2022 Annual Report

To Our Stockholders:

In 2022, we set ambitious goals to advance our mission of improving the lives of patients with serious diseases by pioneering therapies created with our revolutionary PROTAC® protein degradation platform. I believe we have met those goals and set the foundation for future growth.

Throughout the year, we reported promising data across our development programs and continued progressing our broad pipeline of targets in oncology and neurology. We initiated multiple clinical trials across our oncology programs and continued utilizing our PROTAC Discovery Engine to expand the applications of protein degradation, with multiple programs now progressing through investigational new drug (IND)-enabling work. We are proud of the protein degradation discovery and development platform we have built at Arvinas.

Clinical and Development Progress

In November and at the San Antonio Breast Cancer Congress in December, we reported positive results from the Phase 2 cohort expansion portion (VERITAC) of a Phase 1/2 trial with vepdegestrant (or ARV-471) in patients with locally advanced or metastatic estrogen receptor (ER)-positive/human epidermal growth factor receptor 2 (HER2) negative breast cancer (ER+/HER2-). Vepdegestrant targets the ER and is being co-developed with Pfizer. These data continued to show a differentiated profile for vepdegestrant and reinforced its potential to become an important new standard of care for patients with ER+/HER2- breast cancer. We have initiated a Phase 3 trial of vepdegestrant as a monotherapy as a second-line treatment in patients with metastatic breast cancer, and we are exploring the potential of vepdegestrant across the treatment landscape. During the year we also initiated multiple clinical trials with vepdegestrant, including in combination with other targeted therapies, and as a monotherapy in the neoadjuvant setting.

Our novel PROTAC protein degraders targeting the androgen receptor (AR) – bavdegalutamide (ARV-110) and ARV-766 – also made significant progress during the year. In February 2022, we reported Phase 2 data from our ARDENT trial that reinforced our belief that bavdegalutamide has the potential to provide a meaningful clinical benefit to a patient population for which few options exist after the progression of metastatic castrate resistant prostate cancer (mCRPC). The ARV-766 program also continued to advance and based on findings from our Phase 1 dose escalation trial, we initiated a Phase 2 clinical trial of ARV-766 in mCRPC.

Corporate Structure and Community Engagement

We made key leadership hires in 2022 to support our transition to a late-stage development organization. The appointments of John Northcott as Chief Commercial Officer; Lisa Sinclair as Senior Vice President, Corporate Operations; and Paul McInulty as Senior Vice President, Regulatory Affairs, all bring key skills and extensive knowledge into the company.

Our ultimate success as an organization is inherently tied to the communities in which we work, live, and serve. With this in mind, we took steps in 2022 to engage with the Greater New Haven and patient communities. We hosted our inaugural “Arvinas Impact Day,” a company-wide community service day benefitting organizations in the Greater New Haven area, with employees participating in activities that support important priorities for Arvinas, including science, technology, engineering, and math (STEM) initiatives, and the Greater New Haven and patient communities. Arvinas also recognized the efforts of up-and-coming researchers bringing innovation, new approