-cash Interest expense on Royalty financing obligations.....	39,994	22,239	14,249	76,482
Royalty revenues paid and payable.....	<u>(22,237)</u>	<u>(1,931)</u>	<u>—</u>	<u>(24,168)</u>
Balance as of December 31, 2022.....	<u>\$164,981</u>	<u>\$173,651</u>	<u>\$163,023</u>	<u>\$501,655</u>
Effective interest rate.....	22.4%	13.1%	10.6%	

Deferred issuance costs pursuant to the Royalty financing obligations, which consist primarily of advisory and legal fees, totaled \$8,532 and \$8,497 as of December 31, 2022 and 2021, respectively. The Royalty financing obligations liabilities and the associated deferred issuance costs are amortized using the effective interest method over the term of the arrangement, in accordance with the respective guidance. Concurrent with entering into the 2021 RPI Royalty Purchase Agreement, the Company and RPI entered into a Common Stock Purchase Agreement, pursuant to which the Company sold common stock to RPI for a premium of \$4,269. This premium has been deferred and is being amortized through interest expense using the effective interest method over the term of the applicable arrangement. Refer to Note 11 for further details on the common stock sale premium.

Note 9— Debt

Credit Agreement

On December 7, 2020, the Company entered into a \$200,000 Credit Agreement (the “Credit Agreement”) with Athyrium Opportunities III Co-Invest 1 LP (“Athyrium”), as lender and as administrative agent for the lenders. Certain of the Company’s direct and indirect subsidiaries 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, 2022. 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 prior credit facility with MidCap Financial Trust.

The Credit Agreement also provided 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” and, collectively with the Term A Loan and the Term B Loan, the “Term Loans”). Having achieved all required revenue-based milestones, the Company exercised its option to draw upon the additional funding available under the Credit Agreement, borrowing the principal amounts of \$25,000 under the Term B Loan and \$50,000 under the Term C Loan. Both the Term B Loan and the Term C Loan were funded on July 29, 2022 in the aggregate principal amount of \$75,000. The Company incurred deferred debt fees and issuance costs associated with the Term B and Term C Loans of \$3,428. The Term B Loan and the Term C Loan are subject to all the provisions under the Credit Agreement.

On November 19, 2021, the Company entered into an amendment to the Credit Agreement (i) to permit the Company to enter into the 2021 RPI Royalty Purchase Agreement, the OMERS Royalty Purchase Agreement, and the other definitive documentation related thereto and to perform its obligations thereunder; (ii) to require the Company to pay to Athyrium, for the account of the lenders, a make-whole premium plus certain fees set forth in the Credit Agreement in the event that the Company did not draw the Term B Loan or the Term C Loan, as applicable, by the end of the applicable period available to draw the Term B Loan or the Term C Loan, subject to certain exceptions set forth in the Credit Agreement; and (iii) to require the Company to pay to Athyrium, for the account of the lenders, a make-whole premium plus certain fees set forth in the Credit Agreement in the event that the Company either (x) terminated the commitments in respect of the Term B Loan or the Term C Loan, as applicable, on or prior to the end of the applicable period available to draw the Term B Loan or the Term C Loan, or (y) prepays or repays, or is required to prepay or repay, voluntarily or pursuant to mandatory prepayment obligations under the Credit Agreement (e.g., with the proceeds of certain asset sales, certain ORLADEYO out-licensing or royalty monetization transactions (excluding the Royalty Sales), extraordinary receipts, debt issuances, or upon a change of control of the Company and specified other events, subject to certain exceptions), all of the then-outstanding Term Loans, in each case, subject to certain exceptions set forth in the Credit Agreement.

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, which shall be no less than 1.75% and no more than 3.50%, plus 8.25%, or for each interest period in which a PIK Interest Payment is made, the three-month LIBOR plus 10.25%.

The Term Loans accrued interest at an effective interest rate of 12.87% for fiscal year 2022 compared to 12.17% for fiscal year 2021.

The quarter ended December 31, 2022 was the last PIK eligible period. Accordingly, the Company is obligated to make quarterly interest payments on the outstanding principal of the Term Loans as of December 31, 2022. The three-month LIBOR was 4.73% as of December 28, 2022, the LIBOR measurement date for the three-month interest period beginning January 1, 2023. As the LIBOR rate exceeds the LIBOR cap of 3.50%, the 3.50% cap plus 8.25% will be used to record interest expense for the three-month interest period beginning January 1, 2023.

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 Sales), extraordinary receipts, debt issuances, or upon a change of control of the Company and specified other events. 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 Loan 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, 2022, the Company had total borrowings of \$200,000 under the Credit Agreement. Quarterly interest payments under the Credit Agreement for the years ended December 31, 2022 and 2021, totaled \$23,387 and \$16,009, respectively, and have been designated and accounted for as PIK Interest Payments and added to the outstanding principal balance of the borrowing. As of December 31, 2022, borrowings, including the PIK Interest Payments, totaled \$240,452. The principal balance of the borrowings, including PIK amounts, is accruing interest at a rate of 11.88% as of December 31, 2022. The fair value of the debt approximates its carrying value based on prevailing interest rates as of the balance sheet date and is considered as Level 2 in the fair value hierarchy.

As of December 31, 2022 and 2021, deferred debt fees and issuance costs associated with all Term Loans under the Credit Agreement totaled \$12,828 and \$8,483, respectively and are being amortized as interest expense on an effective interest rate method over the remaining term of the Term Loans. When utilizing the effective interest method, in periods in which PIK interest is designated and those amounts are added to the outstanding principal balance of the borrowing, the amortization of the deferred debt fees and issuance costs is accretive. Deferred financing amortization of (\$916) and (\$531), was recognized for the years ended December 31, 2022 and 2021, respectively.

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.

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 10— Lease Obligations

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, 2022. Renewal options for the Company’s leases range from 1 to 5 years in length and begin from 2023 through 2026.

Aggregate lease expense under operating leases was as follows (in thousands):

	<u>Years Ended December 31,</u>	
	<u>2022</u>	<u>2021</u>
Aggregate lease expense	\$2,532	\$1,795

Other supplemental information related to leases was as follows:

	<u>As of December 31, 2022</u>	<u>As of December 31, 2021</u>
Weighted average remaining lease term	8.1 years	9.2 years
Weighted average discount rate	10.96%	11.20%

All of the Company's leases qualify as operating leases. The following table summarizes the presentation in the Consolidated Balance Sheets of the Company's operating leases:

Balance Sheet Location	2022	2021
Assets:		
Operating lease assets, net Other Assets	\$6,806	\$6,472
Liabilities:		
Current operating lease liabilities Lease financing obligation – current liabilities	\$2,369	\$1,819
Non-current operating lease liabilities Lease financing obligation – long-term liabilities	<u>5,804</u>	<u>5,962</u>
Total operating lease liabilities	<u>\$8,173</u>	<u>\$7,781</u>

Operating lease assets are recorded net of accumulated amortization of \$4,349 and \$2,626 as of December 31, 2022 and 2021, respectively. Cash paid for amounts included in the measurement of lease liabilities was \$2,453 and \$1,615 for the years ended December 31, 2022 and 2021, respectively.

Maturities of operating lease liabilities as of December 31, 2022, are as follows (in thousands):

2023	\$ 2,621
2024	1,958
2025	1,541
2026	656
2027	613
Thereafter	<u>6,112</u>
Total lease payments	13,501
Less imputed interest	<u>(5,328)</u>
Total	<u>\$ 8,173</u>

Note 11— Stockholders' Equity

Sales of Common Stock

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 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, 2022.

On March 1, 2021, the Company filed an automatic shelf registration statement on Form S-3 with the SEC. This shelf registration statement became effective automatically upon filing and allows the Company to sell an indeterminate number of securities, including common stock, preferred stock, depositary 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 November 19, 2021, concurrent with the Company entering into the 2021 RPI Royalty Purchase Agreement, the Company and RPI entered into the Common Stock Purchase Agreement, pursuant to which the Company issued 3,846 shares of the Company's common stock to RPI for an aggregate purchase price of \$50,000, at a price of \$13.00 per share, calculated based on the 20-day volume weighted average price. The \$13.00 per share price represented a premium of \$1.11 over the closing price of \$11.89 of the Company's common stock on November 17, 2021, the last trading day prior to the execution of the Common Stock Purchase Agreement. The premium of \$4,269 paid by RPI on the purchase of the Company's common stock has been deferred and is being amortized as a component of interest expense of the 2021 RPI royalty financing obligation.

Note 12— Stock-Based Compensation

As of December 31, 2022, 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 Amended and Restated Employee Stock Purchase Plan ("ESPP"). The Incentive Plan

was most recently amended and restated on April 18, 2022 and approved by the Company’s stockholders on June 7, 2022. The Inducement Plan was most recently amended and restated on August 26, 2022. The ESPP was most recently amended and restated on April 1, 2021 and approved by the Company’s stockholders on May 25, 2021.

Stock-based compensation expense of \$44,701 (\$36,716 of expense related to the Incentive Plan, \$6,550 of expense related to the Inducement Plan, and \$1,435 of expense related to the ESPP) was recognized during 2022, while \$34,640 (\$27,062 of expense related to the Incentive Plan, \$6,055 of expense related to the Inducement Plan, and \$1,523 of expense related to the ESPP) was recognized during 2021 and \$14,794 (\$12,938 of expense related to the Incentive Plan, \$1,494 of expense related to the Inducement Plan, and \$362 of expense related to the ESPP) was recognized during 2020.

There was approximately \$148,700 of total unrecognized compensation expense related to non-vested stock option and restricted stock unit awards granted by the Company as of December 31, 2022. As of December 31, 2022, the Company expected to recognize that expense as follows: \$50,713 in 2023, \$46,329 in 2024, \$34,537 in 2025 and \$17,121 in 2026. In addition, the Company has outstanding performance-based stock options and restricted stock unit awards for which no compensation expense is recognized until “performance” has occurred and the award vests.

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:

	<u>Years Ended December 31,</u>		
	<u>2022</u>	<u>2021</u>	<u>2020</u>
Research and development	\$24,936	\$20,179	\$10,222
Selling, general and administrative	19,765	14,461	4,572
Total stock-based compensation expense	<u>\$44,701</u>	<u>\$34,640</u>	<u>\$14,794</u>

Stock Incentive Plan

The Company grants stock option awards, restricted stock and restricted stock units 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 common stock at the date of grant. 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, 2022, 100%, 85% and 100% of these 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.

In January 2022, the Company issued 221 performance-based restricted stock unit awards. Contingent upon successful achievement of specific commercial or operational objectives in 2022, the awards become eligible for vesting at 50% on the first anniversary of the grant date and 25% on each of the second and third anniversaries of the grant date, until fully vested after three years. During 2022, the Company recognized \$158 of stock compensation expense related to certain milestones within the January 2022 grants for which achievement became probable.

Stock option awards and restricted stock unit awards granted to non-employee directors of the Company generally vest over one year. Stock option awards granted to new non-employee directors when they first join the Company’s Board of Directors generally vest, subject to the terms of the Incentive Plan, in 36 equal monthly installments over a three-year period measured from the grant date. Restricted stock unit awards granted to new non-employee directors when they first join the Company’s Board of Directors generally vest, subject to the terms of the Incentive Plan, in three equal annual installments beginning on the first anniversary of the grant date.

All stock option awards have contractual terms of 10 years. The vesting and 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:

	<u>Awards Available</u>	<u>Options Outstanding</u>	<u>Weighted Average Exercise Price</u>
Balance at December 31, 2019	968	21,050	\$ 5.96
Plan amendment	8,000	—	—
Restricted stock unit awards granted	(31)	—	—
Stock option awards granted	(7,469)	7,469	8.06
Stock option awards exercised	—	(510)	3.56
Stock option awards cancelled	<u>3,124</u>	<u>(3,124)</u>	6.93
Balance at December 31, 2020	4,592	24,885	\$ 6.52
Plan amendment	7,500	—	—
Restricted stock unit awards granted	(1,936)	—	—
Stock option awards granted	(6,753)	6,753	11.57
Stock option awards exercised	—	(2,705)	4.36
Stock option awards cancelled	<u>248</u>	<u>(248)</u>	7.62
Balance at December 31, 2021	3,651	28,685	\$ 7.90
Plan amendment	8,000	—	—
Restricted stock unit awards granted	(2,948)	—	—
Restricted stock unit awards cancelled	254	—	—
Stock option awards granted	(5,784)	5,784	10.70
Stock option awards exercised	—	(2,257)	5.00
Stock option awards cancelled	<u>1,033</u>	<u>(1,033)</u>	10.02
Balance at December 31, 2022	<u>4,206</u>	<u>31,179</u>	\$ 8.56

For stock option awards granted under the Incentive Plan during 2022, 2021, and 2020, the fair value was estimated on the date of grant using a Black-Scholes option pricing model and the assumptions noted in the table following the next subsection. The weighted average grant date fair value of these awards granted during 2022, 2021, and 2020 was \$7.57, \$7.93, and \$5.48, respectively. The fair value of the stock option awards is amortized to expense over the vesting periods using a straight-line expense attribution method. For restricted stock unit awards granted under the Incentive Plan, the fair value of the awards was determined based on the market value of the Company's shares on the grant date. The weighted average grant date fair value of these awards granted during 2022 and 2021 was \$11.20 and \$11.36, respectively. The fair value of the restricted stock unit 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 and restricted stock unit awards to newly-hired employees as inducements material to each employee entering employment with the Company. Awards granted to newly hired employees generally vest 25% each year until fully vested after four years and are subject to the terms and conditions of the Inducement Plan. Each stock option has a term of 10 years. 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:

	<u>Awards Available</u>	<u>Options Outstanding</u>	<u>Weighted Average Exercise Price</u>
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
Plan amendment	1,500	—	—
Stock option awards granted	(1,003)	1,003	13.91
Stock option awards exercised	—	(592)	3.63
Stock option awards cancelled	174	(174)	3.67
Balance at December 31, 2021	900	4,408	\$ 6.20
Plan amendment	1,926	—	—
Restricted stock unit awards granted	(603)	—	—
Restricted stock unit awards cancelled	15	—	—
Stock option awards granted	(1,819)	1,819	13.54
Stock option awards exercised	—	(358)	3.45
Stock option awards cancelled	528	(528)	7.44
Balance at December 31, 2022	<u>947</u>	<u>5,341</u>	\$ 8.80

For stock option awards granted under the Inducement Plan during 2022, 2021, and 2020, 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 2022, 2021, and 2020 was \$9.54, \$9.65, and \$2.73, respectively. The fair value of the stock option awards is amortized to expense over the vesting periods using a straight-line expense attribution method. For restricted stock unit awards granted under the Inducement Plan, the fair value of the awards was determined based on the market value of the Company's shares on the grant date. The weighted average grant date fair value of these awards granted during 2022 was \$13.21. The fair value of the restricted stock unit awards is amortized to expense over the vesting periods using a straight-line expense attribution method. No restricted stock unit awards were granted under the Inducement Plan during 2021 or 2020.

The following table summarizes the key assumptions used by the Company to value the stock option awards granted under all plans during 2022, 2021, and 2020, 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 Incentive and Inducement Plans

	<u>2022</u>	<u>2021</u>	<u>2020</u>
Expected Life	5.5	5.5	5.5
Expected Volatility	84%	84%	84%
Expected Dividend Yield	0.0%	0.0%	0.0%
Risk-Free Interest Rate	3.5%	1.1%	0.4%

The total intrinsic value of stock option awards exercised under the Incentive Plan was \$21,150 during 2022, \$25,484 during 2021, and \$1,562 during 2020. 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. The total intrinsic value of stock option awards exercised under the Inducement Plan was \$3,710 and \$6,700 during 2022 and 2021, respectively. No stock option awards were exercised under the Inducement Plan during 2020.

The following table summarizes, at December 31, 2022, by price range: (1) for stock option awards outstanding under the Incentive and Inducement Plans, 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 Incentive and Inducement Plans, the number of stock option awards exercisable and their weighted average exercise price:

Range	Outstanding			Exercisable	
	Number	Weighted Average Remaining Life	Weighted Average Exercise Price	Number	Weighted Average Exercise Price
\$0 to 3	1,145	6.3	\$ 2.65	777	\$ 2.66
3 to 6	8,653	5.7	4.23	7,183	4.32
6 to 9	9,704	7.2	7.90	6,332	7.70
9 to 12	13,390	8.3	10.89	3,287	11.01
12 to 15	2,189	7.5	13.06	927	12.80
15 to 18	<u>1,439</u>	8.4	16.02	<u>322</u>	15.89
\$0 to 18	<u>36,520</u>	7.3	\$ 8.59	<u>18,828</u>	\$ 7.17

The weighted average remaining contractual life of stock option awards exercisable under the Incentive and Inducement Plans at December 31, 2022 was 5.8 years.

The aggregate intrinsic value of stock option awards outstanding and exercisable under the Incentive and Inducement Plans at December 31, 2022 was \$83,783. 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 Incentive and Inducement 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 Incentive and Inducement Plans was \$33,575 during 2022, \$23,395 during 2021, and \$18,739 during 2020.

As of December 31, 2022, the number of stock option awards vested and expected to vest under the Incentive and Inducement Plans is 32,837. The weighted average exercise price of these stock option awards is \$8.52 and their weighted average remaining contractual life is 7.2 years.

The following table summarizes the changes in the number and weighted-average grant-date fair value of non-vested stock option awards during 2022:

	Non-Vested Stock Option Awards	Weighted Average Grant-Date Fair Value
Balance December 31, 2021	17,532	\$6.06
Stock option awards granted	7,603	8.03
Stock option awards vested	(5,908)	5.68
Stock option awards forfeited	<u>(1,535)</u>	6.24
Balance December 31, 2022	<u>17,692</u>	\$7.02

Employee Stock Purchase Plan

The Company has reserved a total of 7,975 shares of common stock to be purchased under the ESPP, of which 5,792 shares remain available for purchase at December 31, 2022. 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 260, 321, and 246 shares of common stock purchased under the ESPP in 2022, 2021, and 2020, respectively, at a weighted average price per share of \$11.03, \$6.20, and \$2.56, respectively. Expense of \$1,435, \$1,523, and \$362 related to the ESPP was recognized during 2022, 2021, and 2020, 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 2022, 2021, and 2020, were \$6.02, \$2.80, and \$1.47, respectively.

Note 13— Income Taxes

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

	<u>Years Ended December 31,</u>	
	<u>2022</u>	<u>2021</u>
Domestic	\$(225,127)	\$(159,632)
Foreign	<u>(19,256)</u>	<u>(22,177)</u>
Loss before provision for income taxes	<u>\$(244,383)</u>	<u>\$(181,809)</u>

The components of the (benefit) expense for income taxes were as follows:

	<u>Years Ended December 31,</u>	
	<u>2022</u>	<u>2021</u>
Current expense provision:		
U.S. Federal and state	\$2,430	\$2,179
Foreign	<u>292</u>	<u>233</u>
Total current expense provision	2,722	2,412
Deferred expense (benefit) provision:		
U.S. Federal and state	<u>11</u>	<u>(159)</u>
Total expense provision	<u>\$2,733</u>	<u>\$2,253</u>

The differences between the Company’s effective tax rate and the statutory tax rate in 2022, 2021, and 2020, are as follows:

	<u>2022</u>	<u>2021</u>	<u>2020</u>
Income tax benefit at federal statutory rate (21% for 2022, 2021 and 2020) . . .	\$(51,321)	\$(38,175)	\$(38,391)
State and local income taxes net of federal tax benefit	(1,816)	(2,288)	(2,544)
Permanent items	(1,608)	(1,343)	774
Rate change	—	—	(82)
Expiration of attribute carryforwards	—	(1,057)	3,774
Research and development tax credits	(9,793)	(5,994)	(4,080)
Foreign rate differential	1,862	1,940	542
Other	(5,485)	1,216	1,456
Change in valuation allowance	<u>70,894</u>	<u>47,954</u>	<u>38,551</u>
Income tax expense	<u>\$ 2,733</u>	<u>\$ 2,253</u>	<u>\$ —</u>

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:

	<u>2022</u>	<u>2021</u>
Balance at January 1,	\$ 9,729	\$8,230
Additions to current period tax positions	<u>4,115</u>	<u>1,499</u>
Balance at December 31,	<u>\$13,844</u>	<u>\$9,729</u>

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:

	<u>2022</u>	<u>2021</u>
Deferred tax assets:		
Net federal and state operating losses	\$ 101,600	\$ 113,649
Research and development credits	86,321	71,197
Royalty income	115,554	106,007
Stock-based compensation	19,374	14,512
Capitalized R&D	62,794	8,997
Leasing obligations	1,842	1,836
Other	<u>4,354</u>	<u>4,809</u>
Total deferred tax assets	391,839	321,007
Deferred tax liabilities:		
Fixed assets	(717)	(607)
Right of use asset	<u>(1,525)</u>	<u>(1,527)</u>
Total deferred tax liabilities	<u>(2,242)</u>	<u>(2,134)</u>
Valuation allowance.	<u>(389,608)</u>	<u>(318,714)</u>
Net deferred tax assets (liabilities)	<u>\$ (11)</u>	<u>\$ 159</u>

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 valuation allowance against substantially all 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 \$70,894, \$47,954, and \$38,551 in 2022, 2021, and 2020, respectively.

As of December 31, 2022, the Company had U.S. federal operating loss carryforwards of \$408,671, state operating loss carryforwards of \$188,341, foreign net operating losses of \$47,337, and U.S. research and development and orphan drug credit carryforwards of \$100,165, which will expire at various dates from 2023 through 2041. Federal losses, state losses, research and development credit carryforwards began expiring in 2021. The foreign net operating losses have an indefinite carryforward period.

Tax years 2018-2021 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 2022, 2021 and 2020.

As of December 31, 2022, the Company has minimal accumulated undistributed earnings generated by our foreign subsidiaries which have already been subject to local and U.S. tax (as part of the global intangible low-taxed income provisions). We intend to indefinitely reinvest these earnings, as well as future earnings from our foreign subsidiaries to fund our international operations. In addition, we expect future U.S. cash generation will be sufficient to meet future U.S. cash needs.

Note 14— 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 \$3,758, \$2,834, and \$1,569 in 2022, 2021, and 2020, respectively.

Note 15— Collaborative and Other Relationships

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. On September 15, 2021, the Company entered into an amendment to pay for certain additional costs, including additional manufacturing development costs and overhead, and to change the total value of the contract, as amended, to \$47,315 from \$45,931. All options under the contract have been awarded.

In August 2020, NIAID/HHS awarded the Company a new contract, with potential aggregate funding of up 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 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, 2022, a total of \$20,574 has been awarded under exercised options within this contract. The most recent development option was completed as of December 31, 2022.

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 contracts 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. As of December 31, 2022, all of our government funding for galidesivir has expired.

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. The Company initially delivered 20,000 doses of RAPIVAB under this contract in 2019 for a total price of approximately \$13,864. The Company further delivered 20,000 and 9,980 doses of RAPIVAB in 2022 and 2021, respectively, and recorded revenue of \$13,864 and \$6,918 for the years ending December 31, 2022 and December 31, 2021, respectively. As of December 31, 2022, the Company has delivered a total of 49,980 RAPIVAB doses of the 50,000 RAPIVAB doses available under the contract, effectively completing the contract with HHS.

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. The Japanese National Health Insurance System’s (“NHI”) approval of the addition of ORLADEYO to the NHI drug price list in April 2021 triggered a \$15,000 milestone payment from Torii to the Company, which was received in May 2021.

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 commenced 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 is responsible for supplying Torii with its required amounts of ORLADEYO. The activities of the parties pursuant to the Torii Agreement are overseen by a joint steering committee, composed of an equal number of representatives from each party to coordinate the development and commercialization of ORLADEYO in Japan. Torii launched ORLADEYO in Japan on April 23, 2021.

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 Topic 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. For the year ended December 31, 2020, \$1,899 of the \$22,000 upfront payment was recognized as revenue as the services were delivered. Prior to 2020, the Company had recognized as revenue \$20,101 of the \$22,000 upfront payment.

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 United States. 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 United States 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 recognized a 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.

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 is responsible for all development, regulatory, and commercialization costs in Korea and the Company is entitled to 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.

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 candidate from this collaboration is forodesine. The Company has obtained worldwide exclusive rights to develop and ultimately distribute this, 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 collaborations, or commercializes products related to these programs, the Company will owe sublicense fees or royalties on amounts received.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the 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, 2022 and 2021, the related consolidated statements of comprehensive loss, stockholders' deficit and cash flows for each of the three years in the period ended December 31, 2022, 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, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, 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, 2022, 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 February 27, 2023 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 \$87.6 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 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.

Royalty Financing Obligations

Description of the Matter

As described in Note 8 to the consolidated financial statements, the Company entered into Royalty Purchase Agreements ("RPA's") with third parties. Pursuant to the RPA's, the Company received proceeds of approximately \$425 million in exchange for the right to receive royalty payments based on future net revenues of the Company's commercialized drug, Orladeyo, and other drug candidates as specified in the agreements.

The Company recorded the RPA's as non-current liability instruments (royalty financing obligations) on the balance sheet at their carrying value of \$501.7 million as of December 31, 2022, and imputed interest expense associated with these liabilities 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 each arrangement. The interest rates on these instruments 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. In order to amortize the royalty financing obligations, the Company utilizes the prospective method to estimate the future royalties to be paid by the Company to the third parties over the life of the arrangements. Under the prospective method, a new effective interest rate is determined based on the revised estimate of remaining cash flows. The Company periodically assesses the amount and timing of expected royalty payments using a combination of internal projections and forecasts from external sources.

Auditing the royalty financing obligations was complex and highly judgmental due to the estimation uncertainty in determining the effective interest rates. The Company's effective interest rate models includes actual revenues recorded and royalties paid to-date, as well as revenue projections for which future royalties will be paid, which are sensitive to significant assumptions (including population, market penetration, probability of success, and sales price, among others) 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 obligations, including controls over management's review of the revenue projections within the models.

To evaluate the royalty financing obligations, our audit procedures included, among others, assessing the underlying data and assumptions used by the Company in its effective interest rate models. 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 schedules and estimates of royalties using the effective interest method and performed sensitivity analyses to evaluate the changes in the effective interest rates, and associated interest expense, that would result from changes in the assumptions.

Product Sales, net

Description of the Matter As discussed in Note 1, when recognizing revenue, the Company makes an estimate of the net selling price (transaction price), which includes estimates of variable consideration. For the year ended December 31, 2022, the Company recorded net product sales of \$267.7 million. Product sales are recorded net of adjustments for variable consideration including estimated government rebates, managed care rebates, chargebacks, costs of co-payment for assistance programs, and product returns at the time revenue is recorded. Limited historical data is available for use in developing such estimates which are periodically reviewed and adjusted as necessary.

The Company's estimates of variable consideration depend on the identification of key customer contract terms and conditions, as well as estimates of sales volumes to different classes of payors. The revenue recognition process can be complex and can involve judgment related to these estimates as well as to identify and assess the terms and conditions of customer agreements and related government regulations that could affect revenue recognition, as the Company's revenue expands with new customers and new markets.

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 process of recording product sales and related rebates, chargebacks and returns. We also tested management's controls related to the identification and assessment of the terms and conditions of customer agreements and the completeness and accuracy of data utilized in the controls, and the calculations supporting management's estimates.

To test product sales, our audit procedures included, among others, tracing a sample of revenue transactions recognized during the year to source documentation. We also confirmed a sample of outstanding receivable balances directly with the Company's customers. To test management's estimates of variable consideration, we obtained management's calculations for the respective estimates and performed one or more of the following procedures: tested management's estimation process to assess whether the recorded reserve balances are within a reasonable range of estimate, performed retrospective reviews, assessed subsequent events, and tested a sample of credits issued throughout the year.

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

/s/ Ernst & Young LLP
Raleigh, North Carolina
February 27, 2023

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, 2022, 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, 2022, 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, 2022 and 2021, the related consolidated statements of comprehensive loss, stockholders' deficit and cash flows for each of the three years in the period ended December 31, 2022, and the related notes and our report dated February 27, 2023 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
February 27, 2023

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, 2022, 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, 2022, 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, 2022, 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 103 of this 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, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

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 2023 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,*” “*Executive Compensation,*” “*2022 Director Compensation,*” “*Compensation Committee Interlocks and Insider Participation,*” and “*Compensation Committee Report*” in our definitive Proxy Statement for the 2023 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 2023 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 caption “*Corporate Governance*” in our definitive Proxy Statement for the 2023 Annual Meeting of Stockholders and incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

Our independent registered public accounting firm is Ernst & Young LLP, Raleigh, NC, Auditor Firm ID: 42.

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 2023 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 report:

	Page in Form 10-K
Consolidated Balance Sheets at December 31, 2022 and 2021	67
Consolidated Statements of Comprehensive Loss for the years ended December 31, 2022, 2021, and 2020	68
Consolidated Statements of Cash Flows for the years ended December 31, 2022, 2021, and 2020	69
Consolidated Statements of Stockholders' Equity (Deficit) for the years ended December 31, 2022, 2021, and 2020	70
Notes to Consolidated Financial Statements	71
Report of Independent Registered Public Accounting Firm on Consolidated Financial Statements	100
Report of Independent Registered Public Accounting Firm on Internal Control	103

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 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.
3.5	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.
3.6	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.
3.7	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. Incorporated by reference to Exhibit 4.1 to the Company's Form 10-K filed March 1, 2021.

Number	Description
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 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. Stock Incentive Plan (as amended and restated March 19, 2020). Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed May 13, 2020.
10.8&	BioCryst Pharmaceuticals, Inc. Stock Incentive Plan (as amended and restated April 1, 2021). Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed May 26, 2021.
10.9&	BioCryst Pharmaceuticals, Inc. Stock Incentive Plan (as amended and restated as of April 18, 2022). Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed June 7, 2022.
10.10&	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.
10.11&	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.
10.12&	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.
10.13&	Form of Notice of Grant of Non-Employee Director Stock Option and Stock Option Agreement under the BioCryst Pharmaceuticals, Inc. Stock Incentive Plan. Incorporated by reference to Exhibit 10.3 to the Company's 10-Q filed August 5, 2022.

Number	Description
10.14&	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.
10.15&	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 10.2 to the Company's Form 10-Q filed May 7, 2021.
10.16&	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 10.14 to the Company's Form 10-K filed February 28, 2022.
10.17&	Form of Notice of Grant of Non-Employee Director Restricted Stock Unit Award and Restricted Stock Unit Agreement under BioCryst Pharmaceuticals, Inc. Stock Incentive Plan. Incorporated by reference to Exhibit 10.4 to the Company's Form 10-Q filed August 5, 2022.
10.18&	BioCryst Pharmaceuticals, Inc. Employee Stock Purchase Plan (as amended and restated April 1, 2021). Incorporated by reference to Exhibit 10.2 to the Company's Form 8-K filed May 26, 2021.
10.19&	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.
10.20&	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.
10.21&	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.
10.22&	BioCryst Pharmaceuticals, Inc. Inducement Equity Incentive Plan (as amended and restated July 23, 2021). Incorporated by reference to Exhibit 99.1 to the Company's Form S-8 (File No. 333-259919) filed September 30, 2021.
10.23&	BioCryst Pharmaceuticals, Inc. Inducement Equity Incentive Plan (as amended and restated August 31, 2022). Incorporated by reference to Exhibit 99.1 to the Company's Form S-8 (File No. 333-267193) filed August 31, 2022.
10.24&	Form of Notice of Grant of Stock Option and Standard Stock Option Agreement under the BioCryst Pharmaceuticals, Inc. Inducement Equity Incentive Plan. Incorporated by reference to Exhibit 10.16 to the Company's Form 10-K filed March 1, 2021.
(10.25)&	Form of Notice of Grant of Restricted Stock Unit Award and Restricted Stock Unit Agreement under the BioCryst Pharmaceuticals, Inc. Inducement Equity Incentive Plan.
10.26&	BioCryst Pharmaceuticals, Inc. Non-Employee Director Compensation Policy, effective April 18, 2022. Incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed May 9, 2022.
10.27&	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.

Number	Description
10.28&	Executive Relocation Policy. Incorporated by reference to Exhibit 10.2 to the Company's Form 10-K filed March 4, 2008.
10.29&	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.
10.30&	Amended and Restated Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and William P. Sheridan, dated August 4, 2021. Incorporated by reference to Exhibit 10.4 to the Company's Form 10-Q filed August 9, 2021.
10.31&	Amendment No. 1 to the Amended and Restated Letter Agreement between BioCryst Pharmaceuticals, Inc. and William P. Sheridan, dated September 15, 2022. Incorporated by reference to Exhibit 10.4 to the Company's Form 10-Q filed November 4, 2022.
10.32&	Amended and Restated Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and Yarlagadda S. Babu, dated August 4, 2021. Incorporated by reference to Exhibit 10.5 to the Company's Form 10-Q filed August 9, 2021.
10.33&	Amended and Restated Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and Alane P. Barnes, dated August 4, 2021. Incorporated by reference to Exhibit 10.6 to the Company's Form 10-Q filed August 9, 2021.
10.34&	Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and Charles Gayer, dated January 14, 2020. Incorporated by reference to Exhibit 10.26 to the Company's Form 10-K filed March 1, 2021.
10.35&	Amendment No. 1 to the Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and Charles Gayer, dated September 24, 2021. Incorporated by reference to Exhibit 10.10 to the Company's Form 10-Q filed November 4, 2021.
10.36&	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.
10.37&	Amendment No. 1 to the Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and Anthony Doyle, dated September 24, 2021. Incorporated by reference to Exhibit 10.8 to the Company's Form 10-Q filed November 4, 2021.
10.38&	Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and Dr. Helen M. Thackray, dated February 18, 2021. Incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed May 7, 2021.
10.39&	Amendment No. 1 to the Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and Dr. Helen M. Thackray, dated September 24, 2021. Incorporated by reference to Exhibit 10.9 to the Company's Form 10-Q filed November 4, 2021.
10.40†	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 10.28 to the Company's Form 10-K filed March 1, 2021.

Number	Description
10.41†	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 10.29 to the Company's Form 10-K filed March 1, 2021.
10.42	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.
10.43	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.
10.44	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.
10.45	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.
10.46†	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.
10.47†*	Purchase and Sale Agreement, dated as of December 7, 2020, between BioCryst Pharmaceuticals, Inc. and RPI 2019 Intermediate Finance Trust. Incorporated by reference to Exhibit 10.91 to the Company's Form 10-K filed March 1, 2021.
10.48†*	Amendment Number One to Credit Agreement, dated as of November 19, 2021, by and among BioCryst Pharmaceuticals, Inc., as borrower, the guarantors listed on the signature pages thereto, the lenders listed on the signature pages thereto, and Athyrium Opportunities III Co-Invest 1 LP, as administrative agent for the lenders. Incorporated by reference to Exhibit 10.101 to the Company's Form 10-K filed on February 28, 2022.
10.49	Waiver to Credit Agreement, dated as of July 14, 2022, by and among BioCryst Pharmaceuticals, Inc., as borrower, the guarantors listed on the signature pages thereto, the lenders listed on the signature pages thereto, and Athyrium Opportunities III Co-Invest 1 LP, as administrative agent for the lenders. Incorporated by reference to Exhibit 10.1 of the Company's Form 10-Q filed November 4, 2022.
10.50†	Amendment Number Two to Credit Agreement, dated as of August 3, 2022, by and among BioCryst Pharmaceuticals, Inc., as borrower, the guarantors listed on the signature pages thereto, the lenders listed on the signature pages thereto, and Athyrium Opportunities III Co-Invest 1 LP, as administrative agent for the lender. Incorporated by reference to Exhibit 10.2 of the Company's Form 10-Q filed November 4, 2022.
10.51†*	Purchase and Sale Agreement, dated as of November 19, 2021, between BioCryst Pharmaceuticals, Inc. and RPI 2019 Intermediate Finance Trust. Incorporated by reference to Exhibit 10.102 to the Company's Form 10-K filed on February 28, 2022.
10.52†*	Purchase and Sale Agreement, dated as of November 19, 2021, between BioCryst Pharmaceuticals, Inc. and OCM IP Healthcare Holdings Limited. Incorporated by reference to Exhibit 10.103 to the Company's Form 10-K filed on February 28, 2022.

Number	Description
10.53 ^{†*}	Common Stock Purchase Agreement, dated as of November 19, 2021, between BioCryst Pharmaceuticals, Inc. and RPI Intermediate Finance Trust. Incorporated by reference to Exhibit 10.104 to the Company's Form 10-K filed on February 28, 2022.
(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, 2022, 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, 2022 is formatted in Inline XBRL (contained in Exhibit 101).

[†] Certain identified information has been omitted pursuant to Item 601(b)(10) of Regulation S-K because it is both not material and would likely cause competitive harm to the Company if publicly disclosed.

* Certain personally identifiable information has been omitted from this exhibit pursuant to Item 601(a)(6) of Regulation S-K.

& 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 February 27, 2023.

BIOCRYSST 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 February 27, 2023:

<u>Signature</u>	<u>Title(s)</u>
<u>/s/ Jon P. Stonehouse</u> Jon P. Stonehouse	President, Chief Executive Officer and Director (Principal Executive Officer)
<u>/s/ Anthony J. Doyle</u> Anthony J. Doyle	Chief Financial Officer (Principal Financial Officer)
<u>/s/ Michael L. Jones</u> Michael L. Jones	Executive Director, Finance and Principal Accounting Officer (Principal Accounting Officer)
<u>/s/ George B. Abercrombie</u> George B. Abercrombie	Director
<u>/s/ Stephen J. Aselage</u> Stephen J. Aselage	Director
<u>/s/ Steven K. Galson</u> Steven K. Galson, M.D.	Director
<u>/s/ Theresa M. Heggie</u> Theresa M. Heggie	Director
<u>/s/ Nancy J. Hutson</u> Nancy J. Hutson, Ph.D.	Director
<u>/s/ Robert A. Ingram</u> Robert A. Ingram	Director
<u>/s/ Kenneth B. Lee, Jr.</u> Kenneth B. Lee, Jr.	Director
<u>/s/ Alan G. Levin</u> Alan G. Levin	Director
<u>/s/ Amy E. McKee</u> Amy E. McKee, M.D.	Director
<u>/s/ Vincent J. Milano</u> Vincent J. Milano	Director
<u>/s/ Mabelle Sanders</u> Mabelle Sanders	Director



BIOCRYST PHARMACEUTICALS, INC.
4505 Emperor Blvd., Suite 200
Durham, North Carolina 27703

NOTICE OF ANNUAL MEETING OF STOCKHOLDERS
To Be Held June 13, 2023

To the Stockholders of BioCryst Pharmaceuticals, Inc.:

Notice is hereby given that the Annual Meeting of Stockholders of BioCryst Pharmaceuticals, Inc., a Delaware corporation (the "Company"), will be held at our corporate headquarters at 4505 Emperor Blvd., Suite 200, Durham, NC 27703 on Tuesday, June 13, 2023 at 10:00 a.m., Eastern Daylight Time (the "Meeting"), for the following purposes:

1. To elect the four directors nominated in this Proxy Statement to serve for a term ending at the 2026 annual meeting of stockholders and until a successor is duly elected and qualified;
2. To ratify the selection of Ernst & Young LLP as our independent registered public accountants for 2023;
3. To hold an advisory vote regarding executive compensation;
4. To hold an advisory vote on the frequency of future advisory votes on the Company's executive compensation;
5. To approve an amended and restated Stock Incentive Plan, increasing the number of shares available for issuance under the Stock Incentive Plan by 7,000,000 shares; and
6. To transact such other business as may properly come before the Meeting or any adjournment thereof.

THE BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS THAT YOU VOTE IN FAVOR OF PROPOSALS 1, 2, 3 AND 5, AND "1 YEAR" WITH RESPECT TO PROPOSAL 4. The proposals are further described in the accompanying Proxy Statement.

The Board of Directors has fixed the close of business on April 17, 2023 as the record date for the determination of stockholders entitled to receive notice of and to vote at the Meeting or any adjournment thereof. The Meeting may be adjourned from time to time without notice other than announcement at the Meeting, and any business for which notice of the Meeting is hereby given may be transacted at any such adjournment. A list of the stockholders entitled to vote at the Meeting will be open to examination by any stockholder, for any purpose germane to the Meeting, during ordinary business hours, for a period of at least ten days prior to the Meeting at the principal executive offices of the Company, located at 4505 Emperor Blvd, Suite 200, Durham, NC 27703. Stockholders wishing to examine the list may make arrangements to do so by contacting our Corporate Secretary in writing at our principal executive offices or by telephone at (919) 859-1302.

We reserve the right to implement any health and safety measures as we deem prudent or as may be required by applicable laws or government orders. In addition, if we determine that it is not possible or advisable to hold the Meeting in person at our corporate offices on the meeting date, we may make alternative arrangements to hold the Meeting at a different date or time, in a different location, and/or by means of remote communication. In the event we determine it is necessary or appropriate to make alternative arrangements for the Meeting, we will announce the decision to do so in advance, and details on how to participate will be issued by press release, posted on our website, and filed with the Securities and Exchange Commission as additional proxy soliciting material.

Please carefully review the Proxy Card and Proxy Statement.

BY ORDER OF THE BOARD OF DIRECTORS

Alane P. Barnes, Corporate Secretary

Durham, North Carolina
April 27, 2023

ALL STOCKHOLDERS ARE INVITED TO ATTEND THE ANNUAL MEETING IN PERSON. WHETHER OR NOT YOU PLAN TO ATTEND THE MEETING, PLEASE VOTE PROMPTLY. A PERSON GIVING A PROXY HAS THE POWER TO REVOKE IT. IF YOU ATTEND THE MEETING, YOUR PROXY WILL NOT BE COUNTED WITH RESPECT TO ANY MATTER UPON WHICH YOU VOTE IN PERSON.

TABLE OF CONTENTS

	<u>Page</u>
PROXY STATEMENT.....	1
ITEMS TO BE VOTED UPON	4
1. ELECTION OF DIRECTORS	4
2. RATIFICATION OF APPOINTMENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTANTS FOR 2023	8
3. ADVISORY VOTE TO APPROVE EXECUTIVE COMPENSATION	9
4. ADVISORY VOTE ON THE FREQUENCY OF FUTURE ADVISORY VOTES TO APPROVE EXECUTIVE COMPENSATION	10
5. APPROVAL OF AN AMENDED AND RESTATED STOCK INCENTIVE PLAN, INCREASING THE NUMBER OF SHARES AVAILABLE FOR ISSUANCE UNDER THE STOCK INCENTIVE PLAN BY 7,000,000 SHARES.....	11
CORPORATE GOVERNANCE	21
EXECUTIVE OFFICERS	27
COMPENSATION DISCUSSION AND ANALYSIS	29
COMPENSATION COMMITTEE REPORT	38
EXECUTIVE COMPENSATION	39
2022 SUMMARY COMPENSATION TABLE.....	39
GRANTS OF PLAN-BASED AWARDS IN 2022.....	40
OUTSTANDING EQUITY AWARDS AT DECEMBER 31, 2022	41
2022 OPTION EXERCISES AND STOCK VESTED.....	43
POTENTIAL PAYMENTS UPON TERMINATION OR CHANGE IN CONTROL.....	43
CEO PAY RATIO.....	47
PAY VERSUS PERFORMANCE	48
2022 DIRECTOR COMPENSATION.....	52
AUDIT COMMITTEE REPORT	54
SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT.....	55
STOCKHOLDER PROPOSALS.....	57
NO INCORPORATION BY REFERENCE	57
OTHER MATTERS	57
GENERAL INFORMATION.....	57
ANNEX A	A-1

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BIOCRIST PHARMACEUTICALS, INC.
4505 Emperor Blvd., Suite 200
Durham, North Carolina 27703

PROXY STATEMENT

General

This Proxy Statement is furnished in connection with the solicitation of proxies by the Board of Directors (the “Board” or the “Board of Directors”) of BioCryst Pharmaceuticals, Inc. (“BioCryst” or the “Company”) for the Annual Meeting of Stockholders of the Company to be held at our corporate headquarters at 4505 Emperor Blvd., Suite 200, Durham, NC 27703 on Tuesday, June 13, 2023 at 10:00 a.m., Eastern Daylight Time, and at any adjournment thereof (the “Meeting”), and for the purposes set forth in the accompanying Notice of Annual Meeting of Stockholders.

In this document, the words “BioCryst,” the “Company,” “we,” “our,” “ours,” and “us” refer only to BioCryst Pharmaceuticals, Inc. and not to any other person or entity.

We are taking advantage of Securities and Exchange Commission (“SEC”) rules that allow us to deliver proxy materials to our stockholders via the Internet. Under these rules, we are sending our stockholders a one-page notice regarding the Internet availability of proxy materials instead of a full printed set of proxy materials. Our stockholders will not receive printed copies of the proxy materials unless specifically requested. Instead, the one-page notice that our stockholders receive will tell them how to access and review on the Internet all of the important information contained in the proxy materials. This notice also tells our stockholders how to submit their proxy card on the Internet and how to request to receive a printed copy of our proxy materials. We expect to provide notice and electronic delivery of this Proxy Statement to such stockholders on or about April 27, 2023.

We reserve the right to implement any health and safety measures as we deem prudent or as may be required by applicable laws or government orders. In addition, if we determine that it is not possible or advisable to hold the Meeting in person at our corporate offices on the meeting date, we may make alternative arrangements to hold the Meeting at a different date or time, in a different location, and/or by means of remote communication. In the event we determine it is necessary or appropriate to make alternative arrangements for the Meeting, we will announce the decision to do so in advance, and details on how to participate will be issued by press release, posted on our website, and filed with the SEC as additional proxy soliciting material.

Purpose of the Meeting

The matters to be considered at the Meeting are:

1. To elect the four directors nominated in this Proxy Statement to serve for a term ending at the 2026 annual meeting of stockholders and until a successor is duly elected and qualified;
2. To ratify the selection of Ernst & Young LLP as our independent registered public accountants for 2023;
3. To hold an advisory vote regarding executive compensation;
4. To hold an advisory vote on the frequency of future advisory votes on the Company’s executive compensation;
5. To approve an amended and restated Stock Incentive Plan, increasing the number of shares available for issuance under the Stock Incentive Plan by 7,000,000 shares; and
6. To transact such other business as may properly come before the Meeting or any adjournment thereof.

Revocation and Voting of Proxies

Any proxy given pursuant to this solicitation may be revoked by the person giving it at any time prior to the voting thereof, by giving written notice to our Corporate Secretary at our principal executive offices, 4505 Emperor Blvd., Suite 200, Durham, NC 27703 or by voting in person at the Meeting. Attendance at the Meeting will not, by itself, revoke a proxy. All valid, unrevoked proxies will be voted as directed. In the absence of any contrary directions, proxies received by the Board will be voted as follows:

- FOR the election of each of the nominees named in this Proxy Statement for director of the Company;
- FOR ratification of the selection of Ernst & Young LLP as the Company’s independent registered public accountants for 2023;

- FOR approval of the advisory resolution regarding executive compensation;
- FOR “ONE YEAR” with respect to the frequency of holding future advisory votes on executive compensation; and
- FOR approval of the amended and restated Stock Incentive Plan, increasing the number of shares available for issuance under the Stock Incentive Plan by 7,000,000 shares.

With respect to such other matters as may properly come before the Meeting, votes will be cast in the discretion of the appointed proxies.

Voting and Quorum

Only holders of record (referred to in this section as the “Stockholders”) of our common stock (the “Common Stock”) as of the close of business on April 17, 2023 (the “Record Date”) will be entitled to notice of and to vote at the Meeting. At April 17, 2023, there were 188,920,765 shares of Common Stock outstanding. Stockholders are entitled to vote in any one of the following ways:

1. In Person. Stockholders who choose to attend the Meeting can vote in person at the Meeting by presenting a form of photo identification acceptable to the Company and casting a ballot. Registered holders may vote upon presentation of such identification. Beneficial owners who hold their shares through a nominee, such as a broker or a bank, must obtain a proxy from such nominee or other holder of record and present it to the inspector of election with their ballot.
2. By Internet. Stockholders can vote on the Internet by following the instructions provided in the one-page notice regarding the Internet availability of proxy materials.
3. By Mail. Stockholders can vote by mail after requesting a paper copy of the proxy materials, including a proxy card, by following the instructions provided in the one-page notice regarding the Internet availability of proxy materials.
4. By Telephone: Stockholders can vote over the telephone using the toll-free telephone number obtained by accessing the website set forth in the instructions provided in the one-page notice regarding the Internet availability of proxy materials.

Each share of Common Stock is entitled to one vote on all matters on which Stockholders may vote. There is no cumulative voting in the election of directors. The presence, in person or by proxy, of holders of a majority of the outstanding shares of Common Stock entitled to vote at the Meeting is necessary to constitute a quorum at the Meeting. Shares of Common Stock represented by a properly executed and returned proxy will be treated as present at the Meeting for purposes of determining the presence of a quorum without regard to whether the proxy is marked as casting a vote for or against, or withholding authority or abstaining, with respect to a particular matter. In addition, shares of Common Stock represented by “broker non-votes” generally will be treated as present for purposes of determining the presence of a quorum. Broker non-votes are shares of Common Stock held in record name by brokers, banks or other nominees as to which a proxy is received and (i) instructions have not been received from the beneficial owners or persons entitled to vote, (ii) the broker or nominee does not have discretionary power and (iii) the record holder had indicated that it does not have authority to vote such shares on that matter. Under current stock exchange rules, brokers who do not have instructions from their customers may not use their discretion in voting their customers’ shares on certain specific matters that are not considered to be “routine” matters.

Attending the Meeting

Stockholders as of the Record Date are invited to attend the Meeting. Stockholders must present a form of photo identification acceptable to the Company, such as a valid driver’s license or passport, to be admitted to the Meeting. Registered holders may vote upon presentation of such identification. Beneficial owners who hold their shares through a nominee, such as a broker or a bank, must obtain a proxy from such nominee or other holder of record and present it to the inspector of election with their ballot. Each stockholder may appoint only one proxy holder or representative to attend the Meeting on his or her behalf. In addition, we reserve the right to implement any health and safety measures as we deem prudent or as may be required by applicable laws or government orders. In recent years, such safety measures have included, among others, requirements to wear masks and follow social distancing protocols.

The Meeting will begin promptly at 10:00 a.m. Eastern Daylight Time. Please allow ample time for the check-in procedures. Media may attend the Meeting by invitation only. No cameras, audio or video recording equipment, communication devices, or other similar equipment may be brought into the Meeting.

Required Votes, Abstentions, and Broker Non-Votes

Directors will be elected by a plurality of the votes cast. This means that the nominees with the most votes will be elected. Votes may be cast for or withheld from the nominee, but a withheld vote or a broker non-vote will not affect the outcome of the election of directors at the Meeting.

The affirmative vote of the holders of a majority of the shares of Common Stock represented in person or by proxy at the Annual Meeting and voting on the proposal is required for approval of (i) the ratification of our selection of Ernst & Young LLP as our independent registered public accountants for 2023, (ii) the advisory resolution regarding executive compensation, (iii) the amended and restated Stock Incentive Plan, and (iv) the proposal regarding the frequency of holding future advisory votes on executive compensation. Abstentions and broker non-votes will have no effect upon these proposals.

With respect to the proposal regarding the frequency of holding future advisory votes on executive compensation, if none of the alternatives receives an affirmative vote of the holders of a majority of the shares represented in person or by proxy at the Annual Meeting and voting on the proposal, the frequency (every one, two, or three years) that receives the highest number of votes will be deemed to be the frequency that is preferred by stockholders.

Proxy Solicitation

We are making this proxy solicitation both through the mail and Internet, although proxies may be solicited by personal interview, telephone, facsimile, letter, e-mail or otherwise. Certain of our directors, officers and other employees, without additional compensation, may participate in the solicitation of proxies. We will pay the cost of this solicitation, including the reasonable charges and expenses of brokerage firms and others who forward solicitation materials to beneficial owners of Common Stock. We have retained Georgeson LLC, 1290 Avenue of the Americas, 9th Floor, New York, NY 10104] to act as proxy solicitor in conjunction with the Meeting. We have agreed to pay that firm approximately \$15,000 plus reasonable out-of-pocket expenses for their services.

ITEMS TO BE VOTED UPON

1. ELECTION OF DIRECTORS

Our Board of Directors currently consists of 11 directors. Four directors have terms expiring at the Meeting. These four directors are named as director nominees in this Proxy Statement and have been nominated for reelection to the Board to serve for a term ending at the 2026 annual meeting of stockholders, and until their successors shall have been duly elected and qualified. Proxies cannot be voted for more than four nominees. Unless otherwise specified in the accompanying proxy card, the shares voted by proxy will be voted FOR the election of the four persons listed for terms expiring in 2026. The Board expects that all four nominees will be available for election, but if any of the nominees is not available or is unwilling to accept election, it is expected that the proxies will vote for a substitute nominee to be designated by the Board or, if no such designation is made, that the proxies will vote for a lesser number of nominees. The Board has no reason to believe that the persons named will be unable to serve or will decline to serve if elected.

NOMINEES FOR DIRECTOR WITH TERMS EXPIRING AT THE ANNUAL MEETING OF STOCKHOLDERS IN 2026

Name	Age ⁽¹⁾	Position(s) with the Company	Served as Director Since
George B. Abercrombie	68	Director	2011
Theresa M. Heggie	62	Director	2018
Amy E. McKee, M.D.	51	Director	2021
Jon P. Stonehouse	62	Director, President, Chief Executive Officer	2007

The following persons shall continue to serve as directors for the terms indicated:

DIRECTORS WITH TERMS EXPIRING AT THE ANNUAL MEETING OF STOCKHOLDERS IN 2024

Name	Age ⁽¹⁾	Position(s) with the Company	Served as Director Since
Nancy J. Hutson, Ph.D.	73	Director, Chair of the Board	2012
Vincent J. Milano	59	Director	2021
A. Mabelle Sanders	59	Director	2022

DIRECTORS WITH TERMS EXPIRING AT THE ANNUAL MEETING OF STOCKHOLDERS IN 2025

Name	Age ⁽¹⁾	Position(s) with the Company	Served as Director Since
Stephen J. Aselage	72	Director	2019
Steven K. Galson, M.D., MPH.	66	Director	2021
Kenneth B. Lee, Jr	75	Director	2011
Alan G. Levin	61	Director	2020

(1) Age as of April 17, 2023.

Biographical Information of Directors and Director Nominees

Below you can find information, including biographical information, about our current directors, nominees for director, and directors whose terms continue after the Meeting, as well as a discussion of the specific experiences, qualifications, attributes, and skills considered by the Board in concluding that such individuals should serve as directors. Mr. Robert A. Ingram, who previously served as a director with a term expiring at the annual meeting of stockholders in 2024 and as Chairman of the Board, passed away in March 2023. We are saddened by the loss of Mr. Ingram, and we acknowledge and appreciate his many years of service and contributions to the Company.

Nominees for Director with Terms Expiring in 2026

George B. Abercrombie was initially appointed to the Board in October 2011. Mr. Abercrombie has over 30 years of experience as a business leader in the pharmaceutical industry. Mr. Abercrombie held the position of Senior Vice President and Chief Commercial Officer at Innoviva, Inc., a publicly-traded bio-pharmaceutical asset management company, from 2014 to 2018. He served from 2001 to 2009 as the President and Chief Executive Officer of Hoffmann-La Roche Inc., a pharmaceutical company, where he was responsible for leading operations in both the United States and Canada. During his tenure, Mr. Abercrombie also served as a member of the Roche Pharmaceutical Executive Committee, which was responsible for developing and implementing global strategy for the

Pharmaceuticals Division. In 1993, Mr. Abercrombie joined Glaxo Wellcome Inc. (“Glaxo”) as Vice President and General Manager of the Glaxo Pharmaceuticals Division, and was later promoted to Senior Vice President, U.S. Commercial Operations. Prior to joining Glaxo, he spent over ten years at Merck & Co., Inc., where he gained experience in sales and marketing, executive sales management and business development. Mr. Abercrombie began his career as a pharmacist after receiving a bachelor’s degree in pharmacy from the University of North Carolina at Chapel Hill, and later earned an MBA from Harvard University. He formerly served on the boards of directors of Brickell Biotech, Inc., Inspire Pharmaceuticals, Inc., Ziopharm Oncology, Inc., Tranzyme Pharma, Aptus Health, Inc., and DemeRX. Additionally, he is an Adjunct Professor at Duke University’s Fuqua School of Business, a board member of the North Carolina GlaxoSmithKline Foundation, an inaugural member of the Duke University Psychiatry and Behavioral Sciences Advisory Board, a member of the North Carolina Board of Science, Technology and Innovation, and the Chief Executive Officer of Abercrombie Advisors LLC, a pharmaceutical consulting firm. Mr. Abercrombie’s executive experience in the pharmaceutical industry and management positions with major pharmaceutical companies provide an excellent background for service on the Board.

Theresa M. Heggie was initially appointed to the Board in December 2018. Ms. Heggie most recently served as Chief Operating Officer of ProQR Therapeutics NV (“ProQR”), a publicly-traded biotechnology company developing RNA therapies using its proprietary Axiomer RNA-editing platform technology for severe, rare and common diseases, from February 2022 to October 2022, after joining ProQR as Chief Commercial Officer in October 2021. She previously served as Chief Executive Officer of Freeline Therapeutics Holdings plc (“Freeline”), a publicly-traded gene therapy company, from June 2020 to August 2021 and, prior to that, as Senior Vice President, Head of Europe, Middle East, Africa & Canada for Alnylam Pharmaceuticals, Inc., a global commercial-stage biopharmaceutical company, from May 2017 to May 2020. From June 2013 to March 2016, Ms. Heggie served as Chief Strategy and Marketing Officer for Bupa, an international healthcare group. Prior to June 2013, Ms. Heggie served in senior commercial and operating roles at Shire plc (“Shire”), a global specialty biopharmaceutical company, including Senior Vice President, Global Commercial Operations for the rare disease business. Prior to that, Ms. Heggie had responsibility over EMEA rare disease and served as Chief Executive Officer of Jerini AG, a pharmaceutical company, following Shire’s acquisition of the company, and its lead asset, Firazyr[®], for the treatment of hereditary angioedema. Prior to joining Shire, Ms. Heggie spent more than 20 years in a broad range of increasingly senior commercial positions at Janssen Pharmaceuticals and Baxter Healthcare. Ms. Heggie previously served as a non-executive director of Swedish Orphan Biovitrum AB, an international specialty biopharmaceutical company dedicated to rare diseases, from May 2016 to April 2017, as a member of the board of directors of Freeline from June 2020 to August 2021, and as a member of the supervisory board of ProQR from July 2019 to October 2021. Ms. Heggie holds a B.S. degree from Cornell University. Ms. Heggie’s extensive commercial experience in the industry, especially her rare disease commercial experience, provide valuable knowledge and insight to the Board.

Amy E. McKee, M.D. was initially appointed to the Board in September 2021. Since September 2022, she has served as Chief Medical Officer and Global Head, Oncology Center of Excellence at Parexel International Corporation (“Parexel”), a global clinical research organization. She previously served as Vice President, Regulatory Consulting at Parexel from February 2019 to September 2022. Prior to joining Parexel, Dr. McKee served in several leadership roles of increasing responsibility at the U.S. Food and Drug Administration (FDA) from 2008 to February 2019. While at the FDA, Dr. McKee served as a primary reviewer of new drug applications (NDAs) and biologics license applications (BLAs) across multiple divisions and served as both the acting deputy director and supervisory associate director of the Office of Hematology and Oncology products, where she managed four separate divisions performing NDA and BLA reviews. From January 2018 to February 2019, Dr. McKee was the deputy center director for the FDA’s Oncology Center of Excellence, which helps expedite development of innovative medical products of oncologic and hematologic malignancies and supports an integrated approach to their clinical evaluation. She holds an M.D. from Tulane University School of Medicine and a B.A. from Middlebury College. Dr. McKee’s extensive regulatory experience provides valuable knowledge and insight to the Board.

Jon P. Stonehouse joined BioCryst in January 2007 as Chief Executive Officer and Director. He was also named President in July 2007. Prior to joining the Company, he served as Senior Vice President of Corporate Development for Merck KgaA, a pharmaceutical company, since July 2002. His responsibilities included corporate mergers and acquisitions, global licensing and business development, corporate strategy and alliance management. Prior to joining Merck KgaA, Mr. Stonehouse held a variety of roles at Astra Merck/AstraZeneca. Mr. Stonehouse began his career in the pharmaceutical industry as a sales representative and held increasing sales leadership positions at Merck & Co., Inc. In 2011, Mr. Stonehouse joined the advisory board of Genscript, a private bioservices company, and in December 2014, he joined the board of directors of Bellicum Pharmaceuticals, Inc., a publicly-traded clinical stage biopharmaceutical company

focused on novel cellular immunotherapies. Mr. Stonehouse previously served on the advisory board of Precision Biosciences, Inc., a private biotechnology company, from 2008 to 2018. He earned his B.S. in Microbiology at the University of Minnesota. As Chief Executive Officer and President of BioCryst, Mr. Stonehouse brings to the Board an intimate knowledge of our business, and his executive experience in a variety of capacities at major pharmaceutical companies provides industry-specific operational experience that is beneficial to the Board.

Directors with Terms Expiring in 2024

Nancy J. Hutson, Ph.D. was initially appointed to the Board in January 2012 and was elected as Chair of the Board in March 2023. Dr. Hutson brings over 30 years of experience as a seasoned professional and leader within the pharmaceutical industry. She retired from Pfizer, Inc. in 2006 after spending 25 years in several research and leadership positions, most recently serving as Senior Vice President of Global Research & Development (R&D) as well as Director of Pfizer’s pharmaceutical R&D site, Groton/New London Laboratories. Dr. Hutson received a B.A. degree from Illinois Wesleyan University and a Ph.D. in physiology from Vanderbilt University. Dr. Hutson currently serves on the board of directors for Endo International plc, a publicly-traded pharmaceutical company, and PhaseBio Pharmaceuticals, Inc. and Clearside Biomedical, Inc., both publicly-traded biopharmaceutical companies. She also previously served on the board of directors of Inspire Pharmaceuticals, Inc. and Cubist Pharmaceuticals, Inc. Dr. Hutson’s extensive experience in research and development in the pharmaceutical industry provides valuable insight to the Board.

Vincent J. Milano was initially appointed to the Board in July 2021. Mr. Milano most recently served as President and Chief Executive Officer of Idera Pharmaceuticals, Inc. (“Idera”) (now Aceragen, Inc.), a position he held from December 2014 until his resignation in September 2022 following Idera’s acquisition of Aceragen. Prior to joining Idera, Mr. Milano served in roles of increasing responsibility, including most recently as Chairman, President and Chief Executive Officer, at ViroPharma Incorporated, which successfully developed and launched Cinryze for the treatment of hereditary angioedema (“HAE”) in the United States and Europe, prior to its acquisition by Shire Pharmaceuticals in January 2014. Prior to joining ViroPharma, Mr. Milano served as a senior manager at KPMG LLP, an independent registered public accounting firm. He currently serves as chair of the board of directors of Aceragen and as a member of the board of directors of Aclaris Therapeutics, and he is the chairman of the board of Life Science Cares Philadelphia. He previously served on the boards of directors of Spark Therapeutics, Inc. and Vanda Pharmaceuticals Inc. Mr. Milano received his B.S. degree in accounting from Rider College. His rare disease and HAE experience, together with his extensive experience in the pharmaceutical industry, including both as an executive and director, provide valuable knowledge and experience to the Board.

A. Mabelle Sanders was initially appointed to the Board in February 2022. She currently serves as the North Carolina Secretary of Commerce, a position she has held since February 2021. Prior to being appointed as North Carolina’s Secretary of Commerce, Ms. Sanders served as Secretary of the North Carolina Department of Administration from January 2017 to February 2021. Ms. Sanders has over 30 years of pharmaceutical and biotechnology experience with increasing levels of quality assurance and manufacturing operations responsibilities with Biogen, Inc. (“Biogen”), Purdue Pharmaceuticals, and AkzoNobel. Most recently, she led product operations for Biogen’s multiple sclerosis franchise as its Vice President of Multiple Sclerosis Franchise Product Operations, and prior to that, she was Vice President of Manufacturing and General Manager for Biogen’s largest global manufacturing operation. Ms. Sanders currently serves on the board of directors of Novan, Inc. She previously served on the board of directors of Radius Health, Inc. until her recent resignation in August 2022 following its acquisition by a leading healthcare fund. She received a B.S. in biochemistry from North Carolina State University and a master’s degree in health administration from Pfeiffer University. Ms. Sanders’ extensive pharmaceutical and biotechnology experience provide valuable insight and expertise to the Board.

Directors with Terms Expiring in 2025

Stephen J. Aselage was initially appointed to the Board in January 2019. Until January 2019, Mr. Aselage served as Chief Executive Officer of Travers Therapeutics, Inc. (then Retrophin Inc.) (“Travers”), a publicly-traded biopharmaceutical company specializing in identifying, developing and delivering life-changing therapies to people living with rare disease, which he joined in 2012. He has more than 40 years of experience in the biopharmaceutical industry, including substantial rare disease, commercial and business development experience. From 2005 to 2012, Mr. Aselage served as Executive Vice President and Chief Business Officer of BioMarin Pharmaceutical Inc. (“BioMarin”), a biotechnology company. Prior to BioMarin, Mr. Aselage held positions of increasing responsibility at a number of companies, including Bristol Laboratories, Genentech and Sangstat. He currently serves as chairman of the board of Acer Therapeutics Inc., a publicly-traded pharmaceutical company, and previously served on the board of Travers from 2012 until May 2022. Mr. Aselage is also a member of the board of Acuitas Therapeutics, a private biotechnology company.

Mr. Aselage holds a B.S. in biology from the University of Notre Dame and serves on the advisory council of the University of Notre Dame Department of Science. Mr. Aselage's extensive experience as an executive in the industry and his experience with rare disease therapies contribute valuable insight and experience to the Board.

Steven K. Galson, M.D., MPH, was initially appointed to the Board in September 2021. From 2010 to 2021, Dr. Galson served as Senior Vice President, Research and Development, at Amgen, where he also led regulatory affairs. Prior to joining Amgen, Dr. Galson spent more than 20 years in public service roles across the U.S. Department of Health and Human Services, Department of Energy, Environmental Protection Agency, and Centers for Disease Control and Prevention. From 2001 to 2007, Dr. Galson progressed from deputy director, to acting director, to director of the Center for Drug Evaluation and Research at the FDA. From 2007 to 2009, he served as acting surgeon general of the United States. Dr. Galson currently serves on the board of directors of Elephas Biosciences Corporation, a private biosciences company. He previously served on the boards of directors of Vanda Pharmaceuticals Inc., a publicly-traded biopharmaceutical company, and Insilico Medicine, a private pharmaceutical company. Dr. Galson received a B.S. in biochemistry from the State University of New York at Stony Brook, an M.D. from the Mt. Sinai School of Medicine, and a master's degree in public health from the Harvard School of Public Health. Dr. Galson's industry background, research and development experience, and extensive regulatory experience provide valuable knowledge and insight to the Board.

Kenneth B. Lee, Jr. was initially appointed to the Board in June 2011. Mr. Lee has over 40 years of experience counseling management teams, boards of directors and investors of technology-based companies worldwide. He is currently a General Partner with Hatteras Venture Partners, LLC, a venture capital fund focusing on life science companies, which he joined in 2003. Previously, he was President of A.M. Pappas & Associates, LLC, following 29 years with Ernst & Young LLP, where he was most recently Managing Director of the firm's health sciences corporate finance group, and at one time served as the National Director of the Life Sciences Practice. Mr. Lee received a B.A. degree from Lenoir-Rhyne College and an MBA from the University of North Carolina at Chapel Hill. Mr. Lee recently retired from the board of directors of Eyenovia, Inc., a publicly-traded ophthalmic biopharmaceutical company, in September 2022. He has previously served on the boards of the public companies Abgenix, Inc., Aralez, Inc., CV Therapeutics, Inspire Pharmaceuticals, Maxygen, Inc., and OSI Pharmaceuticals and previously served on the boards of the private companies Aerami Therapeutics, Clinipace, Clinverse and A.M. Pappas & Associates. Mr. Lee's experience advising biotechnology companies regarding financial and partnering strategies, his extensive background in finance and his experience serving on the boards of both public and private biotech companies contribute valuable insight and experience to the Board.

Alan G. Levin was initially appointed to the Board in February 2020. Mr. Levin served as Chief Financial Officer of Endo Health Solutions Inc. ("Endo"), a global specialty healthcare company, from June 2009 until September 2013. Prior to joining Endo, Mr. Levin worked with Texas Pacific Group, a leading private equity firm, and one of its start-up investments. Before that, he was Chief Financial Officer of Pfizer, Inc. where he worked for 20 years in a variety of executive positions of increasing responsibility, including Treasurer and Senior Vice President of Finance & Strategic Management for the company's research and development organization. He has been a member of the board of directors of Diffusion Pharmaceuticals Inc., a publicly-traded development stage oncology company, since 2015, and was a member of the board of directors of Aceto Corporation, a former publicly-traded seller and distributor of generic drugs, pharmaceutical ingredients, and performance chemicals, from 2013 to 2019. In addition, Mr. Levin is a member of the advisory board of Auen Therapeutics, a private equity fund, and a member of the board of directors of the Critical Path Institute, a non-profit collaboration between the FDA and the pharmaceutical industry, focused on accelerating development of and streamlining regulatory requirements for innovative medicines. He earned a bachelor's degree from Princeton University and a master's degree in accounting from New York University's Stern School of Business. Mr. Levin is a certified public accountant. Mr. Levin's extensive experience in strategic planning, capital markets, financial reporting, tax planning, and business development contribute valuable insight and experience to the Board.

Recommendation of the Board of Directors

THE BOARD OF DIRECTORS OF THE COMPANY RECOMMENDS A VOTE FOR EACH OF THE FOUR NOMINEES FOR DIRECTOR WITH TERMS EXPIRING IN 2026 NAMED ABOVE.

2. RATIFICATION OF APPOINTMENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTANTS FOR 2023

The Audit Committee of the Board has appointed Ernst & Young LLP as our independent registered public accountants for the fiscal year ending December 31, 2023. Services provided to the Company by Ernst & Young LLP in fiscal 2022 and 2021 are described below.

The Company is asking its stockholders to ratify the selection of Ernst & Young LLP as its independent registered public accountants for 2023. Although ratification is not required by the Company's bylaws or otherwise, the Board is submitting the selection of Ernst & Young LLP to its stockholders for ratification as a matter of good corporate practice.

A representative of Ernst & Young LLP will be present at the Meeting and will have an opportunity to make a statement and/or to respond to appropriate questions from our stockholders.

Fees Paid to Independent Registered Public Accountants

In connection with the audit of the 2022 consolidated financial statements, the Company entered into an engagement agreement with Ernst & Young LLP, which set forth the terms by which Ernst & Young LLP agreed to perform audit services for the Company.

Set forth below is information relating to the aggregate fees paid to Ernst & Young LLP for professional services rendered for the fiscal years ended December 31, 2022 and 2021, respectively.

	<u>2022</u>	<u>2021</u>
(1) Audit Fees	\$1,268,440	\$1,175,506
(2) Audit-related fees.	—	—
(3) Tax fees	80,340	—
(4) All other fees	—	—

Audit Fees

Audit fees represent the aggregate fees billed for professional services rendered by our independent registered public accounting firm for the audit of our annual financial statements and internal control over financial reporting, review of financial statements included in our quarterly reports on Form 10-Q and services that are normally provided in connection with statutory and regulatory filings or engagements, including the issuance of consents in connection with registration statement filings with the SEC and comfort letters in connection with securities offerings. For 2022 and 2021, fees associated with registration statement filings and securities offerings were approximately \$15,000 and \$129,500, respectively.

Tax Fees

Tax fees represent the aggregate fees billed for tax advisory services.

Audit Committee Pre-Approval

It is the policy of the Audit Committee, as set forth in the Audit Committee Charter, to pre-approve, consistent with the requirements of the federal securities laws, all auditing services and non-audit services provided to the Company by its independent registered public accounting firm, other than such non-audit services as are prohibited by law to be performed by the independent registered public accounting firm and other than as provided in the de minimis exception set forth in applicable provisions of the federal securities laws. The Audit Committee may delegate to one or more of its designated members the authority to grant the required pre-approvals, provided that the decisions of any member(s) to whom such authority is delegated to pre-approve an activity shall be presented to the full Audit Committee at each of its scheduled meetings.

Recommendation of the Board of Directors

THE BOARD OF DIRECTORS RECOMMENDS THAT STOCKHOLDERS VOTE FOR RATIFICATION OF THE APPOINTMENT OF ERNST & YOUNG LLP AS THE COMPANY'S INDEPENDENT REGISTERED PUBLIC ACCOUNTANTS FOR 2023.

In the event that the Company's stockholders do not ratify the appointment of Ernst & Young LLP as the Company's independent registered public accountants for 2023, the appointment will be reconsidered by the Audit Committee and the Board. Even if the selection is ratified, the Audit Committee in its discretion may select a different registered public accounting firm at any time during the year if it determines that such a change would be in the best interests of the Company and its stockholders.

3. ADVISORY VOTE TO APPROVE EXECUTIVE COMPENSATION

The Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010 (the “Dodd-Frank Act”) enables our stockholders to vote to approve, on an advisory or non-binding basis, an advisory resolution on the compensation of our Named Executive Officers, as defined herein, as disclosed in this Proxy Statement in accordance with rules promulgated by the SEC. We currently hold an advisory vote on the compensation of our Named Executive Officers every year, and subject to our review and consideration of the voting results of Proposal 4 (Advisory Vote on the Frequency of Future Advisory Votes on Executive Compensation), we expect that, after the Meeting, the next such vote will occur at our 2024 annual meeting of stockholders.

The Company asks that you indicate your support for our executive compensation policies and practices as described in “Compensation Discussion and Analysis” and the accompanying tables and related disclosures in this Proxy Statement. This vote is not intended to address any specific item of compensation, but rather the overall compensation of our Named Executive Officers and the policies and practices described in this Proxy Statement. Your vote is advisory and so will not be binding on the Compensation Committee or the Board of Directors. However, the Compensation Committee and the Board of Directors will review the voting results and take them into consideration when structuring future executive compensation arrangements. The affirmative vote of the holders of a majority of the shares of Common Stock represented in person or by proxy at the Meeting and voting on the proposal will be required for approval.

We believe that the experience, abilities and commitment of our Named Executive Officers are unique in the biotechnology industry, and we recognize the need to fairly compensate and retain a senior management team that has produced excellent operating results over the past several years. Accordingly, the Compensation Committee makes compensation decisions for our executive officers after consideration of the following primary objectives:

- to have a substantial portion of each officer’s compensation contingent upon the Company’s performance as well as upon his or her own level of performance and contribution toward the Company’s performance and long-term strategic goals;
- to reward executives for actions that create short-term and long-term sustainable stockholder value, with a strong focus on Company results;
- to align the interests of our executives with the Company’s corporate strategies, business objectives, and the long-term interests of our stockholders; and
- to attract, incentivize, and retain our executive talent.

Further, our executive compensation program is based on market best practices to ensure that it is appropriately risk-based and competitive with similar companies in our industry. We do not believe that our executive compensation program encourages our management to take excessive risks.

The Board of Directors encourages you to carefully review the information regarding our executive compensation program contained in this Proxy Statement, including the Compensation Discussion and Analysis beginning on page 29, as well as the Summary Compensation Table and other related compensation tables and narrative discussion, appearing on pages 39 through 51, which provide detailed information on the compensation of our Named Executive Officers.

Recommendation of the Board of Directors

THE BOARD OF DIRECTORS RECOMMENDS THAT YOU VOTE FOR THE FOLLOWING RESOLUTION:

“RESOLVED, that the stockholders approve, on an advisory basis, the compensation of the Company’s Named Executive Officers, as disclosed in this Proxy Statement, including the Compensation Discussion and Analysis, the Summary Compensation Table and the related compensation tables, notes and narrative discussion.”

4. ADVISORY VOTE ON THE FREQUENCY OF FUTURE ADVISORY VOTES ON EXECUTIVE COMPENSATION

The Dodd-Frank Act also enables our stockholders to vote, on an advisory or non-binding basis, on how frequently they would like to cast an advisory vote on our executive compensation. By voting on this proposal, stockholders may indicate whether they would prefer to cast an advisory vote on executive compensation every one, two or three years. Stockholders may also abstain from voting on this proposal. The frequency (every one, two, or three years) that receives the highest number of votes will be deemed to be the frequency that is preferred by the stockholders.

After careful consideration, the Board of Directors has determined that holding an advisory vote on executive compensation annually is the most appropriate policy for the Company at this time. The Board, therefore, recommends that stockholders vote for future advisory votes on executive compensation to occur every year. While the Company's executive compensation programs are designed to promote a long-term connection between pay and performance, the Board recognizes that executive compensation disclosures are made annually. Holding an annual advisory vote on executive compensation provides the Company with more direct and immediate feedback on our compensation programs.

Although, as an advisory vote, this proposal is not binding upon the Company or the Board of Directors, the Board of Directors will carefully consider the stockholder vote on this proposal, along with all other expressions of stockholder views it receives on this matter.

Recommendation of the Board of Directors

THE BOARD OF DIRECTORS RECOMMENDS THAT YOU VOTE FOR "ONE YEAR" WITH RESPECT TO THIS PROPOSAL.

5. APPROVAL OF AN AMENDED AND RESTATED STOCK INCENTIVE PLAN, INCREASING THE NUMBER OF SHARES AVAILABLE FOR ISSUANCE UNDER THE STOCK INCENTIVE PLAN BY 7,000,000 SHARES

We are asking our stockholders to approve an amendment and restatement to the BioCryst Pharmaceuticals, Inc. Stock Incentive Plan (as amended and restated, the “Stock Incentive Plan”). As amended and restated, the Stock Incentive Plan increases the number of shares available for issuance under the Stock Incentive Plan by 7,000,000 (the “Share Increase”). We believe that the Share Increase is necessary for the Stock Incentive Plan to support the Company’s continued growth in 2023.

As of April 17, 2023, the total number of shares available under the Stock Incentive Plan, without giving effect to the Share Increase, is 38,925,731. This amount consists of 34,245,351 shares reserved for awards already granted and 4,680,380 shares currently available for future issuance under the Stock Incentive Plan. The shares currently available for future issuance under the Stock Incentive Plan represent less than one-half of our projected needs for the next year, which provides limited availability and flexibility for our equity usage as part of our global, broad-based equity program. The proposed increase would bring the total number of shares available under the Stock Incentive Plan to 11,680,380 as of April 17, 2023, which we currently expect to be sufficient under the Stock Incentive Plan through the 2024 annual meeting of stockholders (subject to a number of factors, including changes in stock price and the pace of the Company’s growth).

On April 24, 2023, our Board approved the Share Increase, subject to stockholder approval at this Meeting. The Stock Incentive Plan, as amended by the Share Increase, is attached as **Annex A** to this Proxy Statement. In addition to the Share Increase, the Stock Incentive Plan, as amended and restated on April 24, 2023, includes certain related and immaterial, administrative revisions.

Share Increase

Equity Usage and Needs

As further explained below, our equity awards are intended to attract, incentivize, retain, and motivate participants in the Stock Incentive Plan and align the interests of our directors, employees, and consultants with those of our stockholders. The long period of retention of awards outlined below by our employees indicates the strong link between these incentives and the long-term success of stockholders and employees alike. Our Board and management believe that equity awards are necessary to remain competitive in our industry and are essential to recruiting and retaining the best talent in a crucial period of growth for the Company. In 2023, we expect to continue our global expansion with the commercialization of ORLADEYO. To achieve these goals, the Company must retain and attract top talent, both in the United States and abroad, and equity is critical to support this continued growth. Accordingly, we believe the increase in shares reserved for issuance under the Stock Incentive Plan pursuant to the Share Increase is necessary to allow the Company to provide customary levels of equity incentives to employees, including, without limitation, the long-term equity incentive awards that the Compensation Committee has historically granted to all employees on an annual basis.

- ***The Company has created a culture of ownership that aligns employees with stockholders by offering every employee equity as an incentive to join the Company and annually at the end of each year.*** Strategic use of a broad-based equity program is core to our compensation philosophy as the Compensation Committee has historically granted long-term equity incentive awards to all employees on an annual basis to, among other things, align our employees’ interests with those of our stockholders by creating a culture of ownership. We believe that employees with a stake in the future success of our business are highly motivated to achieve long-term growth and are well-aligned with the interests of our other stockholders to increase stockholder value. Despite the highly competitive biotech market, we have experienced lower than average turnover, and we believe this is in part due to the long-term retentive nature of equity incentives and this ownership culture.
- ***We are in a highly competitive marketplace for biotech talent, and without the ability to offer competitive equity grants to attract and retain talent, we may lose, or fail to attract, key employees, which could impair our ability to execute on our business strategy and harm stockholder value.*** The Company added approximately 229 employees to its workforce in 2022, increasing its net employee headcount as of December 31, 2022 by approximately 49% compared to December 31, 2021, in connection with the continued commercialization of ORLADEYO® (berotralstat) in the United States and multiple other

markets globally, as well as the advancement of other pipeline molecules. The Company expects to add additional talent in 2023, particularly in its commercial operations and related support functions, as it supports the further expansion of ORLADEYO around the world.

- ***Our ability to attract and retain top talent has been critical to driving the strong launch of ORLADEYO and strong overall performance of the Company and is vital to the continued success of the ORLADEYO global expansion.*** In 2022, ORLADEYO generated approximately \$252 million in net revenue. In 2023, the Company expects ORLADEYO net revenue to be no less than \$320 million, with global peak sales of \$1 billion. To achieve these goals, the Company must retain and attract top talent, and equity is critical to support this continued growth.
- ***Outstanding equity awards have a positive impact on long-term employee ownership and alignment with stockholders.*** The Company's employee stock options have a 10-year term with vesting over four years, and the current average holding period for exercised stock options is approximately six years, with some of our officers and directors, including our CEO, holding many stock options for almost the full 10-year term. Although these longer holding periods can increase overhang (which is considered by the Compensation Committee when making decisions with respect to the Stock Incentive Plan and is discussed further under "Potential Dilution and Burn Rate" below), this long-term employee ownership illustrates the positive impact of equity as a retention tool, which aligns with stockholders. In particular, nearly one-third of all outstanding options (approximately 10.5 million options) are both exercisable and in-the-money as of April 17, 2023, which represents approximately one quarter of our current overhang. While this large portion of our outstanding options drives overhang above the overhang levels of our peers and certain independent stockholder advisory group thresholds, we believe employee retention of these options by employees provides the alignment with stockholders that our equity compensation philosophy seeks to achieve.
- ***Equity is essential to talent acquisition and retention.*** Our Board believes that the increase in the share reserve is necessary to assure that a sufficient reserve of Common Stock is available for issuance to make competitive grants through 2024. For the reasons described above, we rely significantly on equity incentives in order to attract, incentivize, and retain employees, consultants, and non-employee directors, and we believe that such equity incentives are necessary for us to remain competitive in the marketplace for executive talent and for other key individuals. This high level of participation in our broad-based equity compensation program aligns the interests of all of our employees and directors with those of stockholders. However, such a participation rate can drive up overhang at the Company when compared to peers given that only less than 20% of our compensation peer group also grants equity awards to every employee.

Without the approval of the Share Increase, we will not be able to continue providing competitive equity incentives to existing employees or to attract new employees in our competitive market. This could ultimately result in the loss of critical talent and inhibit our ability to meet our future growth objectives. If approved by stockholders, we intend to use the additional shares under the Share Increase to recruit, incentivize, and retain employees.

Potential Dilution and Burn Rate

The Company has demonstrated its focus on limiting potential dilution to current stockholders. Over the past three years, the Company has raised approximately \$1,075 million in cash through mechanisms such as royalty and debt financings as alternatives to equity financings that would have been highly dilutive to stockholders. There were many factors that made these alternative financing approaches attractive, including the ability to bring this cash into the Company without additional equity dilution.

Similarly, when considering the number of shares to add to the Stock Incentive Plan, the Compensation Committee reviewed, among other things, the potential dilution to current stockholders as measured by overhang and burn rate, as well as projected future share usage in light of our growing employee population. We recognize the dilutive impact of our equity compensation programs on our stockholders and continuously aim to balance this concern with the competition for talent, competitive compensation practices, the need to attract and retain talent, and the long-term alignment of our employees with stockholders.

As of April 17, 2023, the Company had a total of 188,920,765 shares of Common Stock outstanding. The potential share dilution from the 7,000,000 additional shares to be reserved for issuance under the Stock Incentive Plan, for which stockholder approval is being requested, is 3.7% of the Company's outstanding shares of Common Stock as of such date. Compared to the potential share dilution associated with the most recent share requests of our

peer companies, this percentage falls between the 25th and 50th percentiles of such requests, which range from approximately 3.7% to approximately 11.9% of the outstanding shares of common stock of the applicable peer companies.

Overhang

Stock Incentive Plan

On a fully diluted basis, the approximately 38,925,731 shares currently available for issuance under the Stock Incentive Plan (without taking into account the Share Increase) represent an overhang of approximately 17% based on the number of outstanding shares of Common Stock and shares underlying outstanding awards under the Stock Incentive Plan as of April 17, 2023, and 68% of the shares underlying outstanding awards under the Stock Incentive Plan are underwater (with an exercise price in excess of the closing price of our Common Stock on April 17, 2023). The outstanding stock options under the Stock Incentive Plan that are underwater have a weighted-average exercise price of \$10.33 per share and individual option exercise prices ranging up to \$17.25 per share, as compared to the \$8.07 per share closing price of our Common Stock on April 17, 2023. If the Share Increase is approved, the additional 7,000,000 shares would increase the overhang of the Stock Incentive Plan to 20%. We calculate these overhang numbers as the total of (a) shares available for future grants under the Stock Incentive Plan plus (b) shares underlying any outstanding awards under the Stock Incentive Plan divided by (c) the total number of shares outstanding plus shares available for issuance under the Stock Incentive Plan plus shares underlying any outstanding awards under the Stock Incentive Plan.

Equity Incentive Plans Generally

This section, including the table below, provides additional information about the aggregate outstanding equity awards under both of our equity incentive plans (i.e., the Stock Incentive Plan and our Inducement Equity Incentive Plan).

	<u>As of April 17, 2023</u>
Total number of shares of Common Stock subject to outstanding stock options	35,752,715
Weighted-average exercise price per share of outstanding stock options.	\$ 8.67
Weighted-average remaining term of outstanding stock options (in years)	7.1
Total number of shares of Common Stock subject to outstanding full value awards	4,630,715
Total number of shares of Common Stock available for grant under Company equity plans . .	5,215,901

While our dilution profile is in the upper quartile of our compensation peer group, certain factors have influenced our current overhang level. First, the Company has historically granted long-term equity incentive awards to all of its employees. We believe this high level of participation in our broad-based equity compensation program aligns the interests of employees and directors with those of stockholders. However, this strong employee ownership philosophy can also drive a high level of overhang when compared with our peers, but we believe it is essential to the future success of the Company and our stockholders. Second, the Company's employee stock options have a 10-year term with vesting occurring over a four-year period, and the current average holding period for exercised stock options is approximately six years, with some of our officers and directors, including our CEO, holding many stock options for almost the full 10-year term. The long vesting period of four years and the strong retention of in-the-money stock options can drive our overhang upwards despite positive outcomes for both employees and stockholders.

For example, our current executive officers held approximately 9,300,325 stock options as of April 17, 2023. Of these outstanding stock options, approximately 3,617,016 stock options, or 39%, are exercisable and in-the-money and have an average age of approximately five years. In addition, approximately 10,469,137, or 29%, of all outstanding stock options are exercisable and in-the-money and have an average age of more than four years. If all exercisable, in-the-money stock options were exercised, our total overhang percentage as of April 17, 2023 would be reduced by an approximate amount of at least 5.5, which would result in an overhang that is below the thresholds that certain independent stockholder advisory groups consider when making voting recommendations on equity incentive plan proposals. However, because our executive officers and other employees continue to hold these options rather than exercising them and selling the underlying shares, which would reduce the overhang, they remain aligned with the long-term interests of our stockholders even though these stock options contribute to overhang.

Further, the outstanding stock options that are underwater, or approximately 66% of all outstanding stock options, have a weighted-average exercise price of \$10.67 per share and individual option exercise prices ranging up to \$17.25 per share, as compared to the \$8.07 per share closing price of our Common Stock on April 17, 2023.

With these factors in mind, the Company is committed to continually incentivizing and retaining all employees through equity compensation while managing overhang and burn rate in order to drive long-term success.

Burn Rate

Our three-year average unadjusted burn rate is approximately 5.9%. As of April 17, 2023, there were approximately 4,680,380 shares available for future grants under the Stock Incentive Plan. Depending on assumptions and various factors, such as stock price, employee population growth, and market conditions, should the Share Increase be approved, it is expected that there will be sufficient shares available under the Stock Incentive Plan to satisfy our equity compensation needs through our 2024 annual meeting of stockholders.

Plan Features that Protect Stockholder Interests

The Stock Incentive Plan provides the following provisions that are favorable to our stockholders and protect stockholder interests:

- ✓ ***Independent Plan Administration.*** The Compensation Committee, comprised solely of non-employee, independent directors, administers the Stock Incentive Plan.
- ✓ ***No “Evergreen” Provision.*** The Stock Incentive Plan does not include an “evergreen” feature pursuant to which the reserve of shares authorized for issuance would automatically be replenished periodically.
- ✓ ***Limitation on Awards to Individuals.*** The Stock Incentive Plan limits the number of shares of Common Stock subject to awards that an individual may receive during each calendar year to 1,500,000 shares.
- ✓ ***Cap on Awards to Directors.*** The Stock Incentive Plan limits the value of the initial and annual awards to be granted to directors to \$1,000,000 and \$750,000, respectively.
- ✓ ***Minimum One-Year Vesting Requirement.*** All awards granted under the Stock Incentive Plan are subject to a minimum one-year vesting period, provided that this limitation shall not apply to up to five percent of the total number of shares available for issuance under the Stock Incentive Plan.
- ✓ ***No Discounted Options or Stock Appreciation Rights.*** Options and stock appreciation rights may not be granted with exercise prices below fair market value.
- ✓ ***No Dividends on Unvested Awards.*** The Stock Incentive Plan prohibits the payment of dividends on unvested awards.
- ✓ ***Clawback.*** Awards issued under the Stock Incentive Plan are subject to any clawback policy of the Company as in effect from time-to-time, including the clawback policy described under “Compensation Discussion and Analysis—Clawback Policy.”
- ✓ ***No Liberal Share Recycling.*** Shares subject to an award will not be available for reuse if such shares are delivered or withheld to satisfy any tax withholding obligation, or not issued upon the settlement of an award or exercise of a stock option.
- ✓ ***No Gross Ups.*** The Stock Incentive Plan does not provide for any tax gross-ups.
- ✓ ***No Repricings.*** No option or stock appreciation right may be repriced, regranted through cancellation, including cancellation in exchange for cash or other awards, or otherwise amended to reduce its option price or exercise price (other than with respect to adjustments made in connection with a transaction or other change in the Company’s capitalization as permitted under the Stock Incentive Plan) without the approval of the stockholders of the Company.
- ✓ ***Double-Trigger on Change of Control.*** The Stock Incentive Plan includes a double-trigger provision for the vesting of any options, restricted stock, or restricted stock units (“RSUs”) upon a change of control; however, if awards are not assumed by the acquirer or successor in connection with such change of control, outstanding awards under the Stock Incentive Plan will be fully vested.
- ✓ ***No Transferability.*** Awards generally may not be transferred, except by will or the laws of descent and distribution, unless approved by the Compensation Committee.

Summary of the Stock Incentive Plan

The principal provisions of the Stock Incentive Plan, including (unless otherwise noted) the terms of the Share Increase, are summarized below. This summary is not complete and is qualified in its entirety by the terms of the Stock Incentive Plan attached as **Annex A** to this Proxy Statement.

Equity Incentive Programs

The Stock Incentive Plan consists of three separate equity incentive programs:

- the Discretionary Option Grant Program;
- the Stock Issuance Program; and
- the Director Grant Program for non-employee Board members.

The principal features of each program are described below. The Compensation Committee or, in the absence of the Compensation Committee, another properly constituted committee of the Board, or the Board itself, has the authority to administer the equity incentive programs under the Stock Incentive Plan, and also has the authority to make grants under these programs to all eligible individuals. The Compensation Committee may by resolution authorize one or more officers of the Company to perform any or all things that the Compensation Committee is authorized and empowered to do or perform under the Stock Incentive Plan, and for all purposes under the Stock Incentive Plan, such officer or officers shall be treated as the Compensation Committee.

The term “plan administrator,” as used in this summary, means, as applicable, the Compensation Committee, another properly constituted committee of the Board, the Board, or one or more officers of the Company, to the extent that any of them is acting within the scope of its administrative jurisdiction under the Stock Incentive Plan.

Share Reserve

As of April 17, 2023, an aggregate of 56,090,000 shares of Common Stock have been reserved for issuance over the term of the Stock Incentive Plan, without giving effect to the Share Increase proposed under the terms of this proposal. The total number of shares available under the Stock Incentive Plan as of April 17, 2023, without giving effect to the Share Increase proposed under the terms of this proposal, is 38,925,731. This amount consists of 34,245,351 shares reserved for awards already granted and 4,680,380 shares of Common Stock currently available for future issuance under the Stock Incentive Plan. Approval of the Share Increase will increase the number of shares available for issuance under the Stock Incentive Plan by 7,000,000 shares.

The shares of Common Stock issuable under the Stock Incentive Plan may be drawn from shares of our authorized but unissued Common Stock or from shares of Common Stock reacquired by us, including shares repurchased on the open market.

No individual may receive options or other awards under the Stock Incentive Plan exceeding 1,500,000 shares in the aggregate in any calendar year.

In the event any change is made to the outstanding shares of Common Stock by reason of any recapitalization, stock dividend, stock split, combination of shares, exchange of shares or other change in corporate structure effected without our receipt of consideration, appropriate adjustments will be made to the securities issuable (in the aggregate and per participant) under the Stock Incentive Plan, the securities in effect under each outstanding option and stock issuance, and where applicable, the option exercise price per share.

Eligibility

Officers and employees, non-employee Board members and independent consultants in our service or the service of our parents or subsidiaries, whether now existing or subsequently established, are eligible to participate in the Discretionary Option Grant Program and the Stock Issuance Program. Non-employee members of the Board are also eligible to participate in the Director Grant Program.

As of April 17, 2023, 5 executive officers, approximately 566 other employees, and 10 non-employee Board members were eligible to participate in the Discretionary Option Grant Program and the Stock Issuance Program. Our 10 non-employee Board members were also eligible to participate in the Director Grant Program.

Valuation

The “fair market value” per share of Common Stock on any relevant date under the Stock Incentive Plan will be deemed to be equal to the closing selling price per share on that date on the Nasdaq Global Select Market. On April 17, 2023, the closing selling price of our Common Stock per share was \$8.07.

Discretionary Option Grant Program

Terms of Options

The Plan Administrator has complete discretion under the Discretionary Option Grant Program to determine which eligible individuals are to receive option grants, the time or times when those grants are to be made, the number of shares subject to each grant, the status of any granted option as either an incentive stock option or a non-statutory option under the federal tax laws, the vesting schedule, if any, for the option grant and the maximum term for which any granted option is to remain outstanding.

Each granted option will have an exercise price per share no less than the fair market value of the option shares on the grant date. No granted option will have a term in excess of ten years, and the option will generally become exercisable in one or more installments over a specified period of service measured from the grant date. However, one or more options may be structured so that they will be immediately exercisable for any or all of the option shares; the shares acquired under those options will be unvested and subject to repurchase by us, at the exercise price paid per share, if the optionee ceases service with us prior to vesting in those shares.

Upon cessation of service, the optionee will have a limited period of time in which to exercise any outstanding options to the extent exercisable for vested shares. The Plan Administrator will have complete discretion to extend the period following the optionee’s cessation of service during which his or her outstanding options may be exercised and/or to accelerate the exercisability or vesting of such options in whole or in part. Such discretion may be exercised at any time while the options remain outstanding, whether before or after the optionee’s actual cessation of service.

Upon the optionee’s cessation of service as a result of death after at least five years of service, all of the optionee’s outstanding options will accelerate and become exercisable in full.

In no event may options (or stock appreciation rights) granted under the Stock Incentive Plan be directly or indirectly repriced without the approval of our stockholders.

Stock Appreciation Rights

The Plan Administrator is authorized to issue tandem stock appreciation rights in connection with option grants made under the Discretionary Option Grant Program. The grant price of a stock appreciation right may not be less than the fair market value of our Common Stock on the date of the grant.

Tandem stock appreciation rights under the Discretionary Option Grant Program provide the holder with the right to surrender an option for an appreciation distribution from the Company. The amount of this distribution will be equal to the excess of:

- (i) the fair market value of the vested shares of Common Stock subject to the surrendered option, over
- (ii) the aggregate exercise price payable for such shares.

An appreciation distribution may, at the discretion of the Plan Administrator, be made in cash or in shares of Common Stock, or a combination thereof.

Stock Issuance Program

Shares may be issued under the Stock Issuance Program through direct and immediate issuance or with vesting upon the completion of a designated service period, the attainment of pre-established performance goals, or a specific period of time after issuance. To the extent a participant ceases service without completing the designated service period or performance goals, we have the right to repurchase the shares at the price paid, if any. However, the Plan Administrator has the discretionary authority at any time to accelerate the vesting of any and all unvested shares outstanding under the program. Share recipients will have full stockholder rights with respect to their shares, including the right to vote the shares and to receive regular cash dividends. Share recipients do not have rights with

respect to unvested shares; however, the Plan Administrator may grant dividend equivalents entitling the holder of such unvested shares to regular cash dividends payable on such shares. Dividends and dividend equivalents are subject to the same vesting schedule and payable at the same time as the shares to which such dividends and dividend equivalents relate.

Shares of Common Stock may also be issued under the program pursuant to RSUs that entitle the recipient to receive shares of Common Stock (or cash in lieu thereof) in the future following the satisfaction of vesting conditions imposed by the Plan Administrator. Outstanding RSUs under the program will automatically terminate, and no shares of Common Stock will be issued in satisfaction of those awards, if the vesting conditions established for the awards are not satisfied. RSU holders do not have stockholder rights with respect to the awards; however, the Plan Administrator may grant dividend equivalents entitling the holder of RSUs to regular cash dividends payable on the underlying shares. Dividend equivalents are subject to the same vesting schedule and payable at the same time as the shares underlying the RSU to which such dividend equivalents relate.

The Plan Administrator has complete discretion under the program to determine which eligible individuals are to receive stock issuances or RSUs, the time or times when those issuances or awards are to be made, the number of shares subject to each issuance or award, the extent to which an RSU will have an accompanying dividend equivalent, and the vesting schedule to be in effect for the stock issuance or RSU.

Director Grant Program

Terms of Equity Grants

Under the Director Grant Program, eligible non-employee Board members, including Board members who are our former employees, are eligible to receive equity grants in connection with their Board service. Each non-employee Board member may receive grants of stock options, RSUs, shares of Common Stock, other awards issuable under the Stock Incentive Plan, or a combination thereof. In no event will the aggregate grant date fair value calculated in accordance with FASB ASC Topic 718 of all awards granted during any calendar year to any non-employee Board member (excluding any awards granted at the election of a non-employee Board member in lieu of all or any portion of retainers or fees otherwise payable to non-employee Board members in cash), together with the amount of any cash fees or retainers paid to such non-employee Board members during such calendar year with respect to such individual's service as a non-employee Board member, exceed \$750,000 or, for a non-employee Board member who first joins the Board, \$1,000,000. In each case, the specific dollar amount of the grant will be as set forth in a Director Compensation Policy approved by the Board.

Each stock option grant, if any, will have an exercise price per share equal to no less than the fair market value per share of Common Stock on the grant date, and no stock option will have a term in excess of ten years.

General Provisions

Acceleration

In the event that we are acquired by merger or asset sale or otherwise undergo a change in control, including a change effected through the successful completion of a tender offer for more than 50% of our outstanding voting stock or a change in the majority of the Board effected through one or more contested elections for Board membership, except as set forth in the terms of the grant, the vesting of each outstanding equity award under the Stock Incentive Plan, in each case granted prior to April 3, 2017, shall automatically accelerate in full. However, all other grants under the Stock Incentive Plan made on or after April 3, 2017 are subject to "double trigger" vesting if the grants are assumed, in which case accelerated vesting will apply only if the grantee's service is terminated by us without "cause" or the grantee due to a "constructive termination" within 90 days preceding or two years following the change in control. If the grants are not assumed in connection with the change in control, they will fully vest upon the change in control.

Payment of Withholding Taxes for Options

The Plan Administrator may provide one or more participants in the Discretionary Option Grant Program and Stock Issuance Program with the right to have us withhold a portion of the shares otherwise issuable to such participants in satisfaction of applicable withholding taxes that attach upon the exercise of options or the vesting of stock issuances or RSUs. Alternatively, the Plan Administrator may allow participants to deliver previously acquired shares of Common Stock in payment of such withholding tax liability.

Amendment and Termination

The Board may amend or modify the Stock Incentive Plan at any time, subject to any required stockholder approval pursuant to applicable laws and regulations (including applicable Nasdaq Global Select Market rules). Unless sooner terminated by the Board, the Stock Incentive Plan will terminate on the earliest of:

- (i) ten years following the date the Stock Incentive Plan is approved by the Board, which will be April 24, 2033 (but any options, stock issuances or other awards outstanding on such date shall remain in effect in accordance with their terms);
- (ii) the date on which all shares available for issuance under the Stock Incentive Plan have been issued as fully vested shares; or
- (iii) the termination of all outstanding options and stock issuances in connection with certain changes in control or ownership of the Company.

New Plan Benefits

As described above, all future grants, including the identification of grant recipients and the sizes and types of grants, will be determined by the Plan Administrator in its discretion, and no arrangements have been made at this time with respect to the shares reserved for issuance under the Stock Incentive Plan. Therefore, the amount of future awards under the Stock Incentive Plan is not yet determinable, and it is not possible to predict the benefits or amounts that will be received by, or allocated to, particular individuals or groups of employees or participants.

Equity Compensation Plan Information

As of April 17, 2023, an aggregate of 56,090,000 shares of Common Stock have been reserved for issuance over the term of the Stock Incentive Plan, without giving effect to the Share Increase proposed under the terms of this proposal. The total number of shares available under the Stock Incentive Plan as of April 17, 2023, without giving effect to the Share Increase proposed under the terms of this proposal is 38,925,731. This amount consists of 34,245,531 shares reserved for awards already granted and 4,680,380 shares of Common Stock available for future issuance under the Stock Incentive Plan.

Information regarding the securities authorized for issuance under our equity compensation plans is presented as of December 31, 2022, which does not give effect to the proposed Share Increase of 7,000,000 shares of Common Stock under the Stock Incentive Plan.

Plan Category	(a) Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights	(b) Weighted- Average Exercise Price of Outstanding Options, Warrants and Rights(\$)	(c) Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (a))
Equity compensation plans approved by security holders . .	34,341,115 ⁽¹⁾	8.56	9,998,778 ⁽²⁾
Equity compensation plans not approved by security holders	<u>5,929,900⁽³⁾</u>	8.80	<u>946,108⁽⁴⁾</u>
Total	<u><u>41,271,015</u></u>	8.59	<u><u>10,944,886</u></u>

- (1) Represents stock option awards and RSUs granted under the Stock Incentive Plan. The number of shares that may be issued pursuant to the Employee Stock Purchase Plan during a given period and the purchase price of such shares cannot be determined in advance of such purchases.
- (2) Consists of 4,206,317 shares available for future issuance under the Stock Incentive Plan and 5,792,461 shares available for future issuance under the Employee Stock Purchase Plan.
- (3) Represents stock option awards and RSUs granted under the Inducement Equity Incentive Plan. For a narrative description of the terms of the Inducement Equity Incentive Plan, see Note 12 to the Company's audited consolidated financial statements for the year ended December 31, 2022, which is included in the Company's Annual Report on Form 10-K filed with the SEC on February 27, 2023.
- (4) Represents shares available for issuance under the Inducement Equity Incentive Plan. For a narrative description of the terms of the Inducement Equity Incentive Plan, see Note 12 to the Company's audited consolidated financial statements for the year ended December 31, 2022, which is included in the Company's Annual Report on Form 10-K filed with the SEC on February 27, 2023.

Federal Income Tax Consequences

The following is a summary of the U.S. federal income tax treatment applicable to us and the participants who receive awards under the Stock Incentive Plan based on the federal income tax laws in effect on the date of this Proxy Statement. This summary is not intended to be exhaustive and does not address all matters relevant to a particular participant based on the participant's specific circumstances. The summary expressly does not discuss the income tax laws of any state, municipality, or non-U.S. taxing jurisdiction, or the gift, estate, excise (including the rules applicable to deferred compensation under Section 409A of the Internal Revenue Code of 1986, as amended (the "Code")), or other tax laws other than U.S. federal income tax law. Because individual circumstances may vary, we recommend that all participants consult their own tax advisor concerning the tax implications of awards granted to them under the Stock Incentive Plan.

Option Grants

Options granted under the Stock Incentive Plan may be either incentive stock options which satisfy the requirements of Section 422 of the Code or non-statutory options which are not intended to meet such requirements. The federal income tax treatment for the two types of options differs as follows:

Incentive Stock Options. No taxable income is recognized by the optionee at the time of the option grant, and no taxable income is generally recognized at the time the option is exercised. The optionee will, however, recognize taxable income in the year in which the purchased shares are sold or otherwise transferred. For federal tax purposes, dispositions are divided into two categories: (i) qualifying and (ii) disqualifying. A qualifying disposition occurs if the sale or other disposition is made after the optionee has held the shares for more than two years after the option grant date and more than one year after the exercise date. If either of these two holding periods is not satisfied, then a disqualifying disposition will result. If the optionee makes a qualifying disposition, the taxable income recognized by the optionee will be treated as a long-term capital gain and we will not be entitled to an income tax deduction. If the optionee makes a disqualifying disposition of the purchased shares, then for the taxable year in which such disposition occurs, the optionee will recognize ordinary income, and we will be entitled to an income tax deduction, in an amount generally equal to the excess of (i) the fair market value of such shares on the option exercise date over (ii) the exercise price paid for the shares.

Non-Statutory Options. No taxable income is recognized by an optionee upon the grant of a non-statutory option. The optionee will in general recognize ordinary income in the year in which the option is exercised, in an amount equal to the excess of the fair market value of the purchased shares on the exercise date over the exercise price paid for the shares.

Subject to limitations imposed by Section 162(m) of the Code, we will generally be entitled to an income tax deduction equal to the amount of ordinary income recognized by the optionee with respect to the exercised non-statutory option. Any such deduction will in general be allowed for the taxable year of the Company in which such ordinary income is recognized by the optionee.

Stock Appreciation Rights

No taxable income is recognized upon receipt of a stock appreciation right. The holder will recognize ordinary income in the year in which the stock appreciation right is exercised, in an amount equal to the appreciation distribution. Subject to limitations imposed by Section 162(m) of the Code, we will generally be entitled to an income tax deduction equal to the appreciation distribution in the taxable year in which the ordinary income is recognized by the optionee.

Stock Issuances

Generally, the issuance of unvested stock will not result in taxable income to the employee. Instead, upon vesting, the fair market value of such shares, less cash or other consideration paid (if any), will be included in the participant's ordinary income as compensation. Any cash dividends or other distributions paid with respect to the stock prior to vesting will also be included in the holder's ordinary income as compensation when paid. The participant may, however, elect under Section 83(b) of the Code, to include in his or her ordinary income at the time the stock is issued the fair market value of such shares less any amount paid. Any cash dividends paid thereafter will be treated as dividend income.

Subject to limitations imposed by Section 162(m) of the Code, we will generally be entitled to an income tax deduction equal to the amount of ordinary income recognized by the participant with respect to the stock issuance. The deduction will in general be allowed for the taxable year of the Company in which such ordinary income is recognized by the participant.

Restricted Stock Units (RSUs)

No taxable income is recognized by a participant upon grant of an RSU. The participant will recognize ordinary income, in the year in which the RSU vests and the underlying stock is issued to the participant, in an amount equal to the fair market value of the shares on the date of issuance. Any cash or other property paid with respect to such shares on the vesting date will also be includible in the participant's ordinary income as compensation at the time of payment. A participant may not make an 83(b) election with respect to an RSU. Subject to limitations imposed by Section 162(m) of the Code, we will generally be entitled to an income tax deduction to the extent the participant recognizes ordinary income with respect to an RSU. The deduction will in general be allowed for the taxable year of the Company in which such ordinary income is recognized by the participant.

Deductibility of Executive Compensation

Section 162(m) of the Code imposes an annual deduction limit of \$1 million on compensation paid by the Company to "covered employees" in any taxable year. This rule may limit the deductibility of awards granted pursuant to the Stock Incentive Plan.

Recommendation of the Board of Directors

THE BOARD OF DIRECTORS DEEMS THE APPROVAL OF THE AMENDED AND RESTATED STOCK INCENTIVE PLAN, INCREASING THE NUMBER OF SHARES AVAILABLE FOR ISSUANCE UNDER THE STOCK INCENTIVE PLAN BY 7,000,000 SHARES, TO BE IN THE BEST INTERESTS OF THE COMPANY AND ITS STOCKHOLDERS AND RECOMMENDS A VOTE FOR APPROVAL OF THE AMENDED AND RESTATED STOCK INCENTIVE PLAN.

CORPORATE GOVERNANCE

Code of Business Conduct

We have a code of business conduct that applies to all our employees as well as to each member of the Board. The code of business conduct is available on our website at www.biocryst.com under the Corporate Governance section. The Company intends to post on its website any amendments to, or waivers from, its code of business conduct. To date, there have not been any waivers by us under the code of business conduct.

Board of Directors

The Company is governed by a Board of Directors, which currently consists of 11 directors as determined by resolution of the Board in accordance with the Company's Certificate of Incorporation. The Board has determined that 10 of the 11 current members of the Board (Messrs. Abercrombie, Aselage, Galson, Lee, Levin, and Milano, Ms. Heggie, Dr. Hutson, Dr. McKee, and Ms. Sanders) are independent as defined by the Nasdaq Global Select Market ("Nasdaq"). In addition, the Board previously determined that Mr. Ingram, who served as director and Chairman of the Board until his passing in March 2023, was independent as defined by Nasdaq. In making its independence determinations, the Board considered a proposed ordinary course, arm's-length transaction with Parexel, where Dr. McKee serves as Chief Medical Officer and Global Head, Oncology Center of Excellence. This transaction falls below the relevant thresholds for independence as defined by Nasdaq, and does not qualify as a related party transaction as contemplated by Item 404(a) of Regulation S-K.

There are no family relationships among any of our directors or our executive officers.

The Board has established the Audit, Compensation, and Corporate Governance and Nominating committees to assist in the oversight of the Company. The Board has adopted charters for each of these committees, which are posted on the Company's website at www.biocryst.com. The Company also makes available on its website its code of business conduct. Printed copies of these charters or the code of business conduct may be obtained, without charge, by contacting the Corporate Secretary, BioCryst Pharmaceuticals, Inc., 4505 Emperor Blvd., Suite 200, Durham, North Carolina 27703.

Board Leadership Structure

The Chair of the Board presides over the Board meetings and any executive session of the non-management directors. An executive session is held at every regularly scheduled Board meeting. Mr. Ingram served as Chairman of the Board until his passing in March 2023. Following Mr. Ingram's passing, the Board elected Dr. Hutson as Chair of the Board and decreased the size of the Board from 12 to 11 members. Dr. Hutson currently serves as the Chair of the Board.

The Company's CEO is responsible for setting the Company's strategic direction and for the day-to-day leadership and performance of the Company, while the Company's independent Chair assists and provides guidance to the CEO. The Company believes that having Dr. Hutson serve as Chair is the most appropriate leadership structure for the Company at this time, based on the current circumstances and direction of the Company and the membership of the Board, including Dr. Hutson's vast experience in the pharmaceutical industry. This leadership structure permits the CEO to focus his attention on managing our business and allows the Chair to function as an important liaison between management and the Board, enhancing the ability of the Board to provide oversight of the Company's management and affairs.

Risk Oversight

The Company does not view risk in isolation, but considers risk as part of its regular consideration of business strategy and business decisions. The Board oversees the Company's risk management function, directly and through its committees. BioCryst approaches risk management by integrating its strategic planning, operational decision making and risk oversight, and by communicating risks and opportunities to the Board. The Board commits substantial time and effort every year to discussing and agreeing upon the Company's strategic plan, and it reconsiders key elements of the strategic plan as warranted in response to significant events and opportunities. As part of the review of the strategic plan, as well as in evaluating events and opportunities that occur during the year, the Board and management also consider the risks relating to the strategic plan.

While the Board has primary responsibility for oversight of the Company's risk management, the Board's standing committees support the Board by regularly addressing various risks in their respective areas of oversight. Specifically, the Audit Committee assists the Board in fulfilling its oversight responsibilities with respect to risk management in the areas of financial reporting, internal controls, compliance with public reporting requirements, and

cybersecurity. The Audit Committee also is responsible for reviewing, discussing and advising the Board with respect to our corporate compliance program and code of business conduct. The Compensation Committee assists the Board in fulfilling its risk management oversight responsibilities with respect to human capital management and risks arising from compensation policies and programs. The Corporate Governance and Nominating Committee assists the Board in fulfilling its risk management oversight responsibilities with respect to risks related to corporate governance matters, including as they relate to the Company's corporate responsibility risk management, strategy, initiatives, and policies. For additional information related to the Compensation Committee's role in evaluating risks related to our executive compensation program, see "Compensation Discussion and Analysis" below.

Committees of the Board

Audit Committee

The Company's Audit Committee currently consists of Mr. Lee, as its Chair, Mr. Abercrombie, Ms. Heggie (since February 2023), Mr. Levin, and Mr. Milano, and is responsible for the review of internal accounting controls, financial reporting, and related matters. In addition, the Audit Committee's responsibilities include, among others, the preapproval of audit and non-audit services; reviewing the Company's policies on enterprise risk assessment and risk management; reviewing the Company's corporate compliance program; reviewing, preapproving and overseeing all related-party transactions; establishing and overseeing procedures for the receipt, retention, and treatment of complaints regarding accounting, internal accounting controls, or auditing matters; determining appropriate funding, to be provided by the Company, for payment of compensation to the independent accountants employed by the Company, any other advisors employed by the Audit Committee, and ordinary administrative expenses of the Audit Committee; reviewing and preapproving any non-GAAP financial disclosures and any pro forma financial disclosures; and reviewing and discussing accounting pronouncements, initiatives, and proposed rule changes relevant to the Company. The Audit Committee also recommends to the Board the independent accountants selected to be the Company's auditors and reviews the audit plan, financial statements, and audit results, and it regularly reviews the independence, and evaluates the performance, of the selected independent accountants. In addition, the Audit Committee oversees the Company's cybersecurity program and receives regular updates on the program from the Company's cybersecurity steering committee.

The Board has adopted an Audit Committee Charter, available on the Company's website, that meets all applicable rules of Nasdaq and the SEC. The Audit Committee members are "independent" directors as defined by Nasdaq and the SEC, meet the heightened independence standards applicable to Audit Committee members under Nasdaq and SEC rules, and meet Nasdaq's financial literacy requirements for audit committee members. The Board has determined that each of Mr. Lee, Mr. Levin, and Mr. Milano qualifies as an "audit committee financial expert," as such term is defined by the SEC. The Audit Committee met six times during 2022.

Compensation Committee

The Company's Compensation Committee currently consists of Dr. Hutson, as its Chair, Mr. Aselage, and Ms. Sanders (since February 2023), and is responsible for the annual review of officer compensation and other incentive programs. Mr. Ingram served as a member of the Compensation Committee until March 2023. The Compensation Committee's responsibilities also include, among others, the review and recommendation to the Board of the compensation for directors serving on the Board and its committees; reviewing and approving the Company's goals and objectives relevant to compensation of executive officers; overseeing the risk assessment of the Company's compensation programs; reviewing compliance with any applicable Company stock ownership guidelines; assessing any conflicts of interest of the compensation consultant retained by the Compensation Committee; overseeing the administration of the Company's clawback of incentive compensation; overseeing engagement with stockholders and proxy advisory firms on executive compensation matters; periodically reviewing the Company's policies and strategies relating to human capital management and making recommendations to the Board with respect thereto; and reviewing and approving any compensatory contracts or similar transactions or arrangements with executive officers and certain other employees. Information describing the Compensation Committee's processes and procedures for considering and determining executive compensation, including the role of consultants in determining or recommending the amount or form of director and executive compensation, is included under the heading "Compensation Discussion and Analysis" below.

The Board has adopted a Compensation Committee Charter, available on the Company's website, that meets all applicable rules of Nasdaq and the SEC. The Compensation Committee members, including Mr. Ingram before his

passing, are “independent” directors as defined by Nasdaq, meet the heightened independence standards applicable to Compensation Committee members under Nasdaq rules, and are “non-employee” directors as defined by SEC rules. The Compensation Committee met five times during 2022.

Compensation Committee Interlocks and Insider Participation

The directors who served as members of the Compensation Committee during 2022 are Dr. Hutson, Mr. Aselage, and Mr. Ingram. None of these directors have ever served as an officer or employee of the Company, and none of these directors had any relationship with the Company during 2022 that would be required to be disclosed pursuant to Item 404 of Regulation S-K. No interlocking relationships exist between our current Board of Directors or Compensation Committee and the board of directors or compensation committee of any other company.

Corporate Governance and Nominating Committee

The Company’s Corporate Governance and Nominating Committee currently consists of Ms. Heggie, as its Chair (since February 2023), Mr. Abercrombie, Dr. Hutson, and Dr. McKee, and is responsible for selecting persons for election or re-election as directors and providing oversight of the corporate governance affairs and policies of the Board of Directors and the Company. Mr. Ingram served as a member of the Corporate Governance and Nominating Committee until March 2023. The Corporate Governance and Nominating Committee’s responsibilities also include, among others, overseeing the evaluation of the Board and management of the Company; assessing the independence of incumbent directors and new director nominees; reviewing the Board’s committee structure and recommending to the Board for its approval directors to serve as members and chair of each committee; reviewing periodically the Board’s leadership structure, including the separation of the Chair of the Board and Chief Executive Officer roles and/or appointment of a lead independent director of the Board; overseeing the annual self-evaluation process of the Board and its committees; reviewing the adequacy of the Certificate of Incorporation and Bylaws of the Company and recommending appropriate amendments to the Board; overseeing the orientation process for new directors and ongoing education for directors; reviewing policies relating to meetings of the Board; and overseeing and reviewing the management continuity planning process, including the review and evaluation of succession plans relating to executive officers, including the Chief Executive Officer. The Corporate Governance and Nominating Committee also is responsible for general oversight of the Company’s corporate responsibility risk management, strategy, initiatives, and policies.

The Board has adopted a Corporate Governance and Nominating Committee Charter, available on the Company’s website, that meets all applicable rules of Nasdaq and the SEC. The Corporate Governance and Nominating Committee members, including Mr. Ingram before his passing, are “independent” directors as defined by Nasdaq. The Corporate Governance and Nominating Committee met four times during 2022.

Other Committees

The Company also has a Commercialization Committee, a Science Committee, and a Finance Committee, each of which convenes from time to time, as needed, to assist the Company and the Board in strategic decision-making regarding product development and commercialization and significant scientific and financial matters. Information about these committees, including committee composition and copies of the committee charters, is available on the Company’s website.

Selection of Board Nominees

The Corporate Governance and Nominating Committee (referred to in this section as the “Committee”) will consider candidates for Board membership suggested by its members and other Board members, as well as management and stockholders. The Committee has established a procedure for submission of suggestions by stockholders and will consider candidates recommended in writing, including biographical information and personal references. All submissions by stockholders should be sent directly to the Chair of the Board, Nancy J. Hutson, Ph.D., at 4505 Emperor Blvd., Suite 200, Durham, North Carolina 27703. The Chair will provide copies of all submissions to the Committee for its consideration.

The Committee reviews all submissions and evaluates them based on predetermined selection criteria to identify prospective nominees. In reviewing candidates to become prospective nominees, the Committee makes an initial determination as to whether to conduct a full evaluation of the candidate based on the information provided to the Committee with the recommendation of the candidate, as well as the Committee’s own knowledge of the candidate, which may be supplemented by inquiries to the person making the recommendation or to others. The preliminary determination is based primarily on the need for additional Board members to fill vacancies or expand the size of the Board and the likelihood that the candidate can satisfy the director selection criteria described below. If the Committee determines, in

consultation with the Chair of the Board and other Board members as appropriate, that additional consideration is warranted, it may request additional information about the candidate’s background and experience. The Committee then evaluates the candidate as a prospective nominee considering our director selection criteria, including:

- the ability of the prospective nominee to represent the interests of the stockholders of the Company;
- the prospective nominee’s standards of integrity, commitment, and independence of thought and judgment;
- the prospective nominee’s ability to dedicate sufficient time, energy, and attention to the diligent performance of his or her duties, including the prospective nominee’s service on other public company boards; and
- the extent to which the prospective nominee contributes to the range of talent, skill, and expertise appropriate for the Board.

In evaluating prospective nominees for Board membership, consideration is given to obtaining a diversity of experience and perspective within the Board. In considering diversity, we look at the entirety of the Board. Although we do not seek constituent or representational directors, the Committee does consider the diversity of the Board whenever we are looking for a new director, including diversity of backgrounds, experience, perspective, race, gender, and ethnicity. The Committee and the Board evaluate the Board’s diversity on a periodic basis as part of their review of the Board as a whole, including to determine whether the composition of the Board satisfies the diversity objectives under Nasdaq Rule 5605(f)(2). For example, our Board conducts annual self-evaluations, which the Committee oversees, designed to solicit directors’ views on a variety of topics, including whether directors as a whole have the appropriate mix of characteristics, business experience, background, and tenure. See “Annual Performance Evaluations” below for additional information about these evaluations. The Committee also regularly assesses the expertise and competencies of the directors by considering, among other things, whether the Board, as a whole, is sufficiently represented by directors with public company board experience; experience serving as a chief executive officer or chief financial officer; strategic and transactional expertise; financial reporting and capital markets expertise; applicable experience with manufacturing, quality, regulatory, and late-stage clinical development matters; rare disease commercial expertise; international rare disease expertise; early-stage clinical and discovery research expertise; pharmaceutical research and development expertise; and information technology expertise, among others. In addition, the Board provides an opportunity for directors to voluntarily disclose any self-identified diversity characteristics. See “Board Diversity Matrix” below. Based on these evaluations, assessments, and self-disclosures, we believe the Board currently is comprised of directors who reflect an appropriate mix of diversity of backgrounds, experience, perspective, race, gender, and ethnicity. The following matrix highlights the expertise and competencies of each director, as reviewed by the Committee, in the areas identified above. The absence of a mark does not necessarily indicate that the director does not possess any relevant expertise or competency in the area.

Expertise/Competency	Abercrombie	Aselage	Galson	Heggie	Hutson	Lee	Levin	McKee	Milano	Stonehouse	Sanders
Public Co. Board Experience	X	X	X	X	X	X	X	X	X	X	X
CEO Experience	X	X		X		X			X	X	
CFO Experience						X	X		X		
Strategic/Transactional Expertise	X	X	X	X	X	X	X	X	X	X	X
Financial Reporting/Capital Markets Expertise	X	X		X		X	X	X	X	X	
Manufacturing	X			X	X		X	X		X	X
Quality	X			X				X		X	X
Rare Disease Commercial Expertise		X		X				X	X	X	
International Rare Disease Expertise		X		X				X	X	X	
Regulatory	X	X	X					X		X	X
Late-Stage Clinical Development	X	X	X	X	X		X	X		X	
Early-Stage Clinical and Discovery Research			X		X			X		X	
Pharmaceutical Research & Development Expertise	X	X	X		X		X	X		X	
IT Expertise	X						X	X		X	

The Committee also considers such other relevant factors as it deems appropriate, including the current composition of the Board, the relevance of the current expertise of the Board, stockholder communications, the balance of management and independent directors, the need for Audit Committee expertise and the evaluations of other prospective nominees. In connection with this evaluation, the Committee determines whether to interview the prospective nominee, and if warranted, one or more members of the Committee, and others as appropriate, interview prospective nominees in person or by telephone. After completing this evaluation and interview, the Committee selects the director nominees for the next annual meeting of stockholders. The Committee recommended the nomination of the four incumbent directors whose terms are expiring at the Annual Meeting for reelection to the Board of Directors.

The Committee also has authority to retain and approve the compensation of search firms to be used to identify director candidates. For example, during 2021, the Committee engaged, and the Company paid fees to, a director search firm to identify qualified director nominees to fill potential new directorship(s) on the Board, with a focus on directors who would add industry experience and/or diversity to the Board. This engagement resulted in the addition of Amy E. McKee, M.D to the Board in September 2021. Dr. McKee is standing for election to the Board at the Meeting,

Board Diversity Matrix

The following Board Diversity Matrix presents our Board diversity statistics in accordance with Nasdaq Rule 5606, as self-disclosed by our directors. While the Board satisfies the minimum objectives of Nasdaq Rule 5605(f)(2) by having at least one director who identifies as female and at least one director who identifies as a member of an Underrepresented Minority (as defined by Nasdaq Rules), the Corporate Governance and Nominating Committee will continue to consider the diversity of the Board in its selection of director nominees, consistent with the procedures described in the preceding section, “Selection of Board Nominees.”

Board Diversity Matrix (As of April 17, 2023)				
Total Number of Directors	11			
	Female	Male	Non-Binary	Did Not Disclose Gender
Part I: Gender Identity				
Directors	4	6	–	1
Part II: Demographic Background				
African American or Black	1	–	–	–
Alaskan Native or Native American	–	–	–	–
Asian	–	–	–	–
Hispanic or Latinx	–	–	–	–
Native Hawaiian or Pacific Islander	–	–	–	–
White	3	6	–	1
Two or More Races or Ethnicities	–	–	–	–
LGBTQ+	1			
Did Not Disclose Demographic Background	–			

Annual Performance Evaluations

The Board has a policy requiring an annual evaluation of the performance of the Board and the committees thereof, including individual assessments of each director’s performance and qualifications. The Board engages third-party evaluators to oversee the individual director assessments from time to time at the discretion of the Corporate Governance and Nominating Committee (referred to in this section as the “Committee”). Generally, as part of these individual director assessments, the third-party evaluators interview each director individually using a list of questions approved by the Committee and report the results of the interviews back to the Committee in the aggregate, protecting the anonymity of each director, which we believe facilitates open and honest responses to the interview questions. The Committee then reviews the results of these assessments in making recommendations to the Board, including with respect to director nominations and Board succession planning.

Stockholder or Other Interested Party Communications

Stockholders or other parties interested in communicating directly with the Board, or specified individual directors, may do so by writing to the Corporate Secretary, 4505 Emperor Blvd., Suite 200, Durham, North Carolina 27703. The Secretary will review all such correspondence and will regularly forward to the Board copies of all such correspondence that, in the opinion of the Secretary, relates to the functions of the Board or its committees or that the Secretary otherwise determines requires their attention. Directors may at any time review a log of all correspondence received by the Company that is addressed to members of the Board and request copies of such correspondence. Concerns relating to accounting, internal controls or auditing matters will immediately be brought to the attention of the Chair of the Audit Committee and handled in accordance with procedures established by the Audit Committee with respect to such matters.

Stock Ownership Guidelines

In June 2022, we amended our stock ownership guidelines to require our Leadership Team members and our non-employee directors (collectively, the “Covered Individuals” and each, a “Covered Individual”) to achieve a minimum ownership amount of Company securities within five years of the later of (i) the effective date of the amended guidelines and (ii) the date the Covered Individual becomes subject to the guidelines. We believe these amended guidelines will help ensure that each of our executive officers, all of whom are members of our Leadership Team, and each of our non-employee directors maintains an equity stake in the Company and, by doing so, appropriately links their interests with those of stockholders and employees. Covered Individuals are required to achieve the following minimum ownership amounts of Company securities, as applicable (the “Minimum Ownership Amount”):

Covered Individual	Minimum Ownership Amount
Chief Executive Officer	3x Base Salary
Other Leadership Team Members	1x Base Salary
Non-Employee Directors	3x Annual Cash Retainer

Shares of Common Stock, unvested RSUs, and earned performance share units count toward achievement of the Minimum Ownership Amount. In addition, shares owned by the Covered Individual’s spouse or in trust for the benefit of the Covered Individual, the Covered Individual’s spouse and/or children count toward achievement of the Minimum Ownership Amount. Unexercised options (vested and unvested) and unearned performance share units do not count toward achievement of the Minimum Ownership Amount.

The Compensation Committee of the Board reviews compliance with the stock ownership guidelines on an annual basis, with compliance to be measured as of December 31 each year, using an average stock price for the preceding 30-day period. As of December 31, 2022, each Covered Individual met the applicable Minimum Ownership Amount under the stock ownership guidelines.

Director Attendance

During 2022, the Board held six meetings. Each member of the Board attended at least 75% of the meetings of the Board and committees of the Board of which he or she was a member. We encourage all members of the Board to attend our annual meetings of stockholders. Our President and Chief Executive Officer, Jon P. Stonehouse, and the former Chairman of the Board, Robert A. Ingram, were each in attendance in person at the 2022 Annual Meeting of Stockholders, and Mr. Levin, Dr. McKee, Mr. Milano, and Ms. Sanders were each in attendance virtually.

Certain Relationships and Related Transactions

Since January 1, 2022, there were no relationships or related transactions requiring disclosure between the Company and any of its directors, executive officers or five percent stockholders. The Audit Committee Charter requires all related party transactions to be pre-approved by the Audit Committee.

Anti-Hedging Policy

We have adopted a policy that prohibits employees (including officers) or directors, or any of their family members, from engaging in any type of short sale or purchasing any financial instrument (including prepaid variable forward contracts, equity swaps, collars, and exchange-traded funds), or otherwise engaging in any transaction that, in either case, hedges or offsets, or is designed to hedge or offset, any decrease in the market value of our equity securities. Such persons may engage in other derivative transactions only if it is determined, to the satisfaction of our Insider Trading Compliance Officer (currently, our Chief Legal Officer and Corporate Secretary), that such transactions are consistent with applicable rules, laws, and our Insider Trading Policy.

EXECUTIVE OFFICERS

Our executive officers are listed below, followed by information, including biographical information, about our executive officers (other than Mr. Stonehouse, whose biographical information appears above under “Election of Directors”).

Name	Age ⁽¹⁾	Position(s)
Jon P. Stonehouse	62	President, Chief Executive Officer, and Director
Anthony J. Doyle	43	Chief Financial Officer and Treasurer
Helen M. Thackray, M.D.	54	Chief Research and Development Officer
Alane P. Barnes	57	Chief Legal Officer and Corporate Secretary
Charles K. Gayer	52	Chief Commercial Officer

(1) Age as of April 17, 2023.

In prior years, we also identified Yarlagadda S. Babu, Ph.D., and William P. Sheridan, MBBS, the Company’s Chief Discovery Officer and Chief Development Officer, respectively, as executive officers of the Company. Although Dr. Babu and Dr. Sheridan continue to serve the Company in these positions, the Board determined during 2022 that they are no longer executive officers of the Company within the meaning of SEC rules.

Biographical Information of Executive Officers

Anthony J. Doyle joined BioCryst in April 2020 as its Chief Financial Officer. Prior to joining BioCryst, Mr. Doyle served as Chief Financial Officer of Worldwide Clinical Trials Holdings, Inc., a full-service global contract research organization, since 2014. From 2012 to 2014, Mr. Doyle was Chief Financial Officer of World Book, a Berkshire Hathaway company. From 2004 to 2012, Mr. Doyle held a series of roles of increasing responsibility at General Electric, moving through financial planning and analysis, controller, audit, tax, and commercial finance rotations in the GE Financial Management and Corporate Audit Staff finance and leadership training programs. He then led risk and pricing for GE Healthcare’s U.S. diagnostic imaging business and served as global program manager for GE Healthcare Solutions, a hospital and healthcare outcomes-based consulting company. Mr. Doyle received his Bachelor’s degree from Dublin City University (Ireland) and his DESEM from Reims Management School (France). Mr. Doyle also has a Graduate Certificate in Corporate Treasury from Dublin City University.

Helen M. Thackray, M.D. joined BioCryst in March 2021 as Chief Research & Development Officer. She previously served as Chief Medical Officer and Senior Vice President of clinical development at GlycoMimetics, Inc., a publicly-traded biotechnology company focused on serious oncology, immunology, and inflammatory conditions, from 2006 to 2021 and led its orphan product, fast track, and breakthrough therapy programs at all stages of development in rare diseases. Prior to joining GlycoMimetics, Dr. Thackray was Vice President of Clinical Development at Biosynexus and served for over a decade on the research ethics review board of the National Center for Healthcare Statistics, part of the Centers for Disease Control and Prevention. Most recently, she has served on the ICH E11A Expert Working Group for the development of a harmonized regulatory guideline for pediatric extrapolation in drug development. She also served as Corporate and Clinical Development Advisor for Veralox Therapeutics from 2018 to 2020. Dr. Thackray is a board-certified pediatrician, serving on the faculty of the Children’s National Medical Center and George Washington University School of Medicine and Health Sciences since 2000. She has authored more than 60 peer-reviewed articles and presentations. Dr. Thackray holds a B.S. degree in biological sciences from Stanford University and an M.D. from the George Washington University School of Medicine and Health Sciences. She completed her pediatric residency and chief residency at Children’s National Medical Center, trained in medical genetics at the National Human Genome Research Institute at the National Institutes of Health, and is a Fellow of the American Academy of Pediatrics. Dr. Thackray served on our Board of Directors from September 2019 to May 2021, and she has served on the Board of Directors of Immunogen, Inc. since September 2021.

Alane P. Barnes joined BioCryst in September 2006 as its General Counsel. She was named Corporate Secretary in 2007, was named Vice President, General Counsel & Corporate Secretary in 2011, and has served as our Chief Legal Officer and Corporate Secretary since 2018. She was named as an executive officer in 2013. Ms. Barnes is responsible for all legal affairs of the Company including SEC compliance, corporate governance, IP strategy and management, licensing transactions, government contract negotiations and management and dispute resolution. She graduated magna cum laude from Cumberland School of Law in 1997 and is a member of Curia Honoris, scholar of

merit. Ms. Barnes received her B.S. in Natural Science with a concentration in biology and chemistry from UAB. Prior to joining the Company, Ms. Barnes worked for the UAB Research Foundation where she managed intellectual property, negotiated license transactions and facilitated the emergence of new companies based on university technology. Prior to employment at the UAB Research Foundation, Ms. Barnes practiced corporate law with a prominent law firm in Birmingham, Alabama. Ms. Barnes is currently a board member of the Research Triangle Area Association of Corporate Counsel and regularly speaks at national conferences regarding the pharmaceutical business and at women's success conferences. She is a 2010 graduate of MOMENTUM, an organization geared toward building leadership in women.

Charles K. Gayer joined BioCryst in August 2015 as its Vice President of Global Strategic Marketing and was promoted to Chief Commercial Officer in January 2020. Prior to joining BioCryst, Mr. Gayer held several U.S. and global commercial leadership roles in competitive rare disease categories at Talecris Biotherapeutics, Inc., a biopharmaceutical company that was acquired in 2011 by Grifols, S.A., a multinational pharmaceutical and chemical manufacturer. At Talecris, he led U.S. alpha-1 antitrypsin deficiency marketing and later European sales and marketing. At Grifols, he led the U.S. marketing team for the combined immune globulin portfolio of the two companies. Prior to joining Talecris, he spent six years at GlaxoSmithKline in a range of professional marketing, consumer marketing and sales roles. Mr. Gayer began his career as a strategic consultant for biopharmaceutical companies and also spent three years as a business analyst at rare disease pioneer Genzyme Corporation. Mr. Gayer received his B.A. in Politics from Princeton University and his M.B.A. from the Fuqua School of Business at Duke University.

COMPENSATION DISCUSSION AND ANALYSIS

Philosophy and Overview of Compensation

The Compensation Committee (referred to in this section as the “Committee”) of the Board of Directors has the responsibility for establishing, implementing, and monitoring adherence with the Company’s compensation philosophy. Our goal is to provide a compensation package that attracts, incentivizes, and retains employees and is designed to align employees’ interests with the Company’s corporate strategies and business objectives and the interests of the stockholders. We refer to the individuals identified below as our “Named Executive Officers” for 2022. The Named Executive Officers include our Chief Executive Officer (“CEO”), our Chief Financial Officer (“CFO”), and our next three most highly compensated executive officers serving in such capacity at the end of 2022. The Named Executive Officers also include our Chief Discovery Officer and our Chief Development Officer. Although Dr. Babu and Dr. Sheridan continue to serve the Company in these positions, the Board determined that they are no longer executive officers of the Company, within the meaning of SEC rules, prior to the end of 2022. The compensation of our Named Executive Officers is discussed in this Compensation Discussion and Analysis and included in the Summary Compensation Table. Our Named Executive Officers for 2022 are:

Name	Title
Jon P. Stonehouse	President and Chief Executive Officer
Anthony J. Doyle	Chief Financial Officer and Treasurer
Helen M. Thackray, M.D.	Chief Research & Development Officer
Alane P. Barnes	Chief Legal Officer and Secretary
Charles K. Gayer	Chief Commercial Officer
Yarlagadda S. Babu, Ph.D.	Chief Discovery Officer
William P. Sheridan, MBBS	Chief Development Officer

Our executive compensation program is based on market best practices and is designed to ensure that it is appropriately risk-based and competitive with similar companies in our industry. The Committee’s primary objectives for our executive compensation program are as follows:

- to have a substantial portion of each officer’s compensation contingent upon the Company’s performance as well as upon his or her own level of performance and contribution toward the Company’s performance and long-term strategic goals;
- to reward executives for actions that create short-term and long-term sustainable stockholder value, with a strong focus on Company results;
- to align the interests of our executives with the Company’s corporate strategies, business objectives, and the long-term interests of our stockholders; and
- to attract, incentivize, and retain our executive talent.

Role of the Compensation Committee and Executive Officers

The Committee has the authority to determine the Company’s compensation philosophy, assess overall corporate performance for the year and its impact on the cash bonus pool, equity award pool, and base salary adjustment pool, and to establish compensation for the Company’s executive officers. The Company does not conduct annual individual performance reviews; rather, compensation decisions for the Named Executive Officers have been determined by the Committee based on its assessment of the performance of the Company. The Committee believes this approach effectively aligns the incentives of the Named Executive Officers with those of the Company’s stockholders and reinforces the highly focused corporate strategy of the Company. The CEO makes recommendations to the Committee with respect to executive officer compensation (excluding himself). Neither the CEO nor any other Named Executive Officer participates in the Committee’s final determination of compensation for executive officers.

Role of Compensation Consultants

It is the practice of the Committee to use a compensation consultant to perform an annual competitive compensation analysis of the Company’s overall compensation practices. Since 2015, the Committee has engaged Aon’s Human Capital Solutions practice, a division of Aon plc (“Aon”), formerly known as Radford, as the

Company’s compensation consultant to conduct the overall analysis of the Company’s compensation practices and those of comparable companies in the biotechnology industry. The Committee has determined that there are no conflicts of interest with respect to the engagement of Aon by the Committee.

Under the direction of the Committee, Aon annually conducts an analysis of overall compensation practices, including benchmark comparisons of base salary, annual incentive targets, and long-term equity incentive compensation against a “peer group” of comparable companies discussed in more detail below. The results of this analysis are reviewed by the Committee in connection with its annual compensation decisions, including base salary determinations, annual incentive targets, and long-term equity grants.

Peer Group and the Use of Market Data

While the Company does not establish compensation levels based solely on benchmarking, pay practices at other companies are an important factor that the Committee considers in assessing the reasonableness of compensation and ensuring that our compensation practices are competitive in the marketplace. In order to evaluate the level of compensation for our Named Executive Officers, the Committee, using information provided by Aon, establishes a peer group of publicly-traded, national, and regional companies in the biopharmaceutical and biotechnology industries (the “Peer Group”) that generally:

- are similar to the Company in terms of one or more of the following: size (i.e., employee headcount, revenue, market capitalization, etc.), stage of development for primary products, cash runway, and research and development investment;
- have named executive officer positions that are comparable to the Company’s in terms of breadth, complexity, and scope of responsibilities; and
- compete with the Company for employee talent.

Each Peer Group company participates in the Radford Biotechnology Survey, an Aon survey of executive total compensation for various corporate positions, which survey is widely used among biotechnology companies. Aon analyzes both survey data and compensation information reported in the public filings of the Peer Group companies for the comparative analysis and adjusts the data to reflect the age of the reported information. In September 2021, the Committee approved the 2021 Peer Group. The 2021 Peer Group, which the Committee used when making determinations for our December 2021 long-term equity incentive awards and 2022 base salary and Annual Incentive Plan (“AIP”) target adjustments, emphasized companies that have launched products within the last three years and are scaling. The Committee believed that, following the Company’s transformation into a commercial-stage biotechnology company with the launch of ORLADEYO in December 2020, such companies would reflect a peer group more closely aligned with the Company’s then-current stage of development. The 2021 Peer Group consisted of the following 20 peer companies, which had market capitalization ranging from approximately \$1 billion to \$8 billion and revenue ranging from approximately \$50 million to \$300 million, consistent with the Company’s increase in market capitalization and revenue in 2021 following the launch of ORLADEYO:

- | | | | |
|---------------------------|---------------------------|----------------------------|-----------------------------|
| • ACADIA Pharmaceuticals | • Atara Biotherapeutics | • Dynavax Technologies | • MacroGenics |
| • Acceleron Pharma | • Biohaven Pharmaceutical | • G1 Therapeutics | • Omeros |
| • Agenus | • Blueprint Medicines | • Inmed | • Ultragenyx Pharmaceutical |
| • Amicus Therapeutics | • Cytokinetics | • Intra-Cellular Therapies | • Vir Biotechnology |
| • Apellis Pharmaceuticals | • Dicerna Pharmaceuticals | • KalVista Pharmaceuticals | • Zogenix |

In September 2022, the Committee approved the 2022 Peer Group. The 2022 Peer Group, which the Committee used when making determinations for our December 2022 long-term equity incentive awards and 2023 base salary and AIP target adjustments, continued to emphasize companies that have launched products within the last three years and are scaling. The 2022 Peer Group targeted growing commercial companies, with market capitalization and revenue ranges adjusted to reflect changes in the Company’s market capitalization and revenue during 2022. The 2022 Peer Group consisted of the following 19 peer companies, which had market capitalization ranging from approximately \$800 million to \$7 billion and revenue ranging from approximately \$70 million to \$610 million:

- ACADIA Pharmaceuticals
- Agenus
- Amicus Therapeutics
- Apellis Pharmaceuticals
- Arrowhead Pharmaceuticals
- Biohaven Pharmaceutical
- Blueprint Medicines
- Corcept Therapeutics
- Cytokinetics
- Deciphera Pharmaceuticals
- Dynavax Technologies
- G1 Therapeutics
- Harmony Biosciences
- Insmed
- Intra-Cellular Therapies
- MacroGenics
- PTC Therapeutics
- Ultragenyx Pharmaceutical
- Vir Biotechnology

Role of the 2022 Advisory Vote on Executive Compensation

At our annual meeting in June 2022, our stockholders approved our “say-on-pay” proposal with more than 90% of the votes cast (exclusive of abstentions and broker non-votes) approving our executive compensation policies as described in our 2022 Proxy Statement filed with the SEC on April 25, 2022. The Committee believes that this vote reflected continued stockholder agreement with the Committee’s overall compensation philosophy and actions, and therefore, the Committee continued to apply similar principles in determining the amounts and types of executive compensation for fiscal 2022, with specific compensation decisions to be made each year in consideration of these principles and the Company’s results and performance. In order to align incentives to stockholder interests, the performance of the Named Executive Officers is evaluated based on the Committee’s assessment of the overall performance of the Company. The Committee will continue to consider the outcome of stockholder say-on-pay votes in making future executive compensation decisions.

Elements of Executive Compensation

The Company’s 2022 compensation program for executive officers was primarily comprised of the following elements:

- base salary;
- annual incentive compensation;
- long-term equity incentive awards; and
- other employee benefits.

Base Salary

The Company provides our employees with base salary to compensate them for services rendered during the fiscal year. In determining the base salary amount for each Named Executive Officer, the Committee primarily considers:

- industry experience, knowledge, and qualifications;
- salary levels in effect for comparable positions within the Company’s industry obtained from the Radford Biotechnology Survey; and
- individual performance of the executive and the general performance of the Company.

The Company’s compensation practice is to generally target the competitive 50th percentile for base salary, annual incentive compensation and long-term equity grants. Base salary levels for our Named Executive Officers may fluctuate from the 50th percentile based on each Named Executive Officer’s particular experience, performance and value to the Company. For example, high-performing, experienced Named Executive Officers may be paid at or above the 75th percentile, while newer Named Executive Officers may be paid at a lower percentile. Base salary amounts are typically reviewed annually as part of the Company’s performance review process as well as upon a promotion or other change in responsibility. To assist the Committee in determining appropriate base salary increases, the Company’s compensation consultant provided competitive base salary levels by analyzing the competitive data described in more detail above.

In setting 2022 salaries, consistent with its philosophy for 2021 salaries and given the highly focused strategy of the Company, the Committee did not conduct individual performance reviews but instead continued to assess the Named Executive Officers based primarily on overall corporate performance while also giving consideration to individual contributions to corporate performance. The Committee also considered the market competitiveness of the

Company's current executive officer base salaries compared to the 2021 Peer Group based on the analysis prepared by Aon. This resulted in each Named Executive Officer receiving an increase in base salary for 2022, which generally reflected a market adjustment to the 50th percentile compared to the 2021 Peer Group or a 3.5% increase, whichever is greater:

Name	Approximate Percentage Increase	2022 Base Salary
Jon P. Stonehouse	9.7%	\$640,000
Anthony J. Doyle.....	3.5%	\$507,978
Helen M. Thackray	4.6%	\$554,200
Alane P. Barnes	7.7%	\$457,200
Charles K. Gayer.....	16.2%	\$448,700
Yarlagadda S. Babu	5.2%	\$483,000
William P. Sheridan	3.5%	\$549,171

In setting 2023 salaries, consistent with its philosophy for 2022 salaries and given the highly focused strategy of the Company, the Committee did not conduct individual performance reviews but instead continued to assess the Named Executive Officers based primarily on overall corporate performance while also giving consideration to individual contributions to corporate performance. The Committee also considered the market competitiveness of the Company's current executive officer base salaries compared to the 2022 Peer Group based on the analysis prepared by Aon. This resulted in all of the Named Executive Officers who were serving as executive officers at the time of such determination receiving the following increases in base salary for 2023, which generally reflect adjustments to the 50th percentile compared to the 2022 Peer Group or a 4% increase, whichever is greater; provided, however, that the CEO requested that his base salary not reflect any adjustment above the base 4% increase:

Name	Approximate Percentage Increase	2023 Base Salary
Jon P. Stonehouse	4.0%	\$665,600
Anthony J. Doyle.....	4.0%	\$528,297
Helen M. Thackray	4.0%	\$576,368
Alane P. Barnes	8.4%	\$495,700
Charles K. Gayer.....	10.4%	\$495,300

Annual Incentive Plan Compensation

It is the Committee's objective to have the entirety of each officer's annual incentive program compensation contingent upon the Company's performance based on the achievement of pre-established corporate performance objectives. Annual incentive payments are made pursuant to the AIP, which provides for a target amount of potential incentive awards for each participant thereunder, which is currently expressed as a percentage of annual base salary. In determining the 2022 AIP payouts for each of the Named Executive Officers, the Committee considered overall corporate performance against pre-established corporate objectives for 2022, individual contributions to corporate performance, and Peer Group market data provided by Aon.

The target percentage for each Named Executive Officer was set based on the data described below. Based on performance, the actual payout can range from zero to any amount relative to the target percentage of annual base salary. The overall amount of the AIP pool each performance year is determined by the Committee and is based on its assessment of Company performance against the current year corporate objectives multiplied by the sum of all participants at target performance. The AIP allows the Committee to use its discretion in setting the size of the AIP pool. The Committee may decide that the pool is as low as zero for a year of poor Company performance and may establish a pool that exceeds target for a year of exceptional Company performance.

The Committee annually reviews with Aon the Peer Group data for non-equity incentive compensation and considers other factors intended to align the AIP with the Committee’s pay-for-performance philosophy. The Committee maintained the existing targets for the Named Executive Officers in the 2022 plan year. In December 2022, the Committee approved an increase in the AIP targets for the Named Executive Officers, beginning with the 2023 plan year. This increase is intended to continue the alignment of the interests of our Named Executive Officers with those of the Company and its stockholders, increase the performance-based component of compensation payable to our Named Executive Officers, and provide a more competitive total target cash compensation for our Named Executive Officers, which still remains below market competitive median levels for total cash compensation. The 2022 AIP target for each of Dr. Babu and Dr. Sheridan was 40% of base salary. The 2022 AIP targets for the Named Executive Officers who are continuing executive officers of the Company were, and their 2023 AIP targets are, as follows:

Name	2022 AIP Target (percentage of base salary)	2023 AIP Target
Jon P. Stonehouse	75%	85%
Anthony J. Doyle	40%	60%
Helen M. Thackray	50%	70%
Alane P. Barnes	40%	60%
Charles K. Gayer	40%	60%

At the time the 2022 AIP targets were set, the Committee believed that payout at the target performance level (100 points) was challenging but achievable and that payout above target represented a “stretch” performance goal, but was nevertheless achievable. In order to further tie individual compensation to Company performance, payout to individuals under the AIP is based on Company performance and awards under the AIP are typically settled in cash. All awards are reviewed and approved by the Committee.

The pre-established corporate objectives for 2022 Company performance are described in the table below. However, the table does not include the target levels with respect to the specific quantitative and qualitative objectives as we believe disclosure of such information would result in competitive harm to the Company.

Objective	Description	Points at Target
1	ORLADEYO. Corporate objectives for ORLADEYO included goals to increase ORLADEYO sales and the number of patients on ORLADEYO, expand into additional markets globally, and advance ORLADEYO clinical programs.	35
2	Complement-Mediated Diseases. Corporate objectives for our complement-mediated diseases program included goals to advance the BCX9930 program, advance BCX10013 into a clinical program, and advance discovery candidates in other complement-mediated disease targets.	35
3	Product Portfolio. Corporate objectives for our product portfolio included goals to advance other rare disease candidates through our discovery program.	10
4	Organization. Corporate organizational objectives included targets for recruiting and retaining employees; gather data from employees to obtain a baseline read on Company culture and work to improve communications with employees.	20
		100

In assessing the Company’s performance against the pre-established 2022 objectives in December 2022, the Committee assessed the completion of the corporate objectives as described in the table below. In assessing 2022 Company performance in light of the 2022 objectives, as well as the achievements of the Company, the Committee attributed the values set forth in the table below to the achievement of each of the Company objectives. In consideration of these results, the Committee awarded payouts under the AIP at 100% of target for each recipient.

<u>Objective</u>	<u>Committee Determination</u>	<u>Rationale</u>	<u>Points Awarded</u>
1	Partially Met	<ul style="list-style-type: none"> • Achieved a doubling of ORLADEYO sales from the previous year and increased the number of patients on ORLADEYO, although actual results were below target numbers set for the AIP. • Filed and received approvals for, and priced and launched, ORLADEYO in multiple countries, exceeding the target number of new regulatory filings set for the AIP. • Advanced ORLADEYO clinical programs, although at a slower pace than target. 	30
2	Partially Met	<ul style="list-style-type: none"> • Faced with an unforeseen safety issue in the pivotal study, the team worked to identify its most likely cause and to determine whether there was a path forward for advancement of the BCX9930 program. This resulted in development and implementation of a new plan for the program and the reopening of enrollment in clinical trials with BCX9930. The Company subsequently discontinued the development of BCX9930 for competitive reasons. • Advanced the BCX10013 program in healthy volunteers, although at a slower pace than target. • Advanced pursuits of oral medicines directed at other targets across the classical, lectin and terminal pathways of the complement system, including C2, exceeding the target set for the AIP. 	30
3	Met	<ul style="list-style-type: none"> • Advanced the BCX9250 program in line with the target set for the AIP, prior to its discontinuation in the fourth quarter of 2022 due to competitive reasons and to redirect the investment to other opportunities. • Advanced another rare disease candidate in the development program, also in line with the target set for the AIP. 	10
4	Exceeds	<ul style="list-style-type: none"> • Exceeded recruiting and retention metrics. • Completed a culture assessment that indicated a strong alignment on Company values and culture across the employee base. • Implemented improved communication programs to further enhance culture. 	30
			100

Long-Term Equity Incentive Awards

All of the Named Executive Officers are eligible to participate in the Company’s periodic awards of equity grants under the Company’s Stock Incentive Plan. These awards are designed to:

- create a greater sense of employee ownership;
- enhance the link between creation of stockholder value and long-term employee compensation;
- provide an opportunity for increased equity ownership by the officers, which increases the alignment of their financial interests with those of our stockholders; and
- maintain competitive levels of total compensation.

The Committee has historically granted equity awards to the executive officers on an annual basis. The overall grant pool is established on an annual basis based, in part, on the Committee’s assessment of competitive equity grant

levels by organization level and the number of employees at each level using competitive data provided by Aon based on its analysis of the Company’s current Peer Group. In determining the amount of each grant, the Committee also considers the Company performance, assessed on an annual basis.

Equity Awards Granted in 2022

In setting the levels of long-term equity incentive awards in December 2022, the Committee assessed the Company’s performance against the corporate performance objectives for 2022, as described above under the caption “Annual Incentive Plan Compensation,” and in reviewing the analysis provided by Aon regarding the Company’s 2022 Peer Group equity compensation practices and the number of shares of Common Stock available for grant under the Company’s Stock Incentive Plan, the Committee determined to grant long-term equity incentive awards at a level representing approximately the 75th percentile of comparative companies based on the 2022 Peer Group data provided by Aon, with certain additional long-term equity incentive awards to be granted to selected individuals in light of the particular individual contributions made by such individuals to 2022 Company performance. The Committee further determined that, after evaluating current trends and reviewing the intended purpose of this program, the long-term equity incentive awards for 2022 performance should consist of a mix of stock options and RSUs. In consideration of the foregoing factors, in December 2022, the Committee awarded options and RSUs to the Named Executive Officers as set forth in the table below.

<u>Name</u>	<u>Options (#)</u>	<u>RSUs (#)</u>
Jon P. Stonehouse	595,000	127,500
Anthony J. Doyle	158,500	34,000
Helen M. Thackray	238,000	81,000
Alane P. Barnes	158,500	34,000
Charles K. Gayer	158,500	34,000
Yarlagadda S. Babu	158,500	64,000
William P. Sheridan	158,500	64,000

Each stock option represents the right to purchase one share of Common Stock at the option exercise price (once the option is vested), and each RSU represents the right to receive one share of Common Stock upon vesting of the RSU. The stock options and RSUs granted to the Named Executive Officers in December 2022 vest 25% annually on each of the first four anniversaries of the date of the grant, until fully vested on the fourth anniversary. The stock options expire ten years after the date of the grant. This provides a reasonable timeframe during which the Named Executive Officers can benefit from the appreciation of the Company’s shares. The exercise price of options granted under the Stock Incentive Plan cannot be less than 100% of the fair market value of the underlying stock on the date of grant.

Other Elements of Compensation

In order to attract and retain key talent and pay market levels of compensation, we offer broad-based retirement, health and welfare employee benefits to our eligible employees, including our Named Executive Officers, subject to the terms and conditions of each benefit program. Our Named Executive Officers are eligible to participate in these benefits on the same basis as other full-time employees.

Medical Insurance. The Company makes available to eligible employees and their dependents group health, dental and vision insurance coverage.

Life and Disability Insurance. The Company makes available disability and life insurance at coverage levels based upon the employee’s level of compensation. In addition, as part of Mr. Stonehouse’s employment agreement, he is entitled to have either a \$1 million life insurance policy payable to his beneficiary upon death, or, if there is no policy in place, we are required to pay his beneficiary \$1 million upon his death. An insurance policy was in place at December 31, 2022.

Defined Contribution Plan. The Company offers a retirement plan designed to meet the requirements under Section 401(k) of the Code. The 401(k) plan permits eligible employees to defer up to 100% of their annual eligible compensation, subject to certain limitations imposed by the Code. Employee elective deferrals are immediately vested and non-forfeitable. The Company makes matching contributions equal to the first 5% of the employee elective deferrals, which vest over a period not to exceed six years.

Stock Purchase Plan. The Company sponsors a broad-based employee stock purchase plan (the “ESPP”), designed to meet the requirements under Section 423 of the Code. The ESPP permits employees to purchase Company stock at a discount through payroll deductions. ESPP participants are granted a purchase right to acquire shares of Common Stock at a price that is 85% of the stock price on either the first day of the stock purchase period or the last day of the stock purchase period, whichever is lower. The purchase dates occur on the last business days of January and July of each year. To pay for the shares, each participant may authorize periodic payroll deductions from 1% to 15% of the employee’s cash compensation, subject to certain limitations imposed by the Code. In addition, no employee may purchase more than 3,000 shares in each purchase period and/or \$25,000 in each calendar year. All payroll deductions collected from the participant during the purchase period are automatically applied to the purchase of Common Stock on the dates indicated above provided the participant remains an eligible employee and has not withdrawn from the ESPP prior to the purchase date.

Other Fringe Benefits. With the exception of the commuting expense reimbursements described below and the relocation expenses described below under the caption “Executive Relocation,” the Company makes certain other fringe benefits available to the Named Executive Officers on the same basis as are made available to its other employees, such as tuition reimbursement and payment of professional dues. The aggregate amount of these other fringe benefits was less than \$10,000 for each Named Executive Officer during 2022.

Executive Relocation. The Board has adopted an Executive Relocation Policy (the “Relocation Policy”) for certain new employees of the Company, including executive officers. The Relocation Policy provides for a house hunting trip, temporary living and trips home for up to 90 days, home selling support or direct reimbursement for some selling expenses, moving costs and temporary storage of goods, customary closing expenses on the new home, a miscellaneous allowance of one month’s salary, not to exceed \$5,000, and gross up of all taxable expenses. The Relocation Policy requires 100% repayment of benefits if the employee leaves or is terminated for cause within 12 months from the hire date. The Company did not pay any relocation expenses to Named Executive Officers in 2022.

Policy Regarding Tax Deductibility of Compensation

Section 162(m) of the Code limits our ability to deduct compensation paid to certain of our current and former Named Executive Officers (the covered employees) for tax purposes to \$1 million annually. The application of Section 162(m) is complex and may change with time (with potentially retroactive effect). While the Committee considers the deductibility of awards as one factor in determining executive compensation, the Committee also looks at many other factors in making its decisions and retains the flexibility to grant awards it determines to be consistent with the Company’s overall compensation philosophy, even if the award is not deductible by the Company for tax purposes.

Policy with Respect to Equity Compensation Awards

The Company grants all equity incentive awards based on the fair market value as of the date of grant. The exercise price for stock option grants and similar awards is determined by reference to the last quoted price per share on the Nasdaq Global Select Market at the close of business on the date of grant.

Clawback Policy

In January 2013, our Board implemented a “clawback” policy. The policy provides that in the event of material noncompliance with financial reporting under the securities laws, we may recover (in whole or in part) any performance-based incentive payments and equity-based performance awards received by any of our named executive officers in the three years prior to a material financial restatement, if the Board determines that such executive officer was personally involved in misconduct with respect to material noncompliance that led to the restatement and that such incentive payment or equity-based performance award would have been lower had it been calculated based on the restated results.

Management and the Board continue to monitor developments on Nasdaq’s proposed listing rules relating to clawback policies and will review and modify the policy as necessary to comply with the final Nasdaq listing rules under Exchange Act Rule 10D-1 prior to the effectiveness of such rules.

Risk Assessment of Compensation Programs

Management of the Company, together with the Company's compensation consultant and outside counsel and Compensation Committee, has examined the Company's compensation program and discussed whether any elements of the program created risks that were reasonably likely to have a material adverse effect on the Company. Following this analysis, management concluded that the elements of the Company's compensation program did not create risks that are reasonably likely to have a material adverse effect on the Company. In its analysis, management considered a number of factors, including primarily: (1) the total value of the payments made under the Company's compensation program for the prior year and (2) that any corporate actions that would potentially lead to achievement of corporate performance objectives would require approval by the Company's Board of Directors, which provides a check on the ability of any individual to take risks that could have a material adverse effect on the Company in an effort to achieve a certain performance objective.

COMPENSATION COMMITTEE REPORT

The Compensation Committee reviewed the Compensation Discussion and Analysis and discussed its contents with Company management. Based on such review and discussions, the Committee recommended that the Compensation Discussion and Analysis be included in this Proxy Statement and incorporated by reference into the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2022.

Nancy J. Hutson, Ph.D., Chair of the Committee

Stephen J. Aselage

A. Mabelle Sanders

EXECUTIVE COMPENSATION

2022 Summary Compensation Table

The following table sets forth the total compensation awarded, paid to, or earned by our Named Executive Officers, as specified by Item 402(a)(3) of Regulation S-K.

Name and Principal Position	Year	Salary (\$)	Bonus (\$)	Stock Awards (\$) ⁽¹⁾	Option Awards (\$) ⁽²⁾	Non-Equity Incentive Plan Compensation (\$) ⁽³⁾	All Other Compensation (\$) ⁽⁴⁾	Total (\$)
Jon P. Stonehouse <i>President, Chief Executive Officer and Director</i>	2022	640,000	—	1,355,325	4,482,254	480,000	25,415 ⁽⁵⁾	6,982,994
	2021	583,495	43,762	1,405,890	4,511,089	492,324	24,665	7,061,225
	2020	566,500	—	—	4,916,022	531,094	21,325	6,034,941
Anthony J. Doyle <i>Chief Financial Officer and Treasurer</i>	2022	507,978	—	361,420	1,194,012	203,191	15,250	2,281,851
	2021	490,800	19,632	857,250	1,287,761	220,860	14,500	2,890,803
	2020	345,455	50,000	—	3,468,225	240,000	14,250	4,117,930
Helen M. Thackray, M.D. <i>Chief R&D Officer</i>	2022	554,200	—	861,030	1,792,902	277,100	12,700	3,497,932
	2021	425,125	236,500	1,519,920	4,395,101	298,125	6,625	6,881,396
Alane P. Barnes ⁽⁶⁾ <i>Chief Legal Officer and Corporate Secretary</i>	2022	457,200	—	361,420	1,194,012	182,880	15,250	2,210,762
Charles K. Gayer ⁽⁶⁾ <i>Chief Commercial Officer</i>	2022	448,700	—	361,420	1,194,012	179,480	15,250	2,198,862
	2021	483,000	—	680,320	1,194,012	193,200	15,250	2,565,782
	2020	458,945	18,358	400,050	1,287,761	206,525	14,500	2,386,139
Yarlagadda S. Babu, Ph.D. ⁽⁷⁾ <i>Chief Discovery Officer</i>	2022	445,578	—	—	1,582,168	222,789	14,250	2,264,785
	2021	549,171	—	680,320	1,194,012	219,668	15,250	2,658,421
	2020	530,600	21,224	400,050	1,287,761	238,770	52,826	2,531,231
William P. Sheridan, MBBS ⁽⁷⁾ <i>Chief Development Officer</i>	2022	515,146	—	—	1,892,951	257,573	14,250	2,679,920
	2021	515,146	—	—	1,892,951	257,573	14,250	2,679,920

- (1) For 2022, these amounts reflect the aggregate grant date fair value, computed in accordance with FASB ASC Topic 718, of RSUs granted pursuant to the Stock Incentive Plan for the fiscal year ended December 31, 2022. Assumptions used in the calculation of these amounts are included in Note 12 to the Company's audited consolidated financial statements for the year ended December 31, 2022, which is included in the Company's Annual Report on Form 10-K filed with the SEC on February 27, 2023.
- (2) For 2022, these amounts reflect the aggregate grant date fair value, computed in accordance with FASB ASC Topic 718, of stock option awards granted pursuant to the Stock Incentive Plan. Assumptions used in the calculation of these amounts are included in Note 12 to the Company's audited consolidated financial statements for the year ended December 31, 2022, which is included in the Company's Annual Report on Form 10-K filed with the SEC on February 27, 2022.
- (3) Represents payments earned under the AIP. Values shown reflect the full calculated payout of the incentive awards under the AIP.
- (4) Except as otherwise noted, the amounts shown reflect the Company contribution for the executive to his or her 401(k) plan.
- (5) Consists of Company contributions to the 401(k) plan and life insurance premiums described above in the Compensation Discussion and Analysis under the caption "Other Elements of Compensation—Life and Disability Insurance." For 2022, such amounts were \$15,250 and \$10,165, respectively.
- (6) The executive was not a named executive officer in 2020 or 2021.
- (7) Although Dr. Babu and Dr. Sheridan continue to serve the Company as Chief Discovery Officer and Chief Development Officer, respectively, the Board determined prior to the end of 2022 that Dr. Babu and Dr. Sheridan are no longer executive officers within the meaning of SEC rules. Information regarding their compensation is included in this Proxy Statement pursuant to Item 402(a)(3)(iv) of Regulation S-K.

Grants of Plan-Based Awards in 2022

The following table provides information about plan-based awards granted during 2022 to our Named Executive Officers.

Name	Grant Date	Compensation Committee Action Date	Estimated Future Payments Under Non-Equity Incentive Plan Awards				All Other Stock Awards: Number of Shares or Units (#) ⁽²⁾	All Other Option Awards: Number of Securities Underlying Options (#) ⁽³⁾	Exercise or Base Price of Option Awards (\$/Sh) ⁽⁴⁾	Grant Date Fair Value of Stock and Option Awards (\$) ⁽⁵⁾
			Threshold (\$)	Target (\$) ⁽¹⁾	Maximum (\$)					
Jon P. Stonehouse	12/19/22	12/18/22	—	—	—	—	595,000	10.63	4,482,254	
	12/19/22	12/18/22	—	—	—	127,500	—	—	1,355,325	
	—	—	—	480,000	—	—	—	—	—	
Anthony J. Doyle.	12/19/22	12/18/22	—	—	—	—	158,500	10.63	1,194,012	
	12/19/22	12/18/22	—	—	—	34,000	—	—	361,420	
	—	—	—	203,191	—	—	—	—	—	
Helen M. Thackray, M.D. . . .	12/19/22	12/18/22	—	—	—	—	238,000	10.63	1,792,902	
	12/19/22	12/18/22	—	—	—	81,000	—	—	861,030	
	—	—	—	277,100	—	—	—	—	—	
Alane P. Barnes	12/19/22	12/18/22	—	—	—	—	158,500	10.63	1,194,012	
	12/19/22	12/18/22	—	—	—	34,000	—	—	361,420	
	—	—	—	182,880	—	—	—	—	—	
Charles K. Gayer	12/19/22	12/18/22	—	—	—	—	158,500	10.63	1,194,012	
	12/19/22	12/18/22	—	—	—	34,000	—	—	361,420	
	—	—	—	179,480	—	—	—	—	—	
Yarlagadda S. Babu, Ph.D. . .	12/19/22	12/18/22	—	—	—	—	158,500	10.63	1,194,012	
	12/19/22	12/18/22	—	—	—	64,000	—	—	680,320	
	—	—	—	193,200	—	—	—	—	—	
William P. Sheridan, MBBS .	12/19/22	12/18/22	—	—	—	—	158,500	10.63	1,194,012	
	12/19/22	12/18/22	—	—	—	64,000	—	—	680,320	
	—	—	—	219,668	—	—	—	—	—	

- (1) Represents possible payouts under our AIP. The amount shown in the “Target” column represents the incentive payment that will be earned if performance is assessed at target. There is no specific “threshold” amount payable for minimal performance under the AIP or “maximum” amount payable for performance in excess of target under the AIP. Payout could be zero if corporate objectives are not met. In addition, the Committee has discretion to establish a payout that exceeds the applicable target percentage of annual base salary if warranted by Company performance.
- (2) Represents RSUs that vest 25% on each of the first four anniversaries of the grant date until fully vested after four years, subject to the executive’s continued service to the Company.
- (3) Stock options vest 25% on each of the first four anniversaries of the grant date until fully vested after four years, and they have a term of ten years, subject in each case to the executive’s continued service to the Company.
- (4) The exercise price is the closing market price of our Common Stock on the grant date.
- (5) See Notes (1) and (2) to the “2022 Summary Compensation Table” above for more information about the assumptions used to determine these amounts.

Outstanding Equity Awards at December 31, 2022

The following table summarizes the equity awards we have granted to our Named Executive Officers that were outstanding as of December 31, 2022.

Name	Option Awards					Stock Awards	
	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable ⁽¹⁾	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options (#)	Option Exercise Price (\$) ⁽²⁾	Option Expiration Date ⁽³⁾	Number of Shares or Units of Stock that Have Not Vested ⁽⁴⁾	Market Value of Shares or Units of Stock that Have Not Vested (\$) ⁽⁵⁾
Jon P. Stonehouse	100,000	—	—	5.45	8/8/2023	—	—
	84,000	—	—	10.80	1/20/2024	—	—
	115,345	—	20,355 ⁽⁶⁾	12.16	1/1/2025	—	—
	162,950	—	—	10.82	12/29/2025	—	—
	337,050	—	—	3.22	5/23/2026	—	—
	500,000	—	—	5.51	2/27/2027	—	—
	300,000	—	—	5.04	12/20/2027	—	—
	675,000	—	—	7.06	12/20/2028	—	—
	235,875	78,625	—	3.23	12/17/2029	—	—
	314,500	—	—	3.23	12/17/2029	—	—
	435,000	435,000	—	8.31	12/15/2030	—	—
	143,625	430,875	—	11.43	12/14/2031	—	—
	—	595,000	—	10.63	12/19/2032	—	—
—	—	—	—	—	219,750	2,522,730	
Anthony J. Doyle	333,500 ⁽⁷⁾	266,500 ⁽⁷⁾	—	3.91	4/30/2030	—	—
	166,250	166,250	—	8.31	12/15/2030	—	—
	41,000	123,000	—	11.43	12/14/2031	—	—
	—	158,500	—	10.63	12/19/2032	—	—
—	—	—	—	—	90,250	1,036,070	
Helen M. Thackray	40,000	—	—	2.86	9/20/29	—	—
	40,000	—	—	5.41	5/12/30	—	—
	100,000	300,000	—	10.17	3/31/2031	—	—
	51,250	153,750	—	11.43	12/14/2031	—	—
	—	238,000	—	10.63	12/19/2032	—	—
—	—	—	—	—	189,000	2,169,720	
Alane P. Barnes	18,000	—	—	10.80	1/20/2024	—	—
	52,700	—	9,300 ⁽⁶⁾	11.13	12/22/2024	—	—
	23,200	—	—	12.16	1/1/2025	—	—
	43,997	—	—	10.82	12/29/2025	—	—
	91,004	—	—	3.22	5/23/2026	—	—
	150,000	—	—	5.51	2/27/2027	—	—
	62,500	—	—	5.04	12/20/2027	—	—
	190,000	—	—	7.06	12/20/2028	—	—
	142,500	47,500	—	3.23	12/17/2029	—	—
	140,000	140,000	—	8.31	12/15/2030	—	—
	41,000	123,000	—	11.43	12/14/2031	—	—
	—	158,500	—	10.63	12/19/2032	—	—
	—	—	—	—	—	75,250	863,870
Charles K. Gayer	75,000	—	—	10.82	8/25/2025	—	—
	6,837	—	—	10.82	12/29/2025	—	—
	14,142	—	—	3.22	5/32/2026	—	—
	50,000	—	—	5.51	2/27/2027	—	—
	27,500	—	—	5.04	12/20/2027	—	—
	65,000	—	—	7.06	12/20/2028	—	—
	79,500	26,500	—	3.23	12/17/2029	—	—
	95,000	95,000	—	8.31	12/15/2030	—	—
	41,000	123,000	—	11.43	12/14/2031	—	—
	—	158,500	—	10.63	12/19/2032	—	—
—	—	—	—	—	94,000	1,079,120	

Name	Option Awards					Stock Awards	
	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable ⁽¹⁾	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Options (#)	Option Exercise Price (\$) ⁽²⁾	Option Expiration Date ⁽³⁾	Number of Shares or Units of Stock that Have Not Vested ⁽⁴⁾	Market Value of Shares or Units of Stock that Have Not Vested (\$) ⁽⁵⁾
Yarlagadda S. Babu	68,000	—	—	5.45	8/8/2023	—	—
	35,000	—	—	10.80	1/20/2024	—	—
	76,500	—	13,500 ⁽⁶⁾	11.13	12/22/2024	—	—
	42,400	—	—	12.16	1/1/2025	—	—
	62,573	—	—	10.82	12/29/2025	—	—
	129,427	—	—	3.22	5/23/2026	—	—
	175,000	—	—	5.51	2/27/2027	—	—
	100,000	—	—	5.04	12/20/2027	—	—
	235,000	—	—	7.06	12/20/2028	—	—
	168,750	56,250	—	3.23	12/17/2029	—	—
	140,000	140,000	—	8.31	12/15/2030	—	—
	41,000	123,000	—	11.43	12/14/2031	—	—
	—	158,500	—	10.63	12/19/2032	—	—
	—	—	—	—	—	90,250	1,036,070
William P. Sheridan	17,000	—	—	5.45	8/8/2023	—	—
	35,000	—	—	10.80	1/20/2024	—	—
	96,050	—	16,950 ⁽⁶⁾	11.13	12/22/2024	—	—
	52,000	—	—	12.16	1/1/2025	—	—
	71,698	—	—	10.82	12/29/2025	—	—
	18,148	—	—	5.51	2/27/2027	—	—
	100,000	—	—	5.04	12/20/2027	—	—
	170,000	—	—	7.06	12/20/2028	—	—
	52,000	44,000	—	3.23	12/17/2029	—	—
	167,500	167,500	—	8.31	12/15/2030	—	—
	41,000	123,000	—	11.43	12/14/2031	—	—
	—	158,500	—	10.63	12/19/2032	—	—
	—	—	—	—	—	90,250	1,036,070

- (1) Except as otherwise noted, stock options vest 25% on each of the first four anniversaries of the grant date until fully vested after four years.
- (2) The option exercise price is equal to the closing price of our Common Stock as reported by Nasdaq on the grant date.
- (3) Except as otherwise noted, options expire ten years after the grant date.
- (4) RSUs vest 25% on each of the first four anniversaries of the grant date until fully vested after four years.
- (5) Based upon a stock price of \$11.48 per share, which was the closing price of our Common Stock as reported by Nasdaq on December 30, 2022 (the last trading day of our fiscal year ended December 31, 2022), multiplied by the number of shares of Common Stock subject to RSUs that had not yet vested.
- (6) Special performance stock options subject to vesting upon successful completion of specific performance objectives described under the caption “2014 Special Performance Award” in the Company’s 2015 Proxy Statement filed on April 10, 2015.
- (7) Options granted under the Inducement Equity Incentive Plan and the Stock Incentive Plan that vested 1/3 on the first anniversary of the grant date, with the remainder vesting in three equal installments on the second, third, and fourth anniversaries of the grant date.

2022 Option Exercises and Stock Vested

The following table provides information on shares acquired during 2022 by our Named Executive Officers upon the exercise of stock options and the vesting of RSUs.

Name	Option Awards		Stock Awards	
	Number of Shares Acquired on Exercise (#)	Value Realized on Exercise (\$) ⁽¹⁾	Number of Shares Acquired on Vesting	Value Realized on Vesting (\$) ⁽²⁾
Jon P. Stonehouse	481,573	5,326,206	30,750	343,478
Anthony J. Doyle	—	—	18,750	209,438
Helen M. Thackray	—	—	36,000	529,370
Alane P. Barnes	—	—	13,750	153,588
Charles K. Gayer	—	—	20,000	223,400
Yarlagadda S. Babu	100,000	1,245,703	8,750	97,738
William P. Sheridan	550,154	4,401,140	8,750	97,738

(1) Value is calculated by multiplying (a) the number of shares acquired upon exercise by (b) the difference between the market price of our Common Stock at the time of exercise (or, for non-cash exercises, the closing price of our Common Stock as reported by Nasdaq on the date of exercise) and the applicable exercise price.

(2) Value is calculated by multiplying (a) the number of shares acquired upon vesting of RSUs by (b) the closing price of our Common Stock as reported by Nasdaq on the applicable vesting date.

Potential Payments upon Termination or Change in Control

The following table sets forth potential payments payable to our Named Executive Officers upon termination of employment. The amounts include compensation payable upon termination without cause, constructive termination, termination following a change in control, and termination in the event of disability or death. None of the Named Executive Officers are entitled to any payments upon termination with cause. The effect of a Named Executive Officer's termination of employment on annual incentive awards under the AIP is subject to determination by the Compensation Committee in its sole discretion. Absent a contrary determination by the Compensation Committee or provisions to the contrary in an employment agreement, all awards under the AIP are forfeited if the executive terminates employment with the Company before the annual incentive awards are paid. The Compensation Committee may, in its discretion, revise, amend, or add to the benefits if it deems it advisable. The amounts shown assume the stock options and RSUs are valued at their last intrinsic value in fiscal 2022 and that termination is effective December 31, 2022, and thus include amounts earned through such time and are estimates of the amounts which would be paid out to the executives upon their termination. The actual amounts to be paid out can only be determined at the time of such executive's separation from the Company. The amounts shown in the table do not include accrued vacation, vested amounts payable under the Company's 401(k) plan, any accrued but unpaid bonus or base salary, benefits under the Company's disability benefit program or life insurance policies, or potential compensation recognized upon exercise of vested options as disclosed in the Outstanding Equity Awards table above.

Name	Benefit	Termination				Change in Control with no Change in Employment Status (\$) ⁽²⁾	Change in Control and Termination (\$) ⁽³⁾
		Without Cause (\$)	Constructive Termination (\$)	Disability (\$)	Death (\$) ⁽¹⁾		
Jon P. Stonehouse	Base salary	1,280,000	1,280,000	1,280,000	—	—	1,280,000
	Target bonus ⁽⁴⁾	960,000	960,000	960,000	—	—	960,000
	Health care premiums ⁽⁵⁾	20,916	20,916	20,916	—	—	20,916
	Equity vesting acceleration ⁽⁶⁾	—	—	—	5,077,630	—	5,077,630
	Total	2,260,916	2,260,916	2,260,916	5,077,630	—	7,338,546
Anthony J. Doyle	Base salary	507,978	507,978	—	—	—	507,978
	Target bonus ⁽⁴⁾	203,191	203,191	—	—	—	203,191
	Health care premiums ⁽⁵⁾	29,691	29,691	—	—	—	29,691
	Equity vesting acceleration ⁽⁶⁾	—	—	—	—	—	3,721,363
	Total	740,860	740,860	—	—	—	4,462,223

Name	Benefit	Termination				Change in Control with no	Change in Control and Termination (\$) ⁽³⁾
		Without Cause (\$)	Constructive Termination (\$)	Disability (\$)	Death (\$) ⁽¹⁾	Change in Employment Status (\$) ⁽²⁾	
Helen M. Thackray . . .	Base salary	554,200	554,200	—	—	—	554,200
	Target bonus ⁽⁴⁾	277,100	277,100	—	—	—	277,100
	Health care premiums ⁽⁵⁾	29,691	29,691	—	—	—	29,691
	Equity vesting acceleration ⁽⁶⁾	—	—	—	—	—	3,962,500
	Total	860,991	860,991	—	—	—	4,832,491
Alane P. Barnes	Base salary	457,200	457,200	—	—	—	457,200
	Target bonus ⁽⁴⁾	182,880	182,880	—	—	—	182,880
	Health care premiums ⁽⁵⁾	29,691	29,691	—	—	—	29,691
	Equity vesting acceleration ⁽⁶⁾	—	—	—	1,843,675	—	1,843,675
	Total	669,771	669,771	—	1,843,675	—	2,513,446
Charles K. Gayer	Base salary	448,700	448,700	—	—	—	448,700
	Target bonus ⁽⁴⁾	179,480	179,480	—	—	—	179,480
	Health care premiums ⁽⁵⁾	29,691	29,691	—	—	—	29,691
	Equity vesting acceleration ⁽⁶⁾	—	—	—	1,739,770	—	1,739,770
	Total	657,871	657,871	—	1,739,770	—	2,397,641
Yarlagadda S. Babu . . .	Base salary	483,000	483,000	—	—	—	483,000
	Target bonus ⁽⁴⁾	193,200	193,200	—	—	—	193,200
	Health care premiums ⁽⁵⁾	29,691	29,691	—	—	—	29,691
	Equity vesting acceleration ⁽⁶⁾	—	—	—	2,089,533	—	2,089,533
	Total	705,891	705,891	—	2,089,533	—	2,795,424
William P. Sheridan . . .	Base salary	549,171	549,171	—	—	—	549,171
	Target bonus ⁽⁴⁾	219,668	219,668	—	—	—	219,668
	Health care premiums ⁽⁵⁾	20,916	20,916	—	—	—	20,916
	Equity vesting acceleration ⁽⁶⁾	—	—	—	2,076,853	—	2,076,853
	Total	789,755	789,755	—	2,076,853	—	2,866,608

- (1) Pursuant to the terms of the Company's Stock Incentive Plan, acceleration of unvested stock options occurs in the event of death only after five years of service.
- (2) Relates to acceleration of the unvested special performance stock options described in Note (6) to the "Outstanding Equity Awards at December 31, 2022" table above and assumes that the applicable change in control event would require stockholder approval upon which such outstanding stock options will not vest, as described under "Equity Vesting Acceleration—Stock Options" below. If the applicable change in control event did not require stockholder approval or the acquiring company did not assume the stock options, then the following amounts reflect the value of the stock options that would accelerate upon such change in control event: (i) for Mr. Stonehouse, \$0; (ii) for Mr. Doyle, \$0; (iii) for Dr. Thackray, \$0; (iv) for Ms. Barnes, \$3,255; (v) for Mr. Gayer, \$0; (vi) for Dr. Babu, \$4,725; and (vii) for Dr. Sheridan, \$5,932.
- (3) Benefits for Mr. Stonehouse are triggered if his employment is terminated without Cause or as a result of Disability or Constructive Termination following a Change of Control. Benefits for the other Named Executive Officers are triggered if their employment is terminated without Cause or if they are Constructively Terminated within six months following a Change of Control. The employment agreement for Mr. Stonehouse provides that if any benefit would be subject to excise tax imposed by section 4999 of the Code or any interest or penalties with respect to such excise tax, the employee shall be entitled to the greater of the employee's net after tax benefit of the entire payment assuming the payment is subject to section 4999 (which payment would be subject to the excise tax) and the employee's net after tax benefit of the payments after the payments are reduced just to the point that there is no section 4999 excise tax. The Company will not pay the excise tax if the payments are subject to section 4999.
- (4) Represents AIP awards at the target percentage for each individual (except with respect to Mr. Stonehouse, who, as described below, receives twice the AIP award at the target percentage in the event of termination without Cause, Constructive Termination, or Disability).
- (5) Represents 12 months of premiums under COBRA.
- (6) Based on the closing price of the Company's stock as of December 30, 2022 (the last trading day of the year ended December 31, 2022).

Employment Agreement Terms

Mr. Stonehouse

Pursuant to the terms of his employment letter agreement, in the event of termination by the Company without Cause, upon non-renewal of the term of the agreement by the Company, as a result of a Constructive Termination, or by the Company as a result of a Disability, Mr. Stonehouse is entitled to severance equal to the product of (x) two and (y) the sum of (i) his annual base salary in effect immediately prior to the effective date of the termination and (ii) his target bonus in effect for the fiscal year of termination, to be paid in equal installments over the regularly scheduled payroll periods of the Company for the two years following the effective date of termination. The Company will also pay the monthly premium for health insurance coverage under COBRA until the earlier of 12 months following the effective date of termination or the date upon which COBRA continuation coverage ceases. If there is a Change of Control, all equity awards granted to Mr. Stonehouse prior to May 23, 2016 vest in full, and if his employment is terminated without Cause or as a result of Disability or Constructive Termination following the Change of Control, he shall receive the benefits described above. The receipt of such benefits is subject to his signing and not revoking a release of any and all claims against the Company, its officers, directors and employees, resigning from the Board, and returning to the Company all of its property and confidential information. To the extent required, the payments described in this paragraph may be delayed for the minimum period and in the minimum manner necessary to avoid the imposition of the tax required by Section 409A of the Code.

For purposes of Mr. Stonehouse's letter agreement:

- “Cause” is defined as: determination by the Board that his employment be terminated for any of the following reasons: (i) a violation of a federal or state law or regulation that materially and adversely impacts the business of the Company; (ii) conviction or plea of no contest to a felony under the laws of the United States or any state; (iii) a breach of the terms of any confidentiality, invention assignment or proprietary information agreement with the Company or with a former employer that materially and adversely impacts the Company; (iv) fraud or misappropriation of property belonging to the Company or its affiliates; or (v) willful misconduct or gross negligence in connection with the performance of his duties; provided, however, that no act or failure to act shall be considered “willful” unless it is done, or omitted to be done in bad faith or without reasonable belief that his action or omission was in the best interests of the Company.
- “Constructive Termination” is defined as resignation of employment within 30 days of the occurrence of any of: (i) a reduction in his responsibilities or any change in his status or title with regard to his employment; (ii) a reduction in his base salary, unless such reduction occurs prior to a Change of Control (as defined below) and is made in connection with a fiscal downturn of the Company pursuant to which the base salaries of all executive officers of the Company are reduced by a comparable percentage; or (iii) a relocation of his principal office to a location more than 50 miles from the location of his then-current principal office.
- “Change of Control” is defined as (i) a merger or consolidation in which the Company is not the surviving entity, except for a transaction the principal purpose of which is to change the State of the Company's incorporation; (ii) the sale, transfer or other disposition of all or substantially all of the assets of the Company in liquidation or dissolution of the Company; (iii) any reverse merger in which the Company is the surviving entity but in which securities possessing more than 50% of the total combined voting power of the Company's outstanding securities are transferred to a person or persons different from the persons holding those securities immediately prior to such merger; or (iv) any person or related group of persons (other than the Company or a person that directly or indirectly controls, is controlled by, or is under common control with, the Company) directly or indirectly acquires beneficial ownership (within the meaning of Rule 13d-3 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”)) of securities possessing more than 50% of the total combined voting power of the Company's outstanding securities pursuant to a tender or exchange offer made directly to the Company's stockholders.
- “Disability” means the inability to perform his duties under the agreement by reason of physical or mental incapacity for 90 days, whether consecutive or not, during any consecutive 12-month period.

Other Named Executive Officers

Pursuant to the terms of their employment letter agreements, in the event of termination by the Company without Cause, or Constructive Termination, Mr. Doyle, Dr. Thackray, Ms. Barnes, Mr. Gayer, and Drs. Babu and Sheridan are entitled to (i) continuation of base salary for one year beyond the effective termination date, payable in accordance

with the Company's regular payroll practices; (ii) payment of one times the executive's annual target bonus under the AIP in effect for the fiscal year in which his or her termination date occurs, payable in equal installments over the regularly scheduled payroll periods of the Company for the one year following the effective date of termination; and (iii) if the executive elects to continue health insurance coverage under COBRA, the monthly premium for such coverage until the earlier of 12 months following the effective date of termination or the date upon which the executive commences employment with another entity. In the event the executive's employment is terminated without Cause or the executive is Constructively Terminated within six months of a Change of Control, he or she is entitled to the benefits described in the table above. The receipt of such benefits is conditioned on the executive signing and not revoking a release of any and all claims, in a form prescribed by the Company and returning to the Company all of its property and confidential information. To the extent required, the payments described in this paragraph may be delayed for the minimum period and in the minimum manner necessary to avoid the imposition of the tax required by Section 409A of the Code.

For purposes of the agreements of Mr. Doyle, Dr. Thackray, Ms. Barnes, Mr. Gayer, and Drs. Babu and Sheridan:

- “*Cause*” means a determination by the Board that his or her employment be terminated for any of the following reasons: (i) failure or refusal to comply in any material respect with lawful policies, standards or regulations of Company; (ii) a violation of a federal or state law or regulation applicable to the business of the Company; (iii) conviction or plea of no contest to a felony under the laws of the United States or any State; (iv) fraud or misappropriation of property belonging to the Company or its affiliates; (v) a breach in any material respect of the terms of any confidentiality, invention assignment or proprietary information agreement with the Company or with a former employer; (vi) failure to satisfactorily perform his or her duties after having received written notice of such failure and at least 30 days to cure such failure; or (vii) misconduct or gross negligence in connection with the performance of his or her duties.
- “*Constructive Termination*” means a resignation of employment within 30 days of the occurrence of any of the following events which occurs within six months following a Change of Control (as defined below): (i) a material reduction in his or her responsibilities; (ii) a material reduction in his or her base salary, unless such reduction is comparable in percentage to, and is part of, a reduction in the base salary of all executive officers of the Company; or (iii) a relocation of his or her principal office to a location more than 50 miles from the location of his or her principal office immediately preceding a Change of Control.
- “*Change of Control*” means (i) the sale, transfer, or other disposition of all or substantially all of the assets of the Company in liquidation or dissolution of the Company; (ii) the consummation of a merger or consolidation of the Company with any other corporation or other entity, other than (I) a merger or consolidation (A) which results in the voting securities of the Company outstanding immediately prior to such merger or consolidation continuing to represent 50% or more of the combined voting power of the surviving entity or the ultimate parent thereof outstanding immediately after such merger or consolidation and (B) immediately following which the individuals who comprise the Board immediately prior thereto constitute 50% or more of the board of directors of the surviving entity or, if the Company or the surviving entity is then a subsidiary, the ultimate parent thereof, or (II) a merger or consolidation effected to implement a recapitalization of the Company (or similar transaction) in which no person is or becomes the beneficial owner (within the meaning of Rule 13d-3 of the Exchange Act), directly or indirectly, of securities of the Company (not including in the securities beneficially owned by such person any securities acquired directly from the Company or its affiliates) representing more than 50% of the combined voting power of the Company's then outstanding securities; (iii) any person or related group of persons (other than the Company or a person that directly or indirectly controls, is controlled by, or is under common control with the Company) directly or indirectly acquires beneficial ownership (within the meaning of Rule 13d-3 of the Exchange Act) of securities possessing more than 50% of the total combined voting power of the Company's outstanding securities pursuant to a tender or exchange offer made directly to the Company's stockholders; or (iv) a change in the composition of the Board over a period of 12 consecutive months such that a majority of the Board members (rounded up to the next whole number) ceases to be comprised of individuals who either (A) have been Board members continuously since the beginning of such period or (B) have been elected or nominated for election as Board members during such period by at least two-thirds of the Board members described in clause (A) who were still in office at the time such election or nomination was approved by the Board.

Equity Vesting Acceleration

Stock Options

In the event of termination of service other than on account of death or disability, each executive has three months to exercise any options exercisable prior to the termination in service. In the event of permanent disability, the executive will be able to exercise all outstanding options vested at the time of such disability in their entirety within the earlier of 12 months or the expiration of the option. In the event of death, the executor of the executive's estate will be able to exercise all of the outstanding options in their entirety within the earlier of 12 months or the expiration of the option. If the executive has completed five years of service, all outstanding options vest in their entirety at death, but with less than five years of service, only the portion of the option that was exercisable at the time of death will be exercisable during the 12-month period. If the executive is no longer an employee of the Company, but prior to the last date of employment continues service with the Company in another capacity, such as service as a consultant or service as a member of the Board of Directors, his or her outstanding options will continue to vest and be exercisable until three months after separation from such service or expiration of the option.

With respect to stock options granted prior to May 23, 2016, the standard stock option terms provide for full acceleration of vesting upon a change in control not approved by stockholders, such as: (i) acquisition of over 50% of the combined voting power of the Company and (ii) change in composition of the Board over a period of 24 consecutive months or less such that a majority of the Board members ceases as a result of one or more contested elections. In the event of an acquisition such as: (i) a merger or consolidation, (ii) the sale, transfer or other disposition of all or substantially all of the assets of the Company in liquidation or dissolution of the Company, or (iii) any reverse merger in which the Company is the surviving entity but in which securities possessing more than 50% of the total combined voting power of the Company's outstanding securities are transferred to a person or persons different from the persons holding those securities immediately prior to such merger, then the unvested options of the optionees granted prior to May 23, 2016 are accelerated unless the options are assumed by the acquiring company. However, all other options are subject to "double-trigger" vesting if the options are assumed after a change in control, in which case accelerated vesting will apply only if the optionee's service is terminated by us without "cause" or by the optionee due to a "constructive termination" within 90 days preceding or two years following the change in control. If the options are not assumed in connection with the change in control, they will fully vest upon the change in control.

RSUs

In the event of termination of service, outstanding RSUs will automatically terminate and no shares of Common Stock will be issued in satisfaction of those awards. However, the Compensation Committee has discretionary authority to issue shares of Common Stock in satisfaction of one or more outstanding RSUs as to which the designated service requirement is not attained. Such authority may be exercised at any time, whether before or after the executive's termination of service.

CEO Pay Ratio

The following is a reasonable estimate, prepared under applicable SEC rules, of the ratio of the annual total compensation of our CEO to the median of the annual total compensation of our other employees. We determined our median employee based on 2022 annual base salary and 2022 cash incentive awards for each of our 530 employees (excluding the CEO) as of December 31, 2022. Of these 530 employees, 459 employees are located in the United States and 71 employees are located outside the United States. No foreign employees were excluded in the process of identifying our median employee. For employees paid other than in U.S. dollars, we converted their compensation to U.S. dollars using the applicable yearly average exchange rates published by the Internal Revenue Service, and we did not make any cost-of-living adjustment.

The annual total compensation of our median employee (other than the CEO) for 2022, calculated in accordance with Item 402(c)(2)(x) under Regulation S-K, was \$258,689. As disclosed in the Summary Compensation Table included in this Proxy Statement, our CEO's annual total compensation for 2022 was \$6,982,994. Based on the foregoing, the ratio of the 2022 annual total compensation of our CEO to the median of the annual total compensation of all other employees was 27 to 1. Given the different methodologies that various public companies use to determine an estimate of their pay ratio, the estimated ratio reported above should not be used as a basis for comparison between companies.

Pay Versus Performance

As required by Section 953(a) of the Dodd-Frank Act, and Item 402(v) of Regulation S-K, we are providing the following information about the relationship between executive “compensation actually paid” and certain financial performance of the Company. For further information concerning the Company’s pay-for-performance philosophy and how the Company aligns executive compensation with the Company’s performance, refer to the “Compensation Discussion and Analysis” section above.

Year	Summary Compensation Table Total for PEO (\$) ⁽¹⁾	Compensation Actually Paid to PEO (\$) ⁽²⁾	Average Summary Compensation Table Total for Non-PEO NEOs (\$) ⁽³⁾	Average Compensation Actually Paid to Non-PEO NEOs (\$) ⁽⁴⁾	Value of Initial Fixed \$100 Investment Based On:			ORLADEYO Sales (\$ in thousands) ⁽⁸⁾
					Total Stockholder Return (\$) ⁽⁵⁾	Peer Group Total Stockholder Return (\$) ⁽⁶⁾	Net Income (Loss) (\$ in thousands) ⁽⁷⁾	
2022	6,982,994	4,009,070	2,568,935	1,452,633	332.75	153.08	(247,116)	249,689
2021	7,061,225	17,053,230	4,523,739	7,254,142	401.45	137.47	(184,062)	121,865
2020	6,034,941	10,853,629	2,353,552	3,630,213	215.94	110.52	(182,814)	133

- (1) These amounts represent the amounts reported for our CEO, Jon P. Stonehouse, in the “Total” column of the Summary Compensation Table in each applicable year.
- (2) These amounts represent the amount of “compensation actually paid” to Mr. Stonehouse, as computed in accordance with Item 402(v) of Regulation S-K, and do not reflect the total compensation actually realized or received by Mr. Stonehouse. In accordance with these rules, these amounts reflect total compensation as set forth in the Summary Compensation Table for each year, adjusted as shown below. Equity values are calculated in accordance with FASB ASC Topic 718, and the valuation assumptions used to calculate fair values did not materially differ from those disclosed at the time of grant.

Compensation Actually Paid to PEO	2022	2021	2020
Summary Compensation Table Total	6,982,994	7,061,225	6,034,941
(Less), value of “Stock Awards” and “Option Awards” reported in Summary Compensation Table	(5,837,579)	(5,916,979)	(4,916,022)
Plus, year-end fair value of outstanding and unvested equity awards granted in the year	6,400,540	7,409,280	4,291,310
Plus (less), year-over-year change in fair value of outstanding and unvested equity awards granted in prior years	(1,953,028)	5,604,968	2,621,407
Plus (less), year-over-year change in fair value (from the end of the prior year through the vesting date) of equity awards granted in prior years that vested in the year	(1,583,857)	2,894,736	2,821,993
Compensation Actually Paid to Jon P. Stonehouse	4,009,070	17,053,230	10,853,629

- (3) These amounts represent the average of the amounts reported for the Company’s named executive officers (referred to as “NEOs” in this section) as a group (excluding Mr. Stonehouse) in the “Total” column of the Summary Compensation Table in each applicable year. The names of each of the NEOs included for these purposes in each applicable year are as follows: (i) for 2022, Mr. Doyle, Dr. Thackray, Ms. Barnes, Mr. Gayer, Dr. Babu, and Dr. Sheridan; (ii) for 2021, Mr. Doyle, Dr. Thackray, Dr. Babu, Dr. Sheridan, and Megan T. Sniecinski, the Company’s former Chief Business Officer; and (iii) for 2020, Thomas R. Staab II, the Company’s former CFO, Mr. Doyle, Dr. Babu, Dr. Sheridan, and Ms. Sniecinski. Refer to the “2021 Summary Compensation Table” and “2020 Summary Compensation Table” in our proxy statements for our 2022 and 2021 annual stockholder meetings, respectively, for additional information regarding our NEOs for 2021 and 2020, respectively.
- (4) These amounts represent the average amount of “compensation actually paid” to the NEOs identified in note 3 above as a group, as computed in accordance with Item 402(v) of Regulation S-K and do not reflect the average of the total compensation actually realized or received by these NEOs. In accordance with these rules, these amounts reflect “Total Compensation” as set forth in the respective Summary Compensation Table for each year, adjusted as shown below. Equity values are calculated in accordance with FASB ASC Topic 718, and the valuation assumptions used to calculate fair values did not materially differ from those disclosed at the time of the grant.

Average Compensation Actually Paid to Non-PEO NEOs	2022	2021	2020
Average Summary Compensation Table Total	2,568,935	4,523,739	2,353,552
Less, average value of “Stock Awards” and “Option Awards” reported in Summary Compensation Table	(1,844,815)	(3,677,542)	(1,642,946)
Plus, average year-end fair value of outstanding and unvested equity awards granted in the year	2,020,092	2,998,786	1,849,354
Plus (less), average year-over-year change in fair value of outstanding and unvested equity awards granted in prior years	(813,831)	1,691,604	871,718
Plus (less), average year-over-year change in fair value (from the end of the prior year through the vesting date) of equity awards granted in prior years that vested in the year	(477,748)	1,773,047	363,631
Less, average prior year-end fair value for any equity awards forfeited in the year	—	(55,492)	(165,096)
Average Compensation Actually Paid to Non-PEO NEOs	1,452,633	7,254,142	3,630,213

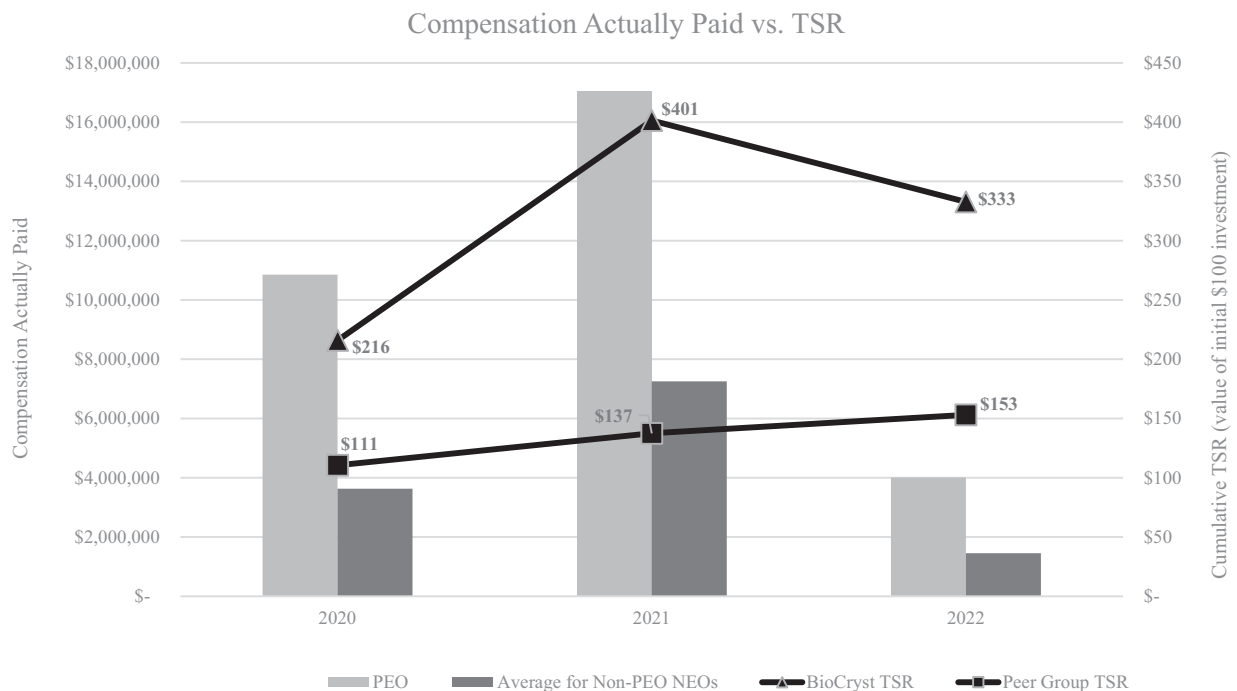
- (5) Total Stockholder Return (TSR) measures the change in a \$100 investment in our Common Stock based on its closing price of \$3.45 on December 31, 2019 and its year-end closing price thereafter. TSR is calculated by dividing (a) the difference between the share price of Common Stock at the end of each fiscal year shown and the beginning of the measurement period by (b) the share price of Common Stock at the beginning of the measurement period. The beginning of the measurement period for each applicable year is December 31, 2019.
- (6) The peer group used for this purpose is the CRSP Total Return Index for Nasdaq Pharmaceutical Stocks.
- (7) The dollar amounts reported represent the amount of net loss reflected in the Company’s audited financial statements for the applicable year.
- (8) Item 402(v)(2)(vi) of Regulation S-K requires that we designate a “Company-Selected Measure,” which, in our assessment, represents the most important financial performance measure (that is not otherwise required to be disclosed in the “Pay Versus Performance” table) used to link “compensation actually paid” to our NEOs, for the most recently completed fiscal year, to Company performance. For these purposes, we have selected ORLADEYO sales. The numbers in this column represent product sales of ORLADEYO and do not include royalty revenue from sales of ORLADEYO in Japan by our collaborative partner, Torii Pharmaceutical Co., Ltd. ORLADEYO is an oral, once-daily therapy discovered and developed by us for the prevention of hereditary angioedema attacks. It was first approved by the U.S. Food and Drug Administration in December 2020, and we began shipping it to patients with a prescription in the United States that same month.

Description of Certain Relationships between Information Presented in the Pay Versus Performance Table

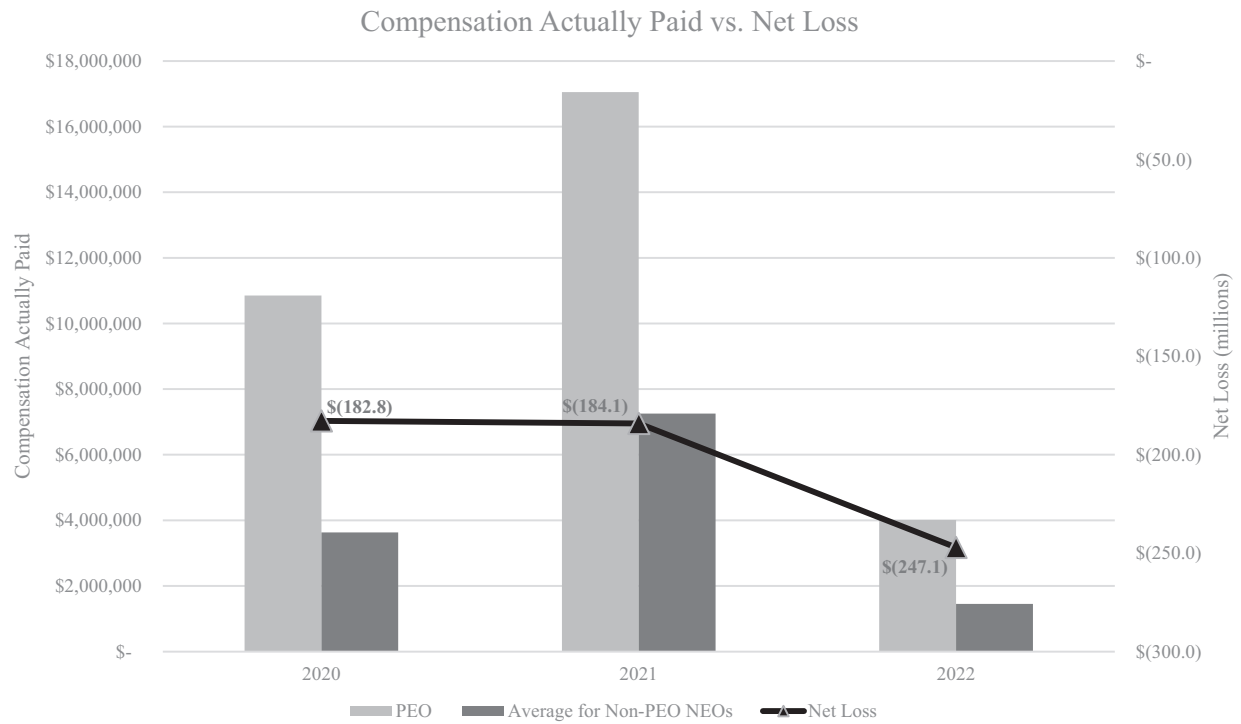
As described in more detail in the “Compensation Discussion and Analysis” section above, the Company’s executive compensation program reflects a variable-pay-for-performance philosophy. It is based on market best practices and is designed to ensure that it is appropriately risk-based and competitive with similar companies in our industry. The Company’s primary objectives for our executive compensation program are described on page 29 of the “Compensation Discussion and Analysis,” and the pre-established corporate objectives used to determine the variable component of executive compensation for 2022 (i.e., cash bonus under the AIP and 2022 long-term equity grants) are described on page 33. While the Company uses several performance measures to align executive compensation with Company performance, not all of those Company measures are presented in the “Pay Versus Performance” table above. Further, not all of the Company’s performance measures are “financial performance measures” as defined above in note 8 to the “Pay Versus Performance” table. For example, as a growing commercial-stage biotechnology company that discovers and commercializes novel, oral, small-molecule medicines, some of our performance measures relate to developments in the Company’s product pipeline and to building a robust and adaptable organization. The Company generally seeks to incentivize long-term performance of the Company as a whole and, therefore, does not specifically align the Company’s performance measures with “compensation actually paid” (as computed in accordance with Item 402(v) of Regulation S-K) for a particular year, which can be impacted in large part by changes in stock price.

In accordance with SEC rules, the Company is providing the following descriptions of the relationships between information presented in the “Pay Versus Performance” table.

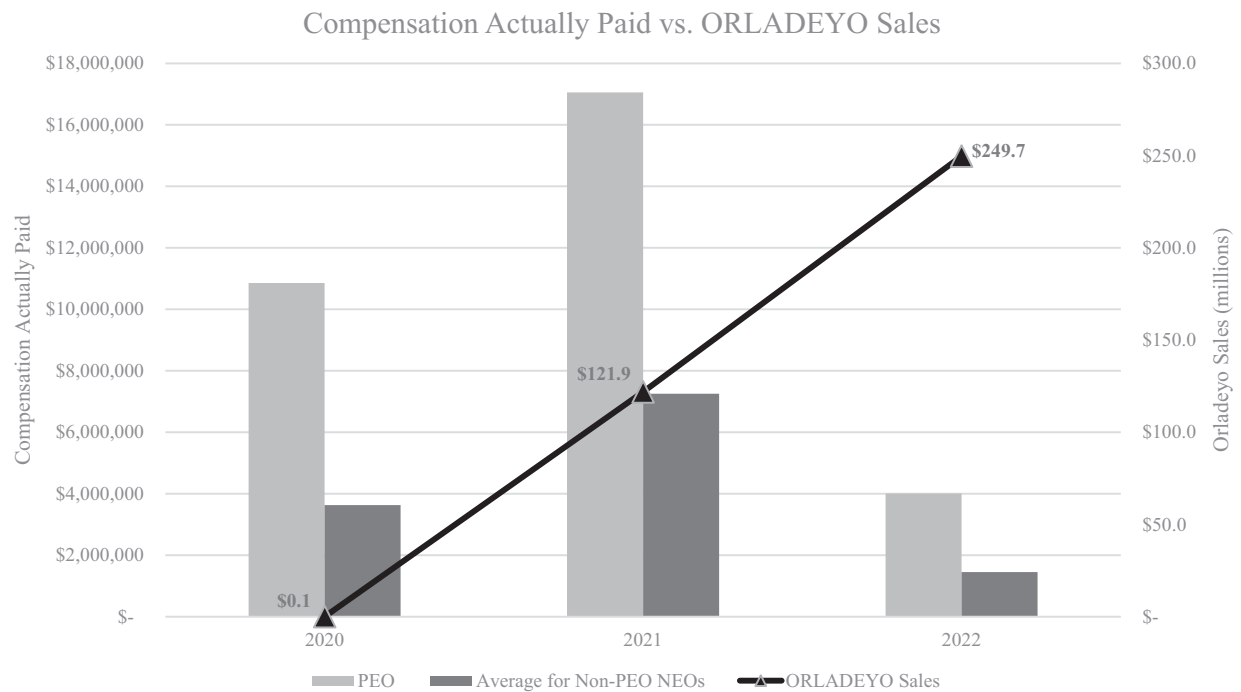
Compensation Actually Paid, Cumulative TSR, and Peer Group TSR



Compensation Actually Paid and Net Loss



Compensation Actually Paid and ORLADEYO Sales



Performance Measures

As disclosed above under “Description of Certain Relationships between Information Presented in the Pay Versus Performance Table,” the Company uses several performance measures to align executive compensation with Company performance, not all of which are presented in the “Pay Versus Performance” table. These performance measures include the pre-established corporate objectives for 2022, as described in the “Compensation Discussion and Analysis” section, and reflect the Company’s variable pay-for-performance philosophy. As a growing company that engages heavily in research and development, the majority of our corporate objectives were not “financial performance measures,” as defined by SEC rules. However, they did include one financial performance measure for ORLADEYO sales. Accordingly, the most important financial performance measure(s) used by the Company to link executive “compensation actually paid” to the Company’s NEOs, for the most recently completed fiscal year, to the Company’s performance is as follows:

- ORLADEYO sales.

In addition to our financial performance measures, the Company views stock price as a key driver of value for all of our equity awards and, in particular, the stock options, which have no value unless the stock price appreciates from the date of grant.

2022 DIRECTOR COMPENSATION

The following table provides information related to the compensation of our non-employee directors during fiscal 2022.

Name	Fees Earned (\$)	Stock Awards \$(1)(2)	Option Awards \$(3)(4)	Total (\$)
George B. Abercrombie	71,014	138,824	227,510	437,348
Stephen J. Aselage	81,014 ⁽⁵⁾	138,824	227,510	447,348
Steven K. Galson, M.D., MPH	58,514	138,824	227,510	424,848
Theresa M. Heggie	51,014 ⁽⁵⁾	138,824	227,510	417,348
Nancy J. Hutson, Ph.D.	78,514	138,824	227,510	444,848
Robert A. Ingram	98,514 ⁽⁵⁾	138,824	227,510	464,848
Kenneth B. Lee, Jr.	71,014	138,824	227,510	437,348
Alan G. Levin	68,514 ⁽⁵⁾	138,824	227,510	434,848
Amy E. McKee, M.D.	56,014	138,824	227,510	422,848
Vincent J. Milano	68,514 ⁽⁵⁾	138,824	227,510	434,848
A. Mabelle Sanders ⁽⁶⁾	44,945	138,824	544,884	728,654

(1) Each non-employee director serving at the time of the Company's 2022 annual meeting of stockholders received an automatic annual grant of RSUs under the Stock Incentive Plan, in accordance with the terms of the Company's Director Compensation Policy, for 12,866 shares of Common Stock, which RSUs vest on the 12-month anniversary of the grant date, subject to the terms of the Stock Incentive Plan. As of December 31, 2022, each non-employee director had RSUs covering 12,866 shares of Common Stock.

(2) The amounts in this column reflect the aggregate grant date fair value computed in accordance with FASB ASC Topic 718 of RSUs pursuant to the Stock Incentive Plan granted in 2022. Assumptions used in the calculation of these amounts are included in Note 12 to the Company's audited consolidated financial statements for the year ended December 31, 2022, which are included in the Company's Annual Report on Form 10-K filed with the SEC on February 27, 2023.

(3) Options are granted to new directors automatically in accordance with our Stock Incentive Plan at the time they became a director. Prior to April 2022, new directors received an option to purchase 80,000 shares of Common Stock, prorated from the date of appointment until the next scheduled annual meeting, which options vest, subject to the terms of the Stock Incentive Plan, in 36 equal monthly installments over a three-year period measured from the grant date.

Each non-employee director serving at the time of the Company's 2022 annual meeting of stockholders received an automatic annual grant of stock options under the Stock Incentive Plan, in accordance with the terms of the Company's Director Compensation Policy, to purchase 30,022 shares of Common Stock, which options vest on the 12-month anniversary of the grant date, subject to the terms of the Stock Incentive Plan. As of December 31, 2022, each director had options outstanding to purchase the following number of shares: Mr. Abercrombie: 200,022; Mr. Aselage: 165,022; Dr. Galson: 90,022; Ms. Heggie: 170,022; Dr. Hutson: 170,022; Mr. Ingram: 248,772; Mr. Lee: 275,022; Mr. Levin: 125,022; Dr. McKee: 83,355; Mr. Milano: 96,689; and Ms. Sanders: 56,689.

(4) The amounts in this column reflect the aggregate grant date fair value computed in accordance with FASB ASC Topic 718 of stock options pursuant to the Stock Incentive Plan granted in 2022. Assumptions used in the calculation of these amounts are included in Note 12 to the Company's audited consolidated financial statements for the year ended December 31, 2022, which are included in the Company's Annual Report on Form 10-K filed with the SEC on February 27, 2023.

(5) As of our 2021 annual meeting of stockholders, Mr. Aselage elected to receive 50%, and Ms. Heggie and Messrs. Ingram and Levin each elected to receive 100%, of their respective retainers in the form of shares of our Common Stock in lieu of cash. As of our 2022 annual meeting of stockholders, Ms. Heggie and Mr. Milano elected to receive 50%, and Messrs. Ingram and Levin each elected to receive 100%, of their respective retainers in the form of shares of our Common Stock in lieu of cash. Accordingly, in 2022, the Company issued the following number of shares of Common Stock in lieu of cash retainers: to Mr. Aselage, 770 shares in lieu of \$8,632 of cash; to Ms. Heggie, 2,576 shares in lieu of \$30,389 of cash; to Mr. Ingram, 6,575 shares in lieu of \$78,514 of cash; to Mr. Levin, 3,614 shares in lieu of \$43,514 of cash; and to Mr. Milano, 1,020 shares in lieu of \$13,125 of cash.

(6) Ms. Sanders joined the Board effective February 8, 2022 and received an automatic new director option grant under the Stock Incentive Plan for 26,667 shares of Common Stock.

Narrative to Director Compensation Table

Directors who are employees of the Company do not receive any additional compensation for their services as a director. Non-employee directors of the Company receive compensation for their services as a director in accordance with the terms of the Company's Director Compensation Policy and the Stock Incentive Plan. The Director Compensation Policy was originally adopted by the Board on April 18, 2022 and may be revised or amended by the Board in its discretion; provided, however, that, in accordance with the terms of the Stock Incentive Plan, the aggregate grant date fair value of all awards granted under the Stock Incentive Plan during any calendar year to any non-employee director (excluding any awards granted at the election of the director in lieu of all or any portion of

cash retainers or fees otherwise payable to the director in cash), together with the amount of any cash fees or retainers paid to such director during such calendar year with respect to the director's service as a non-employee director, cannot exceed \$750,000 (or, for a non-employee director who first joins the Board, \$1,000,000).

Retainer Fees

Non-employee directors receive an annual retainer fee consisting of four equal installment payments paid in arrears on a quarterly basis. Annual retainers are also paid in arrears to members of Board committees and committee Chairs on a quarterly basis. Directors are also reimbursed for expenses incurred in attending Board or committee meetings and while representing the Company in conducting certain business. Prior to April 18, 2022, the annual retainer fee was \$40,000 (\$75,000 for the Chair). Beginning April 18, 2022, the annual retainer fee increased to \$45,000 (\$80,000 for the Chair). Fees are not paid for attending committee meetings. The annual retainers for committee members and Chairs are as follows:

<u>Committee</u>	<u>Member Retainer</u>	<u>Chair Retainer</u>
Audit Committee	\$10,000	\$20,000
Compensation Committee	\$ 7,500	\$15,000
Commercialization Committee	\$ 7,500	\$15,000
Finance Committee	\$ 7,500	\$15,000
Science Committee	\$ 7,500	\$15,000
Corporate Governance and Nominating Committee.	\$ 5,000	\$10,000

Directors are given the opportunity to elect to receive, in lieu of cash retainers, a number of shares of our Common Stock equivalent in value to the Board retainer earned by such director. Directors can elect to receive either 50% or 100% of their Board retainer (excluding any committee retainers) in the form of Common Stock. These shares are distributed four times a year, in line with the quarterly cash retainer payments. The number of shares to be distributed is determined using the closing price of our Common Stock on the last business day of the applicable three-month period. Elections to receive Company shares in lieu of cash for a year shall be made as of the date of each annual meeting of the Company's stockholders, effective until the subsequent annual meeting.

Equity Compensation

New directors who join the Board are eligible to receive an initial equity grant equal to \$500,000 upon their appointment to the Board, prorated based on the date of appointment relative to the Company's annual meeting of stockholders and payable 70% in stock options and 30% in RSUs. In addition, on the date of each annual meeting of the Company's stockholders, continuing directors are eligible to receive an equity grant equal to \$325,000, payable 70% in stock options and 30% in RSUs. Initial equity grants in the form of options vest in 36 equal monthly installments, and initial equity grants in the form of RSUS vest in three equal annual installments, in each case over a three-year period measured from the grant date, subject to the terms of the Stock Incentive Plan. Annual equity grants vest on the 12-month anniversary of the grant date, subject to the terms of the Stock Incentive Plan. Following a grantee's cessation of Board service for any reason, each stock option vested at the time of cessation of Board service will remain exercisable for the remainder of the ten-year term of that option.

AUDIT COMMITTEE REPORT

The Audit Committee of the Board of Directors has furnished the following report, in accordance with rules established by the Securities and Exchange Commission (“SEC”), for inclusion in this Proxy Statement.

In fulfilling its oversight responsibilities, the Audit Committee reviewed and discussed with management the audited consolidated financial statements in the Company’s Annual Report on Form 10-K for the year ended December 31, 2022, including a discussion of the quality, not just the acceptability, of the accounting principles, the reasonableness of significant judgments, and the clarity of disclosures in the financial statements. In addition, the Audit Committee reviewed and discussed with the Company’s management the internal audit plan for the year ended December 31, 2022. Furthermore, the Audit Committee reviewed and discussed with the Company’s management and Ernst and Young LLP the evaluation of the Company’s design and functioning of its internal control over financial reporting, including the required Section 404 testing undertaken by Company management and Ernst and Young LLP with respect to the Company’s internal control over financial reporting. The Audit Committee reviewed with Ernst & Young LLP, who are responsible for expressing an opinion on the conformity of those audited financial statements with generally accepted accounting principles, their judgments as to the quality, not just the acceptability, of the Company’s accounting principles and such other matters as are required to be discussed with the Audit Committee under generally accepted auditing standards. In addition, the Audit Committee has discussed with Ernst & Young LLP the matters required to be discussed by applicable requirements of the Public Company Accounting Oversight Board (PCAOB) and the SEC. The Audit Committee has received the written disclosures and the letter from Ernst & Young LLP required by applicable requirements of the PCAOB regarding Ernst & Young LLP’s communications with the Audit Committee concerning independence, and has discussed with Ernst & Young LLP their independence. The Audit Committee also considered the compatibility of non-audit services with Ernst & Young LLP’s independence.

The Audit Committee discussed with Ernst & Young LLP the overall scope and plans for their audit. The Audit Committee regularly meets with Ernst & Young LLP, with and without management present, to discuss the results of their examination, their evaluation of the Company’s internal controls, and the overall quality of the Company’s financial reporting.

In reliance on the reviews and discussions referred to above, the Audit Committee recommended to the Board that the audited consolidated financial statements be included in the Company’s Annual Report on Form 10-K for the year ended December 31, 2022 for filing with the SEC. The Audit Committee and the Board approved the selection of Ernst & Young LLP as the Company’s independent registered public accounting firm for 2022 and has approved the retention of Ernst & Young LLP as the principal accounting firm to be used by the Company throughout the fiscal year ending December 31, 2023.

The Audit Committee currently consists of Mr. Lee, as Chair, Mr. Abercrombie, Ms. Heggie, Mr. Levin, and Mr. Milano. Ms. Heggie was appointed to the Audit Committee on February 28, 2023 and did not participate in the reviews and discussions referred to above with respect to the Company’s audited consolidated financial statements for the year ended December 31, 2022.

Kenneth B. Lee, Jr., Chair of the Committee

George B. Abercrombie

Alan G. Levin

Vincent J. Milano

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

Except as otherwise indicated in the notes to the table, the following table sets forth information regarding beneficial ownership of the Company's Common Stock as of April 17, 2023, by (i) each director, (ii) each of the Named Executive Officers, (iii) all directors and executive officers of the Company as a group, and (iv) each person known to the Company to be the beneficial owner of more than five percent of our Common Stock. Unless otherwise noted below, the address for each person listed in the table is the principal executive offices of the Company.

<u>Name and Address of Beneficial Owner</u>	<u>Amount and Nature of Beneficial Ownership⁽¹⁾</u>	<u>Percent of Class⁽²⁾</u>
5% Stockholders		
Baker Bros. Advisors LP and related persons 860 Washington Street, 3rd Floor New York, NY 10014	19,262,707 ⁽³⁾	10.2%
BlackRock, Inc. 55 East 52nd Street New York, NY 10055	14,918,955 ⁽⁴⁾	7.9%
The Vanguard Group 100 Vanguard Blvd. Malvern, PA 19355	14,204,395 ⁽⁵⁾	7.5%
State Street Corporation One Lincoln Street Boston, MA 02111	11,126,861 ⁽⁶⁾	5.9%
Directors and Named Executive Officers		
George B. Abercrombie	212,088 ⁽⁷⁾	*
Stephen J. Aselage	211,616 ⁽⁸⁾	*
Steven K. Galson, M.D., MPH	77,890 ⁽⁹⁾	
Theresa M. Heggie	201,711 ⁽¹⁰⁾	*
Nancy J. Hutson, Ph.D.	247,961 ⁽¹¹⁾	*
Kenneth B. Lee, Jr.	312,140 ⁽¹²⁾	*
Alan G. Levin	144,077 ⁽¹³⁾	*
Amy E. McKee, M.D.	72,519 ⁽¹⁴⁾	*
Vincent J. Milano	102,592 ⁽¹⁵⁾	*
A. Mabelle Sanders	54,740 ⁽¹⁶⁾	*
Jon P. Stonehouse	4,112,334 ⁽¹⁷⁾	2.1%
Anthony J. Doyle	785,401 ⁽¹⁸⁾	*
Helen M. Thackray, M.D.	374,525 ⁽¹⁹⁾	*
Alane P. Barnes	1,114,109 ⁽²⁰⁾	*
Charles K. Gayer	608,031 ⁽²¹⁾	*
Yarlagadda S. Babu, Ph.D.	1,541,941 ⁽²²⁾	*
William P. Sheridan, MBBS.	523,609 ⁽²³⁾	*
All current executive officers and directors as a group (15 persons)	8,632,434 ⁽²⁴⁾	4.4%

(*) Less than one percent.

(1) Gives effect to the shares of Common Stock each indicated stockholder has the right to acquire as of April 17, 2023 or within 60 days from that date though the exercise of options and other rights beneficially held by such stockholder on that date.

(2) Ownership percentage is reported based on 188,920,765 shares of Common Stock issued and outstanding on April 17, 2023, plus, as to the holder thereof only and no other person, the number of shares (if any) that the person has the right to acquire as of April 17, 2023 or within 60 days from that date through the exercise of options and other rights.

(3) From Schedule 13G/A filed with the SEC on February 14, 2023. Includes the aggregate number of shares of Common Stock beneficially owned along with shares of Common Stock that may be immediately acquired as follows: 1,586,778 shares held by 667, L.P. ("667"), 17,469,270 shares held by Baker Brothers Life Sciences, L.P. ("Life Sciences" and together with 667, the "Funds"), 77,913 shares directly held by each of Julian C. Baker and Felix J. Baker, and 50,833 shares held by Dr. Stephen R. Biggar, an employee of Baker Bros. Advisors LP ("Advisors") and former director of the Company. The shares held by the Funds include a total of 6,396,063 shares issuable upon exercise of pre-funded warrants held by such entities. By virtue of their power to control the investment decisions of the Funds, each of

Advisors, Baker Bros. Advisors (GP) LLC, Julian C. Baker and Felix J. Baker may be deemed to be beneficial owners of shares owned by the Funds and may be deemed to have sole power to vote or direct the vote of and sole power to dispose or direct the disposition of such securities. Dr. Biggar previously served on the BioCryst board as a representative of the Funds. The policy of the Funds and Advisors does not permit employees to receive compensation for serving as a director of the Company. Therefore, Dr. Biggar has no pecuniary interest in any stock options or shares of Common Stock directly held by him. The Funds are instead entitled to the pecuniary interest in any stock options and shares of Common Stock received as director compensation.

- (4) From Schedule 13G/A filed with the SEC on February 3, 2023 indicating that 14,918,955 shares are held by BlackRock, Inc. and certain subsidiaries. No such subsidiary has the right to receive, or the power to direct the receipt of, dividends from, or the proceeds from the sale of, more than five percent of our Common Stock. BlackRock, Inc. may be deemed to have sole power to vote or to direct the vote of 14,641,999 shares of Common Stock and sole power to dispose or to direct the disposition of 14,918,955 shares of Common Stock.
- (5) From Schedule 13G/A filed with the SEC on February 9, 2023 indicating that 14,204,395 shares of Common Stock are held by The Vanguard Group. The Vanguard Group may be deemed to have shared power to vote or to direct the vote of 258,134 shares of Common Stock, sole power to dispose or to direct the disposition of 13,754,831 shares of Common Stock, and shared power to dispose or to direct the disposition of 449,564 shares of Common Stock.
- (6) From Schedule 13G/A filed with the SEC on February 6, 2023 indicating that 11,126,861 shares of Common Stock are held by State Street Corporation and certain subsidiaries. No such subsidiary has the right to receive, or the power to direct the receipt of, dividends from, or the proceeds from the sale of, more than five percent of our Common Stock. State Street Corporation may be deemed to have shared power to vote or to direct the vote of 10,687,585 shares of our Common Stock and shared power to dispose or to direct the disposition of 11,126,861 shares of our Common Stock.
- (7) Includes (i) 200,022 shares issuable to Mr. Abercrombie upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date and (ii) 12,866 shares issuable to Mr. Abercrombie upon vesting of RSUs within 60 days from April 17, 2023.
- (8) Includes (i) 165,022 shares issuable to Mr. Aselage upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date and (ii) 12,866 shares issuable to Mr. Aselage upon vesting of RSUs within 60 days from April 17, 2023.
- (9) Includes (i) 65,024 shares issuable to Dr. Galson upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date and (ii) 12,866 shares issuable to Dr. Galson upon vesting of RSUs within 60 days from April 17, 2023.
- (10) Includes (i) 170,022 shares issuable to Ms. Heggie upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date and (ii) 12,866 shares issuable to Ms. Heggie upon vesting of RSUs within 60 days from April 17, 2023.
- (11) Includes (i) 170,022 shares issuable to Dr. Hutson upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date and (ii) 12,866 shares issuable to Dr. Hutson upon vesting of RSUs within 60 days from April 17, 2023.
- (12) Includes (i) 260,022 shares issuable to Mr. Lee upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date and (ii) 12,866 shares issuable to Mr. Lee upon vesting of RSUs within 60 days from April 17, 2023.
- (13) Includes (i) 125,022 shares issuable to Mr. Levin upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date and (ii) 12,866 shares issuable to Mr. Levin upon vesting of RSUs within 60 days from April 17, 2023.
- (14) Includes (i) 59,653 shares issuable to Dr. McKee upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date and (ii) 12,866 shares issuable to Dr. McKee upon vesting of RSUs within 60 days from April 17, 2023.
- (15) Includes (i) 70,766 shares issuable to Mr. Milano upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date and (ii) 12,866 shares issuable to Mr. Milano upon vesting of RSUs within 60 days from April 17, 2023.
- (16) Includes (i) 41,874 shares issuable to Ms. Sanders upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date and (ii) 12,866 shares issuable to Ms. Sanders upon vesting of RSUs within 60 days from April 17, 2023.
- (17) Includes 3,272,290 shares issuable to Mr. Stonehouse upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date.
- (18) Includes 674,250 shares issuable to Mr. Doyle upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date.
- (19) Includes 331,250 shares issuable to Dr. Thackray upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date.
- (20) Includes 954,901 shares issuable to Ms. Barnes upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date.
- (21) Includes 453,979 shares issuable to Mr. Gayer upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date.
- (22) Includes 1,273,650 shares issuable to Dr. Babu upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date.
- (23) Includes 517,560 shares issuable to Dr. Sheridan upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date.
- (24) Includes (i) 7,014,119 shares issuable to all of our executive officers and directors upon exercise of stock options that are exercisable as of April 17, 2023 or within 60 days from that date and (ii) 128,660 shares issuable to our directors upon vesting of RSUs within 60 days from April 17, 2023.

STOCKHOLDER PROPOSALS

Proposals of stockholders intended to be presented at our 2024 Annual Meeting of Stockholders (the “2024 Annual Meeting”) must be received by the Company by December 29, 2023 to be considered for inclusion in our Proxy Statement relating to such meeting. Proposals for inclusion in the Proxy Statement must comply with the Exchange Act, including Rule 14a-8.

A stockholder must notify the Company of any proposal (including director nominations) that the stockholder intends to present, other than by inclusion in our proxy materials, at our 2024 Annual Meeting. To be timely, the notice must be delivered to the Company’s Corporate Secretary at the Company’s principal executive offices no earlier than February 14, 2024 and no later than March 15, 2024. In order for the proposal to be eligible for consideration at the 2024 Annual Meeting, the notice must include the information required by the Company’s bylaws, including, with respect to director nominations, specific information regarding both the stockholder making the nomination and the director nominee. These dates and notice requirements also apply to any stockholder nominations for directors to be included on a universal proxy card for election at our 2024 Annual Meeting. In addition to satisfying the advance notice provisions of our bylaws, a stockholder who intends to solicit proxies in support of director nominees submitted under these advance notice provisions must provide the notice required by Exchange Act Rule 14a-19(b) to the Corporate Secretary at the Company’s principal executive offices no later than April 14, 2024.

NO INCORPORATION BY REFERENCE

In the Company’s filings with the SEC, information is sometimes “incorporated by reference.” This means that the Company is referring you to information that has previously been filed with the SEC and that the information should be considered part of a particular filing. As provided in regulations promulgated by the SEC, the “Audit Committee Report,” the “Compensation Committee Report,” and the “Pay Versus Performance” disclosures contained in this Proxy Statement specifically are not incorporated by reference into any other filings with the SEC. In addition, this Proxy Statement includes the Company’s website address. This website address is intended to provide inactive, textual references only. The information on the Company’s website is not part of this Proxy Statement.

OTHER MATTERS

Management does not intend to present to the Meeting any matters other than those previously mentioned herein and does not presently know of any matters that will be presented by other parties. If other matters should properly come before the Meeting, it is intended that the holders of the proxies will act in respect thereto and in accordance with their best judgment.

GENERAL INFORMATION

Some banks, brokers and other nominee record holders may be participating in the practice of “householding” Proxy Statements and annual reports. This means that only one copy of the one-page notice regarding the Internet availability of proxy materials may have been sent to multiple stockholders in your household. You may have a separate copy of this document sent to you by contacting the Corporate Secretary, BioCryst Pharmaceuticals, Inc., 4505 Emperor Blvd., Suite 200, Durham, North Carolina 27703, (919) 859-1302. If you prefer to receive separate copies of the one-page notice regarding the Internet availability of proxy materials in the future, or if you are receiving multiple copies and would like to receive only one copy for your household, you should contact your bank, broker or other nominee holder, or you may contact us at the above address.

Stockholders may obtain a copy of the Notice of Annual Meeting, Proxy Statement, Form of Proxy, and our Annual Report on Form 10-K, free of charge, by writing to the Corporate Secretary at the address stated above or by visiting www.proxyvote.com.

BY ORDER OF THE BOARD OF DIRECTORS

Alane P. Barnes, Chief Legal Officer and
Corporate Secretary

Durham, North Carolina
April 27, 2023

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BIOCRIST PHARMACEUTICALS, INC.
STOCK INCENTIVE PLAN
(AS AMENDED AND RESTATED AS OF APRIL 24, 2023)
ARTICLE ONE
GENERAL PROVISIONS

I. PURPOSES OF THE PLAN

A. This Stock Incentive Plan (the “Plan”), formerly the “BioCryst Pharmaceuticals, Inc. 1991 Stock Option Plan,” is intended to promote the interests of BioCryst Pharmaceuticals, Inc., a Delaware corporation (the “Company”), by providing a method whereby (i) employees (including officers and directors) of the Company (or its parent or subsidiary corporations), (ii) non-employee members of the board of directors of the Company (the “Board”) (or of any parent or subsidiary corporations) and (iii) consultants and other independent contractors who provide valuable services to the Company (or any parent or subsidiary corporations) may be offered the opportunity to acquire a proprietary interest, or otherwise increase their proprietary interest, in the Company as an incentive for them to remain in the service of the Company (or any parent or subsidiary corporations).

B. For purposes of the Plan, the following provisions shall be applicable in determining the parent and subsidiary corporations of the Company:

(i) Any corporation (other than the Company) in an unbroken chain of corporations ending with the Company shall be considered to be a **parent** corporation of the Company, provided each such corporation in the unbroken chain (other than the Company) owns, at the time of the determination, stock possessing fifty percent (50%) or more of the total combined voting power of all classes of stock in one of the other corporations in such chain.

(ii) Each corporation (other than the Company) in an unbroken chain of corporations beginning with the Company shall be considered to be a **subsidiary** of the Company, provided each such corporation (other than the last corporation) in the unbroken chain owns, at the time of the determination, stock possessing fifty percent (50%) or more of the total combined voting power of all classes of stock in one of the other corporations in such chain.

C. The Plan, as amended and restated, was approved and adopted by the Board, effective on April 24, 2023, in order to increase by 7,000,000 the number of shares of the Company’s common stock, par value \$0.01 per share (the “Common Stock”), available for issuance under the Plan, subject to approval by the Company’s stockholders at the Company’s Annual Meeting of Stockholders on June 13, 2023, and to make certain other changes.

II. STRUCTURE OF THE PLAN

A. The Plan shall be divided into three separate equity programs:

(i) the Discretionary Option Grant Program specified in Article Two, pursuant to which eligible persons may, at the discretion of the Plan Administrator, be granted options to purchase shares of Common Stock,

(ii) the Stock Issuance Program specified in Article Three, pursuant to which eligible persons may, at the discretion of the Plan Administrator, be issued shares of Common Stock directly or through the issuance of restricted stock units (“RSUs”) that provide for the issuance of shares of Common Stock if the applicable vesting criteria are satisfied, and

(iii) the Director Grant Program specified in Article Four, pursuant to which non-employee members of the Board may receive grants of awards.

B. Unless the context clearly indicates otherwise, the provisions of Articles One and Five of the Plan shall apply to all equity programs under the Plan and shall accordingly govern the interests of all individuals under the Plan.

III. ADMINISTRATION OF THE PLAN

A. The Plan shall be administered by the Committee who shall be the Compensation Committee of the Board or, in the absence of a Compensation Committee, a properly constituted committee or the Board itself (the administrator is referred to herein as the “Committee” or the “Plan Administrator”). Any power of the Committee may also be exercised by the Board, except to the extent that the grant or exercise of such authority would cause any award or transaction to become subject to (or lose an exemption under) the short-swing profit recovery provisions of Section 16 of the Securities Exchange Act of 1934, as amended (the “1934 Act”). To the extent that any permitted action taken by the Board conflicts with action taken by the Committee, the Board action shall control. The Committee may by resolution authorize one or more officers of the Company to perform any or all things that the Committee is authorized and empowered to do or perform under the Plan, and for all purposes under this Plan, such officer or officers shall be treated as the Committee; provided, however, that the resolution so authorizing such officer or officers shall specify the total number of awards (if any) such officer or officers may award pursuant to such delegated authority, and any such award shall be subject to the form of award agreement theretofore approved by the Compensation Committee. No such officer shall designate himself or herself as a recipient of any awards granted under authority delegated to such officer. In addition, the Compensation Committee may delegate any or all aspects of the day-to-day administration of the Plan to one or more officers or employees of the Company or any subsidiary or affiliate, and/or to one or more agents.

B. Subject to the express provisions of this Plan, the Committee shall be authorized and empowered to do all things that it determines to be necessary or appropriate in connection with the administration of this Plan, including, without limitation: (i) to prescribe, amend and rescind rules and regulations relating to this Plan and to define terms not otherwise defined herein; (ii) to determine which persons are grantees, to which of such grantees, if any, awards shall be granted hereunder and the timing of any such awards; (iii) to grant awards to grantees and determine the terms and conditions thereof, including the number of shares of Common Stock subject to awards and the exercise or purchase price of such shares and the circumstances under which awards become exercisable or vested or are forfeited or expire, which terms may but need not be conditioned upon the passage of time, continued employment, the satisfaction of performance criteria, the occurrence of certain events (including events which constitute a Change in Control to the extent permitted hereunder), or other factors; (iv) to establish and verify the extent of satisfaction of any performance goals or other conditions applicable to the grant, issuance, exercisability, vesting and/or ability to retain any award; (v) to prescribe and amend the terms of the agreements or other documents evidencing awards made under this Plan (which need not be identical) and the terms of or form of any document or notice required to be delivered to the Company by grantees under this Plan; (vi) to determine the extent to which adjustments are required pursuant to Article One; (vii) to interpret and construe this Plan, any rules and regulations under this Plan and the terms and conditions of any award granted hereunder, and to make exceptions to any such provisions for the benefit of the Company; (viii) to approve corrections in the documentation or administration of any award; and (ix) to make all other determinations deemed necessary or advisable for the administration of this Plan.

C. All decisions, determinations and interpretations by the Committee regarding the Plan, any rules and regulations under the Plan and the terms and conditions of or operation of any award granted hereunder, shall be final and binding on all grantees, beneficiaries, heirs, assigns or other persons holding or claiming rights under the Plan or any award. The Committee shall consider such factors as it deems relevant, in its sole and absolute discretion, to making such decisions, determinations and interpretations including, without limitation, the recommendations or advice of any officer or other employee of the Company and such attorneys, consultants and accountants as it may select.

D. The Committee may delegate all or a portion of their duties hereunder to one or more individuals or committees. Any reference to the Committee or the Plan Administrator shall refer to such individual(s) or committee(s) to the extent of such delegation.

IV. ELIGIBILITY

A. The persons eligible to participate in the Discretionary Option Grant and Stock Issuance Programs shall be limited to the following:

- (i) officers and other employees of the Company (or its parent or subsidiary corporations);

(ii) individuals who are consultants or independent advisors and who provide valuable services to the Company (or its parent or subsidiary corporations); and

(iii) non-employee members of the Board (or of the board of directors of parent or subsidiary corporations), subject to the limits set forth in Section II.A. of Article Four.

B. Only Board members who are not employees of the Company (or any parent or subsidiary) shall be eligible to receive grants pursuant to the Director Grant Program specified in Article Four.

C. The Plan Administrator shall, within the scope of its administrative jurisdiction under the Plan, have full power and authority to determine (i) whether to grant options in accordance with the Discretionary Option Grant Program or to effect stock issuances in accordance with the Stock Issuance Program, (ii) which eligible persons are to receive option grants under the Discretionary Option Grant Program, the time or times when such option grants are to be made, the number of shares to be covered by each such grant, the status of the granted option as either an incentive stock option (“Incentive Option”) which satisfies the requirements of Section 422 of the Internal Revenue Code of 1986, as amended (the “Code”) or a non-statutory option not intended to meet such requirements, the time or times when each such option is to become exercisable, the vesting schedule (if any) applicable to the option shares and the maximum term for which such option is to remain outstanding, and (iii) which eligible persons are to receive stock issuances under the Stock Issuance Program, the time or times when such issuances are to be made, the number of shares to be issued to each grantee, the vesting schedule (if any) applicable to the shares and the consideration for such shares.

V. STOCK SUBJECT TO THE PLAN

A. Shares of the Company’s Common Stock shall be available for issuance under the Plan and shall be drawn from either the Company’s authorized but unissued shares of Common Stock or from reacquired shares of Common Stock, including shares repurchased by the Company on the open market. The maximum number of shares of Common Stock which may be issued over the term of the Plan, as amended and restated, shall not exceed 63,090,000 shares, subject to adjustment from time to time in accordance with the provisions of this Section V. The total number of shares available under the Plan, as amended and restated, as of April 24, 2023 is 38,875,731. This amount consists of 34,135,014 shares reserved for awards already issued, 4,740,717 shares of Common Stock available for future issuance under the Plan, and the increase of 7,000,000 shares of Common Stock authorized by the Board (subject to approval by the Company’s stockholders at the Annual Meeting of Stockholders on June 13, 2023).

B. In no event shall the number of shares of Common Stock for which any one individual participating in the Plan may receive options, separately exercisable stock appreciation rights and direct stock issuances and RSUs exceed 1,500,000 shares of Common Stock in the aggregate in any calendar year. For purposes of such limitation, however, no stock options granted prior to the date the Common Stock was first registered under Section 12 of the 1934 Act (the “Section 12(g) Registration Date”) shall be taken into account.

C. Should an outstanding option under this Plan expire or terminate for any reason prior to exercise in full, the shares subject to the portion of the option not so exercised shall be available for subsequent option grant or direct stock issuances or RSUs under the Plan. Unvested shares issued under the Plan and subsequently repurchased by the Company, at the original issue price paid per share, pursuant to the Company’s repurchase rights under the Plan, or shares underlying terminated RSUs, shall be added back to the number of shares of Common Stock reserved for issuance under the Plan and shall accordingly be available for reissuance through one or more subsequent option grants or direct stock issuances or RSUs under the Plan. However, shares subject to an award under the Plan may not again be made available for issuance under the Plan if such shares are: (i) shares that were subject to a stock-settled stock appreciation right and were not issued upon the net settlement or net exercise of such stock appreciation right, (ii) shares used to pay the exercise price of an option, (iii) shares delivered to or withheld by the Company to pay the withholding taxes related an award, or (iv) shares repurchased on the open market with the proceeds of an option exercise. Shares of Common Stock subject to any option surrendered for an appreciation distribution under Section IV of Article Two or Section II.B.1.(iv) of Article Four shall not be available for subsequent issuance under the Plan.

D. In the event any change is made to the Common Stock issuable under the Plan by reason of any stock split, stock dividend, recapitalization, combination of shares, exchange of shares or other change affecting the outstanding Common Stock as a class without receipt of consideration, then appropriate adjustments shall be

made to (i) the maximum number and/or class of securities issuable under the Plan, (ii) the maximum number and/or class of securities for which any one individual participating in the Plan may be granted stock options, separately exercisable stock appreciation rights, and direct stock issuances and RSUs under the Plan from and after the Section 12(g) Registration Date, (iii) the number and/or class of securities and price per share in effect under each outstanding option and stock appreciation right under the Plan, (iv) the number and/or class of securities in effect under each outstanding direct stock issuance and RSU under the Plan, and (v) the number and/or class of securities for which grants are subsequently to be made per non-employee Board member under the Director Grant Program. The purpose of such adjustments shall be to preclude the enlargement or dilution of rights and benefits under the Plan.

E. The fair market value per share of Common Stock on any relevant date under the Plan shall be determined in accordance with the following provisions:

(i) If the Common Stock is not at the time listed or admitted to trading on any national securities exchange but is traded in the over-the-counter market, the fair market value shall be the mean between the highest bid and lowest asked prices (or, if such information is available, the closing selling price) per share of Common Stock on the date in question in the over-the-counter market, as such prices are reported on the Nasdaq National Market, the Nasdaq Global Select Market or any successor system. If there are no reported bid and asked prices (or closing selling price) for the Common Stock on the date in question, then the mean between the highest bid price and lowest asked price (or the closing selling price) on the last preceding date for which such quotations exist shall be determinative of fair market value.

(ii) If the Common Stock is at the time listed or admitted to trading on any national securities exchange, then the fair market value shall be the closing selling price per share of Common Stock on the date in question on the securities exchange determined by the Plan Administrator to be the primary market for the Common Stock, as such price is officially quoted in the composite tape of transactions on such exchange. If there is no reported sale of Common Stock on the exchange on the date in question, then the fair market value shall be the closing selling price on the exchange on the last preceding date for which such quotation exists.

(iii) If the Common Stock is at the time neither listed nor admitted to trading on any securities exchange nor traded in the over-the-counter market, then the fair market value shall be determined by the Plan Administrator after taking into account such factors as the Plan Administrator shall deem appropriate.

VI. MINIMUM VESTING

Notwithstanding any other provision of this Plan to the contrary, in no event shall any award granted pursuant to this Plan vest prior to the twelve (12)-month anniversary of the date of grant, other than in connection with the grantee's death or permanent disability or, to the extent permitted hereunder, in connection with a Change in Control (provided that this limitation shall not apply with respect to up to five percent (5%) of the shares of Common Stock available for issuance under this Plan following approval of the Plan at the Company's Annual Meeting of Stockholders on June 13, 2023). The minimum vesting period set forth in this Section VI may not be waived or superseded by any provision in an award or other agreement.

ARTICLE TWO DISCRETIONARY OPTION GRANT PROGRAM

I. TERMS AND CONDITIONS OF OPTIONS

Options granted pursuant to this Article Two shall be authorized by action of the Plan Administrator and may, at the Plan Administrator's discretion, be either Incentive Options or non-statutory options. Individuals who are not Employees may only be granted non-statutory options under this Article Two. Each option granted shall be evidenced by one or more instruments in the form approved by the Plan Administrator. Each such instrument shall, however, comply with the terms and conditions specified below, and each instrument evidencing an Incentive Option shall, in addition, be subject to the applicable provisions of Section II of this Article Two.

A. Option Price.

1. The option price per share shall be fixed by the Plan Administrator. In no event, however, shall the option price per share be less than one hundred percent (100%) of the fair market value per share of Common Stock on the date of the option grant.

2. The option price shall become immediately due upon exercise of the option and shall, subject to the provisions of Section IV of this Article Two and the instrument evidencing the grant, be payable through one of the following methods (or a combination thereof):

(i) full payment in cash or check drawn to the Company's order;

(ii) full payment in shares of Common Stock held by the optionee for the requisite period necessary to avoid a charge to the Company's earnings for financial reporting purposes and valued at fair market value on the Exercise Date (as such term is defined below);

(iii) full payment through a combination of shares of Common Stock held by the optionee for the requisite period necessary to avoid a charge to the Company's earnings for financial reporting purposes and valued at fair market value on the Exercise Date and cash or cash equivalent;

(iv) full payment through a broker-dealer sale and remittance procedure pursuant to which the optionee (I) shall provide irrevocable written instructions to a designated brokerage firm to effect the immediate sale of the purchased shares and remit to the Company, out of the sale proceeds available on the settlement date, sufficient funds to cover the aggregate option price payable for the purchased shares plus all applicable Federal and State income and employment taxes required to be withheld by the Company in connection with such purchase and (II) shall provide written directives to the Company to deliver the certificates for the purchased shares directly to such brokerage firm in order to complete the sale transaction; or

(v) such other method as permitted by the Plan Administrator.

For purposes of this subparagraph 2, the Exercise Date shall be the date on which written notice of the option exercise is delivered to the Company. Except to the extent the sale and remittance procedure is utilized in connection with the exercise of the option, payment of the option price for the purchased shares must accompany such notice.

B. Term and Exercise of Options.

Each option granted under this Article Two shall be exercisable at such time or times, during such period, and for such number of shares as shall be determined by the Plan Administrator and set forth in the instrument evidencing the option grant. No such option, however, shall have a maximum term in excess of ten (10) years from the grant date. During the lifetime of the optionee, the option, together with any stock appreciation rights pertaining to such option, shall be exercisable only by the optionee and shall not be assignable or transferable by the optionee except for a transfer of the option by will or by the laws of descent and distribution following the optionee's death and, for the avoidance of doubt, may not be transferred to a third party for cash or other value. However, the Plan Administrator shall have the discretion to provide that a non-statutory option may, in connection with the optionee's estate plan, be assigned in whole or in part during the optionee's lifetime either (i) as a gift to one or more members of optionee's immediate family, to a trust in which optionee and/or one or more such family members hold more than fifty percent (50%) of the beneficial interest or an entity in which more than fifty percent (50%) of the voting interests are owned by optionee and/or one or more such family members, or (ii) pursuant to a domestic relations order. The assigned portion shall be exercisable only by the person or persons who acquire a proprietary interest in the option pursuant to such assignment. The terms applicable to the assigned portion shall be the same as those in effect for this option immediately prior to such assignment and shall be set forth in such documents issued to the assignee as the Plan Administrator may deem appropriate.

C. Termination of Service.

1. Except to the extent otherwise provided pursuant to Section V of this Article Two or pursuant to an applicable award agreement, the following provisions shall govern the exercise period applicable to any options held by the optionee at the time of cessation of Service or death.

(i) Should the optionee cease to remain in Service for any reason other than death or permanent disability, then the period for which each outstanding option held by such optionee is to remain exercisable shall be limited to the three (3)-month period following the date of such cessation of Service. However, should optionee die during the three (3)-month period following his or her

cessation of Service, the personal representative of the optionee's estate or the person or persons to whom the option is transferred pursuant to the optionee's will or in accordance with the laws of descent and distribution shall have a twelve (12)-month period following the date of the optionee's death during which to exercise such option.

(ii) In the event such Service terminates by reason of permanent disability (as defined in Section 22(e)(3) of the Internal Revenue Code), then the period for which each outstanding option held by the optionee is to remain exercisable shall be limited to the twelve (12)-month period following the date of such cessation of Service.

(iii) Should the optionee, after completing five (5) full years of Service, die while in Service, then the exercisability of each of his or her outstanding options shall automatically accelerate so that each such option shall become fully exercisable with respect to the total number of shares of Common Stock at the time subject to such option and may be exercised for all or any portion of such shares. The personal representative of the optionee's estate or the person or persons to whom the option is transferred pursuant to the optionee's will or in accordance with the laws of descent and distribution shall have a twelve (12)-month period following the date of the optionee's death during which to exercise such option.

(iv) In the event such Service terminates by reason of death prior to the optionee obtaining five (5) full years of Service, then the period for which each outstanding vested option held by the optionee at the time of death shall be exercisable by the optionee's estate or the person or persons to whom the option is transferred pursuant to the optionee's will shall be limited to the twelve (12)-month period following the date of the optionee's death.

(v) Under no circumstances, however, shall any such option be exercisable after the specified expiration date of the option term.

(vi) Each such option shall, during such limited exercise period, be exercisable for any or all of the shares for which the option is exercisable on the date of the optionee's cessation of Service. Upon the expiration of such limited exercise period or (if earlier) upon the expiration of the option term, the option shall terminate and cease to be exercisable. However, each outstanding option shall immediately terminate and cease to remain outstanding, at the time of the optionee's cessation of Service, with respect to any shares for which the option is not otherwise at that time exercisable or in which the optionee is not otherwise vested.

(vii) Should (i) the optionee's Service be terminated for misconduct (including, but not limited to, any act of dishonesty, willful misconduct, fraud or embezzlement) or (ii) the optionee make any unauthorized use or disclosure of confidential information or trade secrets of the Company or its parent or subsidiary corporations, then in any such event all outstanding options held by the optionee under this Article Two shall terminate immediately and cease to be exercisable.

2. The Plan Administrator shall have complete discretion, exercisable either at the time the option is granted or at any time while the option remains outstanding, to permit one or more options held by the optionee under this Article Two to be exercised, during the limited period of exercisability provided under subparagraph 1 above, not only with respect to the number of shares for which each such option is exercisable at the time of the optionee's cessation of Service but also with respect to one or more subsequent installments of purchasable shares for which the option would otherwise have become exercisable had such cessation of Service not occurred.

3. For purposes of the foregoing provisions of this Section I.C (and for all other purposes under the Plan):

(i) The optionee shall be deemed to remain in the **Service** of the Company for so long as such individual renders services on a periodic basis to the Company (or any parent or subsidiary corporation) in the capacity of an Employee, a non-employee member of the board of directors or an independent consultant or advisor, unless the agreement evidencing the applicable option grant specifically states otherwise.

(ii) The optionee shall be considered to be an **Employee** for so long as such individual remains in the employ of the Company or one or more of its parent or subsidiary corporations, subject to the control and direction of the employer entity not only as to the work to be performed but also as to the manner and method of performance.

D. Stockholder Rights.

An optionee shall have no stockholder rights with respect to any shares covered by the option until such individual shall have exercised the option and paid the option price for the purchased shares. Without limitation, an optionee shall not have any right to receive dividends with respect to an unexercised option.

E. No Repricing.

No option or stock appreciation right may be repriced, regranted through cancellation, including cancellation in exchange for cash or other awards, or otherwise amended to reduce its option price or exercise price (other than with respect to adjustments made in connection with a transaction or other change in the Company's capitalization as permitted under this Plan) without the approval of the stockholders of the Company.

F. Repurchase Rights.

The shares of Common Stock acquired upon the exercise of options granted under this Article Two may be subject to repurchase by the Company in accordance with the following provisions:

1. The Plan Administrator shall have the discretion to grant options which are exercisable for unvested shares of Common Stock under this Article Two. Should the optionee cease Service while holding such unvested shares, the Company shall have the right to repurchase any or all those unvested shares at the option price paid per share. The terms and conditions upon which such repurchase right shall be exercisable (including the period and procedure for exercise and the appropriate vesting schedule for the purchased shares) shall be established by the Plan Administrator and set forth in the instrument evidencing such repurchase right.

2. All of the Company's outstanding repurchase rights shall automatically terminate, and all shares subject to such terminated rights shall immediately vest in full, upon the occurrence of any Corporate Transaction under Section III of this Article Two, except to the extent: (i) any such repurchase right is expressly assigned to the successor corporation (or parent thereof) in connection with the Corporate Transaction or (ii) such termination is precluded by other limitations imposed by the Plan Administrator at the time the repurchase right is issued.

3. The Plan Administrator shall have the discretionary authority, exercisable either before or after the optionee's cessation of Service, to cancel the Company's outstanding repurchase rights with respect to one or more shares purchased or purchasable by the optionee under this Discretionary Option Grant Program and thereby accelerate the vesting of such shares in whole or in part at any time.

II. INCENTIVE OPTIONS

The terms and conditions specified below shall be applicable to all Incentive Options granted under this Article Two. Incentive Options may only be granted to individuals who are Employees of the Company. Options which are specifically designated as "non-statutory" options when issued under the Plan shall not be subject to such terms and conditions.

A. **Dollar Limitation.** The aggregate fair market value (determined as of the respective date or dates of grant) of the Common Stock for which one or more options granted to any Employee under this Plan (or any other option plan of the Company or its parent or subsidiary corporations) may for the first time become exercisable as incentive stock options under the Federal tax laws during any one calendar year shall not exceed the sum of One Hundred Thousand Dollars (\$100,000). To the extent the Employee holds two or more such options which become exercisable for the first time in the same calendar year, the foregoing limitation on the exercisability of such options as incentive stock options under the Federal tax laws shall be applied on the basis of the order in which such options are granted. Should the number of shares of Common Stock for which any Incentive Option first becomes exercisable in any calendar year exceed the applicable One Hundred Thousand Dollar (\$100,000) limitation, then that option may nevertheless be exercised in such calendar year for the excess number of shares as a non-statutory option under the Federal tax laws.

B. **10% Stockholder.** If any individual to whom an Incentive Option is granted is the owner of stock (as determined under Section 424(d) of the Internal Revenue Code) possessing 10% or more of the total combined voting power of all classes of stock of the Company or any one of its parent or subsidiary corporations, then the option price per share shall not be less than one hundred and ten percent (110%) of the fair market value per share of Common Stock on the grant date, and the option term shall not exceed five (5) years, measured from the grant date.

C. **Termination of Employment.** Any portion of an Incentive Option that remains outstanding (by reason of the optionee remaining in the Service of the Company, pursuant to the Plan Administrator's exercise of discretion under Section V of this Article Two, or otherwise) more than 3 months following the date an optionee ceases to be an Employee of the Company shall thereafter be exercisable as a non-statutory option under federal tax laws.

Except as modified by the preceding provisions of this Section II, the provisions of Articles One, Two and Five of the Plan shall apply to all Incentive Options granted hereunder.

III. CORPORATE TRANSACTIONS/CHANGES IN CONTROL

A. For purposes of this Section III (and for all other purposes under the Plan), a Corporate Transaction shall be deemed to occur in the event of:

- (1) a merger or consolidation in which the Company is not the surviving entity, except for a transaction the principal purpose of which is to change the State of the Company's incorporation,
- (2) the sale, transfer or other disposition of all or substantially all of the assets of the Company in liquidation or dissolution of the Company, or
- (3) any reverse merger in which the Company is the surviving entity but in which securities possessing more than fifty percent (50%) of the total combined voting power of the Company's outstanding securities are transferred to a person or persons different from the persons holding those securities immediately prior to such merger.

The exercisability of each option outstanding under this Article Two that was granted before April 3, 2017 shall automatically accelerate so that each such option shall, immediately prior to the specified effective date for the Corporate Transaction, become fully exercisable with respect to the total number of shares of Common Stock at the time subject to such option and may be exercised for all or any portion of such shares.

B. Immediately after the consummation of the Corporate Transaction, all outstanding options under this Article Two shall fully vest, terminate and cease to be outstanding, except to the extent continued or assumed (as applicable) by the Company or the successor corporation or its parent company. The Plan Administrator shall have complete discretion to provide, on such terms and conditions as it sees fit, for a cash payment to be made to any optionee on account of any option terminated in accordance with this paragraph, in an amount equal to the excess (if any) of (A) the fair market value of the shares subject to the option as of the date of the Corporate Transaction, over (B) the aggregate exercise price of the option.

C. Each outstanding option under this Article Two which is assumed in connection with the Corporate Transaction or is otherwise to continue in effect shall be appropriately adjusted, immediately after such Corporate Transaction, to apply and pertain to the number and class of securities which would have been issued to the option holder, in consummation of such Corporate Transaction, had such person exercised the option immediately prior to such Corporate Transaction. Appropriate adjustments shall also be made to the option price payable per share, provided the aggregate option price payable for such securities shall remain the same. In addition, the class and number of securities available for issuance under the Plan following the consummation of the Corporate Transaction shall be appropriately adjusted. Any such options that are so continued or assumed in connection with a Corporate Transaction shall be treated as follows: if the grantee's employment is terminated by the Company without Cause or the grantee resigns due to a Constructive Termination, in either case within the ninety (90) day period preceding or the two (2) year period following the Corporate Transaction, the exercisability of such option shall automatically accelerate, and the Company's outstanding repurchase rights under this Article Two shall immediately terminate; provided, however, that if the Company, the acquirer or

successor refuses to continue (or, as applicable, assume) the option in connection with the Corporate Transaction, the exercisability of such option under this Article Two shall automatically accelerate, and the Company's outstanding repurchase rights under this Article Two shall immediately terminate upon the occurrence of such Corporate Transaction.

D. The grant of options under this Article Two shall in no way affect the right of the Company to adjust, reclassify, reorganize or otherwise change its capital or business structure or to merge, consolidate, dissolve, liquidate or sell or transfer all or any part of its business or assets.

E. In the event of a Change in Control: (1) options granted under this Article Two prior to May 23, 2016 shall be subject to the provisions of the Plan as in effect prior to such date, and (2) options granted on or after May 23, 2016 shall be treated as follows: if the grantee's employment is terminated by the Company without Cause or the grantee resigns due to a Constructive Termination, in either case within the ninety (90) day period preceding or the two (2) year period following the Change in Control, the exercisability of such option shall automatically accelerate, and the Company's outstanding repurchase rights under this Article Two shall immediately terminate; provided, however, that if the acquiror or successor refuses to assume the option in connection with the Change in Control, the exercisability of such option under this Article Two shall automatically accelerate, and the Company's outstanding repurchase rights under this Article Two shall immediately terminate upon the occurrence of such Change in Control. In the event that the acquiror or successor refuses to assume the option in connection with the Change in Control, the Plan Administrator shall have complete discretion to provide, on such terms and conditions as it sees fit, for a cash payment to be made to any optionee on account of any option terminated in accordance with this paragraph, in an amount equal to the excess (if any) of (A) the fair market value of the shares subject to the option as of the date of the Change in Control, over (B) the aggregate exercise price of the option.

F. For purposes of this Section III (and for all other purposes under the Plan), a Change in Control shall be deemed to occur in the event:

(1) any person or related group of persons (other than the Company or a person that directly or indirectly controls, is controlled by, or is under common control with, the Company) directly or indirectly acquires beneficial ownership (within the meaning of Rule 13d-3 of the 1934 Act) of securities possessing more than fifty percent (50%) of the total combined voting power of the Company's outstanding securities pursuant to a tender or exchange offer made directly to the Company's stockholders; or

(2) there is a change in the composition of the Board over a period of twenty-four (24) consecutive months or less such that a majority of the Board members (rounded up to the next whole number) ceases, by reason of one or more contested elections for Board membership, to be comprised of individuals who either (A) have been Board members continuously since the beginning of such period or (B) have been elected or nominated for election as Board members during such period by at least two-thirds of the Board members described in clause (A) who were still in office at the time such election or nomination was approved by the Board.

G. All options accelerated in connection with the Corporate Transaction or Change in Control (either at the time of the Corporate Transaction or Change in Control or as otherwise provided in this Section III) shall remain fully exercisable until the expiration or sooner termination of the option term.

H. The portion of any Incentive Option accelerated under this Section III in connection with a Corporate Transaction or Change in Control shall remain exercisable as an incentive stock option under the Federal tax laws only to the extent the dollar limitation of Section II of this Article Two is not exceeded. To the extent such dollar limitation is exceeded, the accelerated portion of such option shall be exercisable as a non-statutory option under the Federal tax laws.

I. For purposes of this Article Two and for purposes of Article Three:

1. "Cause" means, unless otherwise provided in the applicable award agreement, the Company's termination of the grantee's employment for any of the following reasons: (i) failure or refusal to comply in any material respect with lawful policies, standards or regulations of the Company; (ii) a violation of a federal or state law or regulation applicable to the business of the Company; (iii) conviction or plea of no contest to a felony under the laws of the United States or any State; (iv) fraud or misappropriation of property belonging to the Company or its affiliates; (v) a breach in any material respect of the terms of any confidentiality, invention assignment or proprietary information agreement with the Company or with a former employer, (vi) failure to satisfactorily perform the grantee's duties after having received written notice of such failure and at least thirty (30) days to cure such failure, or (vii) misconduct or gross negligence in connection with the performance of the grantee's duties.

2. "Constructive Termination" means, unless otherwise provided in the applicable award agreement, the grantee's resignation of employment with the Company within ninety (90) days of the occurrence of any of the following: (i) a material reduction in the grantee's responsibilities; (ii) a material reduction in the grantee's base salary; or (iii) a relocation of the grantee's principal office to a location more than 50 miles from the location of the grantee's existing principal office.

IV. STOCK APPRECIATION RIGHTS

A. Provided and only if the Plan Administrator determines in its discretion to implement the stock appreciation right provisions of this Section IV, one or more optionees may be granted the right, exercisable upon such terms and conditions as the Plan Administrator may establish, to surrender all or part of an unexercised option granted under this Article Two in exchange for a distribution from the Company in an amount equal to the excess of (i) the fair market value (on the option surrender date) of the number of shares in which the optionee is at the time vested under the surrendered option (or surrendered portion thereof) over (ii) the aggregate option price payable for such vested shares. The distribution may be made in shares of Common Stock valued at fair market value on the option surrender date, in cash, or partly in shares and partly in cash, as the Plan Administrator shall determine in its sole discretion.

B. The shares of Common Stock subject to any option surrendered for an appreciation distribution pursuant to this Section IV shall not be available for subsequent option grant under the Plan.

C. **Stockholder Rights.** A stock appreciation right holder shall have no stockholder rights with respect to any shares covered by the stock appreciation right until such individual shall have exercised the stock appreciation right and received the acquired shares. Without limitation, a stock appreciation right holder shall not have any right to receive dividends with respect to a stock appreciation right.

V. EXTENSION OF EXERCISE PERIOD

The Plan Administrator shall have full power and authority, exercisable either at the time the option is granted or at any time while the option remains outstanding, to extend the period of time for which any option granted under this Article Two is to remain exercisable following the optionee's cessation of Service or death from the limited period in effect under Section I.C.1 of Article Two to such greater period of time as the Plan Administrator shall deem appropriate; provided, however, that in no event shall such option be exercisable after the specified expiration date of the option term.

ARTICLE THREE STOCK ISSUANCE PROGRAM

I. STOCK ISSUANCE TERMS

Shares of Common Stock may be issued under the Stock Issuance Program through direct and immediate issuances without any intervening option grants. Each such stock issuance shall be evidenced by a Stock Issuance Agreement which complies with the terms specified below. Shares of Common Stock may also be issued under the Stock Issuance Program pursuant to restricted stock units ("RSUs"), which are awards granted to eligible individuals that entitle them to shares of Common Stock (or cash in lieu thereof) in the future following the satisfaction of vesting conditions imposed by the Plan Administrator.

A. Vesting Provisions.

1. The Plan Administrator may issue shares of Common Stock under the Stock Issuance Program which are to vest in one or more installments over the grantee's period of Service or upon attainment of specified performance objectives. Alternatively, the Plan Administrator may issue RSUs under the Stock Issuance Program which shall entitle the recipient to receive a specified number of shares of Common Stock upon the attainment of one or more Service and/or performance goals established by the Plan Administrator. Upon the attainment of such Service and/or performance goals, fully-vested shares of Common Stock shall be issued in satisfaction of those RSUs.

2. Any new, substituted or additional securities or other property (including money paid other than as a regular cash dividend) issued by reason of any stock dividend, stock split, recapitalization, combination of shares, exchange of shares or other change affecting the outstanding Common Stock as a class without the Company's receipt of consideration, shall be issued or set aside with respect to the shares of unvested Common Stock granted to a grantee or subject to a grantee's RSUs, subject to (i) the same vesting requirements applicable to the grantee's unvested shares of Common Stock or RSUs, and (ii) such escrow arrangements as the Plan Administrator shall deem appropriate.

3. The grantee shall have full stockholder rights with respect to any shares of Common Stock issued to the grantee under the Stock Issuance Program, whether or not the grantee's interest in those shares is vested, except that the grantee shall not have dividend rights with respect to such shares prior to the vesting of such shares. However, the Plan Administrator may provide for a grantee to receive one or more dividend equivalents with respect to such shares, entitling the grantee to all regular cash dividends payable on such shares of Common Stock, which amounts shall be (i) subject to the same vesting requirements applicable to the shares of Common Stock granted hereunder, and (ii) payable upon vesting of the shares to which such dividend equivalents relate.

4. The grantee shall not have any stockholder rights with respect to any shares of Common Stock subject to an RSU. However, the Plan Administrator may provide for a grantee to receive one or more dividend equivalents with respect to such shares, entitling the grantee to all regular cash dividends payable on the shares of Common Stock underlying the RSU, which amounts shall be (i) subject to the same vesting requirements applicable to the shares of Common Stock underlying the RSU, and (ii) payable upon issuance of the shares to which such dividend equivalents relate.

5. Should the grantee cease to remain in Service while holding one or more unvested shares of Common Stock issued under the Stock Issuance Program or should the performance objectives not be attained with respect to one or more such unvested shares of Common Stock, then those shares shall be immediately surrendered to the Company for cancellation, and the grantee shall have no further stockholder rights with respect to those shares. To the extent the surrendered shares were previously issued to the grantee for consideration paid in cash, the Company shall repay to the grantee the cash consideration paid for the surrendered shares.

6. Except as prohibited by the last sentence of paragraph 1 above, the Plan Administrator may in its discretion waive the surrender and cancellation of one or more unvested shares of Common Stock which would otherwise occur upon the cessation of the grantee's Service or the non-attainment of the performance objectives applicable to those shares. Such waiver shall result in the immediate vesting of the grantee's interest in the shares of Common Stock as to which the waiver applies. Such waiver may be effected at any time, whether before or after the grantee's cessation of Service or the attainment or non-attainment of the applicable performance objectives.

7. Outstanding RSUs under the Stock Issuance Program shall automatically terminate, and no shares of Common Stock shall actually be issued in satisfaction of those awards, if the Service and/or performance goals established for such awards are not attained. The Plan Administrator, however, shall, except as prohibited by the last sentence of paragraph 1 above, have the discretionary authority to issue shares of Common Stock in satisfaction of one or more outstanding RSUs as to which the designated Service and/or performance goals are not attained. Such authority may be exercised at any time, whether before or after the grantee's cessation of Service or the attainment or non-attainment of the applicable performance objectives.

II. CORPORATE TRANSACTION/CHANGE IN CONTROL

A. All of the Company's outstanding repurchase rights under the Stock Issuance Program shall terminate automatically, and all the shares of Common Stock subject to those terminated rights shall immediately vest in full, in the event of any Corporate Transaction, except to the extent (i) those repurchase rights are to be assigned to the successor corporation (or parent thereof) in connection with such Corporate Transaction, or (ii) such accelerated vesting is precluded by other limitations imposed in the Stock Issuance Agreement, unless the Plan Administrator determines to waive such limitations.

B. Each award which is assigned in connection with (or is otherwise to continue in effect after) a Corporate Transaction shall be appropriately adjusted such that it shall apply and pertain to the number and class of securities issued to the grantee in consummation of the Corporate Transaction with respect to the shares granted to grantee under this Article Three.

C. In the event of a Change in Control, shares of restricted stock and RSUs shall be treated as follows: if the grantee's employment is terminated by the Company without Cause or the grantee resigns due to a Constructive Termination, in either case within the ninety (90) day period preceding or the two (2) year period following the Change in Control, the vesting of such restricted stock and RSUs shall automatically accelerate (and all of the shares of Common Stock subject to such RSUs shall be issued to grantees), and the Company's outstanding repurchase rights under this Article Three shall immediately terminate; provided, however, that if the acquiror or successor refuses to assume the shares of restricted stock or RSUs or substitute an award of equivalent value (as determined by the Committee in its discretion) in connection with the Change in Control, the vesting of such restricted stock or RSUs under this Article Three shall automatically accelerate (and all of the shares of Common Stock subject to such RSUs shall be issued to grantees). To the extent any shares of restricted stock or RSUs vest in whole or in part based on the achievement of performance criteria, the amount that shall vest in accordance with the proviso to clause (2) of the immediately-preceding sentence shall vest based on the higher of actual performance goal attainment through the date of the Change in Control or a prorated amount using target performance and based on the time elapsed in the performance period as of the date of the Change in Control.

III. STOCKHOLDER RIGHTS

A. Individuals who are granted shares of Common Stock pursuant to this Article Three shall be the owners of such shares for all purposes while holding such Common Stock, and may exercise full voting rights with respect to those shares at all times while held by the individuals. Individuals who have been granted RSUs shall have no voting rights with respect to Common Stock underlying RSUs unless and until such Common Stock is reflected as issued and outstanding shares on the Company's stock ledger.

B. Individuals who are granted shares of Common Stock pursuant to this Article Three shall not have dividend rights with respect to such shares prior to the vesting of such shares. However, the Plan Administrator may provide for a grantee to receive one or more dividend equivalents with respect to such shares, entitling the grantee to all regular cash dividends payable on such shares of Common Stock, which amounts shall be (i) subject to the same vesting requirements applicable to the shares of Common Stock granted hereunder, and (ii) payable upon vesting of the shares to which such dividend equivalents relate.

IV. SHARE ESCROW / LEGENDS

Unvested shares may, in the Plan Administrator's discretion, be held in escrow by the Company until the grantee's interest in such shares vests or may be issued directly to the grantee with restrictive legends on the certificates evidencing those unvested shares.

ARTICLE FOUR DIRECTOR GRANT PROGRAM

I. ELIGIBILITY

The individuals eligible to receive grants pursuant to the provisions of this Article Four shall be (i) those individuals who, after the effective date of this amendment and restatement, first become non-employee Board members, whether through appointment by the Board, election by the Company's stockholders, or by continuing to

serve as a Board member after ceasing to be employed by the Company, and (ii) those individuals already serving as non-employee Board members on the effective date of this amendment and restatement. As used herein, a “non-employee” Board member is any Board member who is not employed by the Company on the date in question.

II. TERMS AND CONDITIONS OF DIRECTOR GRANTS

A. **Grants.** Grants under this Article Four shall be made pursuant to a Director Compensation Policy adopted by the Board (the “Director Compensation Policy”) and may be in the form of non-statutory options, RSUs, shares of Common Stock, other awards issuable under the Plan or a combination thereof, as determined by the Committee. In no event shall the aggregate grant date fair value (calculated in accordance with FASB ASC Topic 718) of all awards granted under the Plan during any calendar year to any non-employee Board member (excluding any awards granted at the election of a non-employee Board member in lieu of all or any portion of cash retainers or fees otherwise payable to non-employee Board members in cash), together with the amount of any cash fees or retainers paid to such non-employee Board members during such calendar year with respect to such individual’s service as a non-employee Board member, exceed \$750,000 (or, for a non-employee Board member who first joins the Board, \$1,000,000).

B. Terms and Conditions of Grants.

1. Options.

(i) Term. Each option granted under this Article Four shall be exercisable at such time or times, during such period, and for such number of shares as shall be set forth in the Director Compensation Policy or as otherwise determined by the Plan Administrator and set forth in the instrument evidencing the option grant. No such option, however, shall have a maximum term in excess of ten (10) years from the grant date.

(ii) Option Price. The option price per share shall be fixed by the Plan Administrator. In no event, however, shall the option price per share be less than one hundred percent (100%) of the fair market value per share of Common Stock on the date of the option grant. The option price shall become immediately due upon exercise of the option and shall, subject to Section II.B.1.(iv) of this Article Four and the instrument evidencing the grant, be payable in any manner set forth in Section I.A.2 of Article Two.

(iii) Non-Transferability. During the lifetime of the optionee, each option grant, together with any limited stock appreciation right pertaining to such option, shall be exercisable only by the optionee and shall not be assignable or transferable by the optionee, except to the extent such option or the limited stock appreciation right is assigned or transferred (i) by will or by the laws of descent and distribution following the optionee’s death, or (ii) during optionee’s lifetime either (A) as a gift in connection with the optionee’s estate plan to one or more members of optionee’s immediate family, to a trust in which optionee and/or one or more such family members hold more than fifty percent (50%) of the beneficial interest or to an entity in which more than fifty percent (50%) of the voting interests are owned by optionee and/or one or more such family members, or (B) pursuant to a domestic relations order. The portion of any option assigned or transferred during optionee’s lifetime shall be exercisable only by the person or persons who acquire a proprietary interest in the option pursuant to such assignment. The terms applicable to the assigned portion shall be the same as those in effect for this option immediately prior to such assignment and shall be set forth in such documents issued to the assignee as the Plan Administrator may deem appropriate.

(iv) Stock Appreciation Rights. With respect to each option granted under this Article Four, each optionee shall have the right to surrender all or part of the option (to the extent not then exercised) in exchange for a distribution from the Company in an amount equal to the excess of (i) the fair market value (on the option surrender date) of the number of shares in which the grantee is at the time vested under the surrendered option (or surrendered portion thereof) over (ii) the aggregate option price payable for such vested shares. The distribution shall be made in shares of Common Stock valued at fair market value on the option surrender date.

(v) No Repricing. No option or stock appreciation right may be repriced, regranted through cancellation, including cancellation in exchange for cash or other awards, or otherwise amended to

reduce its option price or exercise price (other than with respect to adjustments made in connection with a transaction or other change in the Company's capitalization as permitted under this Plan) without the approval of the stockholders of the Company.

2. **Grants Generally.**

(i) **Stockholder Rights.** The holder of an option grant under this Article Four shall have none of the rights of a stockholder with respect to any shares subject to such option until such individual shall have exercised the option and paid the exercise price for the purchased shares, and the holder of RSUs granted under this Article Four shall have none of the rights of a stockholder with respect to any shares subject to such RSUs until shares have been delivered in settlement thereof. Without limitation, a grantee shall not have any right to receive dividends with respect to an unexercised option or unsettled RSUs.

(ii) **Corporate Transactions/Changes in Control.** In connection with a Corporate Transaction or a Change in Control, grants under this Article Four shall be treated in the manner specified in Article Two (with respect to options) or Article Three (with respect to shares of Common Stock and RSUs), as applicable.

(iii) Subject to the terms of the Plan, the terms and conditions of the grants under this Article Four shall be determined by the Plan Administrator consistent with the Director Compensation Policy.

ARTICLE FIVE
PERFORMANCE GOALS

I. GENERAL

The Plan Administrator may establish performance criteria and level of achievement versus such criteria that shall determine the number of shares of Common Stock or RSUs to be granted, retained, vested, issued or issuable under or in settlement of or the amount payable pursuant to an award hereunder. In addition, the Plan Administrator may specify that an award or a portion of an award shall be subject to measures based on one or more performance criteria selected by the Committee and specified at the time the award is granted. The Committee shall certify the extent to which any performance criteria have been satisfied, and the amount payable as a result thereof, prior to payment, settlement or vesting of any award subject thereto. Notwithstanding satisfaction of any performance goals, the number of shares of Common Stock issued under or the amount paid under an award may, to the extent specified in the applicable award agreement, be reduced by the Committee on the basis of such further considerations as the Committee in its sole discretion shall determine.

II. PERFORMANCE CRITERIA

For purposes of this Plan, performance criteria may include, among others, any one or more of the following performance criteria, either individually, alternatively or in any combination, applied to either the Company as a whole or to a business unit or subsidiary, either individually, alternatively or in any combination, and measured either quarterly, annually or cumulatively over a period of years, on an absolute basis or relative to a pre-established target, to previous years' results or to a designated comparison group, in each case as specified by the Committee: (i) revenue growth; (ii) earnings before interest, taxes, depreciation and amortization; (iii) earnings before interest, taxes and amortization; (iv) operating income; (v) pre- or after-tax income; (vi) cash flow; (vii) cash flow per share; (viii) net income; (ix) earnings per share; (x) return on equity; (xi) return on invested capital; (xii) return on assets; (xiii) economic value added (or an equivalent metric); (xiv) share price performance; (xv) total shareholder return; (xvi) improvement in or attainment of expense levels; (xvii) improvement in or attainment of working capital levels; (xviii) debt reduction; (xix) progress for advancing drug discovery and/or drug development programs; or (xx) implementation, completion or attainment of measurable objectives with respect to research, development, manufacturing, commercialization, products or projects, or production volume levels. The Committee (A) shall appropriately adjust any evaluation of performance under applicable performance criteria to eliminate the effects of charges for restructurings, discontinued operations, extraordinary items and all items of gain, loss or expense determined to be extraordinary or unusual in nature or related to the acquisition or disposal of a segment of a business or related to a change in accounting principle all as determined in accordance with standards established by opinion No. 30 of the Accounting Principles Board (APB Opinion No. 30) or other applicable or successor accounting provisions, as well as the cumulative effect of accounting changes, in each case as determined in accordance with generally accepted accounting principles or identified in the Company's financial statements or notes to the financial

statements, and (B) may appropriately adjust any evaluation of performance under applicable performance criteria to exclude any of the following events that occurs during a performance period: (i) asset write-downs, (ii) litigation, claims, judgments or settlements, (iii) the effect of changes in tax law or other such laws or provisions affecting reported results, (iv) the adverse effect of work stoppages or slowdowns, (v) accruals for reorganization and restructuring programs and (vi) accruals of any amounts for payment under this Plan or any other compensation arrangement maintained by the Company.

ARTICLE SIX **MISCELLANEOUS**

I. AMENDMENT OF THE PLAN

The Board shall have complete and exclusive power and authority to amend or modify the Plan in any or all respects whatsoever. However, no such amendment or modification shall, without the consent of the holders, adversely affect rights and obligations with respect to options at the time outstanding under the Plan. In addition, certain amendments may require stockholder approval pursuant to applicable laws or regulations.

II. TAX WITHHOLDING

A. The Company's obligation to deliver shares or cash upon the exercise of stock options or stock appreciation rights or upon the grant or vesting of direct stock issuances or RSUs under the Plan shall be subject to the satisfaction of all applicable Federal, State and local income and employment tax withholding requirements.

B. The Plan Administrator may, in its discretion and upon such terms and conditions as it may deem appropriate, provide any or all holders of outstanding options or stock issuances under the Plan (other than the grants under Article Four) with the election to have the Company withhold, from the shares of Common Stock otherwise issuable upon the exercise or vesting of such awards, a whole number of such shares with an aggregate fair market value equal to the minimum amount necessary (or, if determined by the Plan Administrator in its discretion and to the extent adverse accounting treatment does not result, at the maximum applicable individual statutory tax rates) to satisfy the Federal, State and local income and employment tax withholdings (the "Taxes") incurred in connection with the acquisition or vesting of such shares. In lieu of such direct withholding, one or more grantees may also be granted the right to deliver whole shares of Common Stock to the Company in satisfaction of such Taxes. Any withheld or delivered shares shall be valued at their fair market value on the applicable determination date for such Taxes.

III. EFFECTIVE DATE AND TERM OF PLAN

A. The Plan, as amended and restated, shall be effective on the date specified in the Board of Directors resolution adopting the Plan. Except as provided below, each option issued and outstanding under the Plan immediately prior to such effective date shall continue to be governed solely by the terms and conditions of the agreement evidencing such grant, and nothing in this restatement of the Plan shall be deemed to affect or otherwise modify the rights or obligations of the holders of such options with respect to their acquisition of shares of Common Stock thereunder. The Plan Administrator shall, however, have full power and authority, under such circumstances as the Plan Administrator may deem appropriate (but in accordance with Section I of this Article Five), to extend one or more features of this amendment and restatement to any options outstanding on the effective date.

B. Unless sooner terminated in accordance with the other provisions of this Plan, the Plan shall terminate upon the earlier of (i) ten (10) years following the date this amendment and restatement of the Plan is approved by the Board or (ii) the date on which all shares available for issuance under the Plan shall have been issued or cancelled pursuant to the exercise, surrender or cash-out of the options granted hereunder. If the date of termination is determined under clause (i) above, then any options or stock issuances outstanding on such date shall continue to have force and effect in accordance with the provisions of the agreements evidencing those awards.

C. Options may be granted with respect to a number of shares of Common Stock in excess of the number of shares at the time available for issuance under the Plan, provided each granted option is not to become exercisable, in whole or in part, at any time prior to stockholder approval of an amendment authorizing a sufficient increase in the number of shares issuable under the Plan.

IV. USE OF PROCEEDS

Any cash proceeds received by the Company from the sale of shares pursuant to options or stock issuances granted under the Plan shall be used for general corporate purposes.

V. REGULATORY APPROVALS

A. The implementation of the Plan, the granting of any option hereunder, and the issuance of stock (i) upon the exercise or surrender of any option or (ii) under the Stock Issuance Program shall be subject to the procurement by the Company of all approvals and permits required by regulatory authorities having jurisdiction over the Plan, the options granted under it and the stock issued pursuant to it.

B. No shares of Common Stock or other assets shall be issued or delivered under the Plan unless and until there shall have been compliance with all applicable requirements of Federal and state securities laws, including (to the extent required) the filing and effectiveness of the Form S-8 registration statement for the shares of Common Stock issuable under the Plan, and all applicable listing requirements of any stock exchange (or the Nasdaq National Market, the Nasdaq Global Select Market or any successor system, if applicable) on which Common Stock is then trading.

VI. NO EMPLOYMENT/SERVICE RIGHTS

Neither the action of the Company in establishing or restating the Plan, nor any action taken by the Plan Administrator hereunder, nor any provision of the Plan shall be construed so as to grant any individual the right to remain in the employ or service of the Company (or any parent or subsidiary corporation) for any period of specific duration, and the Company (or any parent or subsidiary corporation retaining the services of such individual) may terminate such individual's employment or service at any time and for any reason, with or without cause.

VII. MISCELLANEOUS PROVISIONS

A. Except to the extent otherwise expressly provided in the Plan, the right to acquire Common Stock or other awards under the Plan may not be assigned, encumbered or otherwise transferred by any grantee.

B. Awards issued under the Plan shall be subject to any clawback policy of the Company as in effect from time-to-time.

C. The provisions of the Plan relating to the exercise of options and the issuance and/or vesting of shares shall be governed by the laws of the State of Delaware without resort to that state's conflict-of-laws provisions, as such laws are applied to contracts entered into and performed in such State.

D. The Plan is intended to be an unfunded plan. Grantees are and shall at all times be general creditors of the Company with respect to their awards. If the Committee or the Company chooses to set aside funds in a trust or otherwise for the payment of awards under the Plan, such funds shall at all times be subject to the claims of the creditors of the Company in the event of its bankruptcy or insolvency.

E. **Awards to Non-U.S. Employees.** The Committee shall have the power and authority to determine which subsidiary corporations shall be covered by this Plan and which employees outside the United States shall be eligible to participate in the Plan. The Committee may adopt, amend, or rescind rules, procedures, or sub-plans relating to the operation and administration of the Plan to accommodate the specific requirements of local laws, procedures, and practices. Without limiting the generality of the foregoing, the Committee is specifically authorized to adopt rules, procedures, and sub-plans with provisions that limit or modify rights on death, disability, or retirement or on termination of employment; available methods of exercise or settlement of an award; payment of income, social insurance contributions and payroll taxes; the withholding procedures and handling of any stock certificates or other indicia of ownership which vary with local requirements. The Committee may also adopt rules, procedures or sub-plans applicable to particular subsidiary corporations or locations.

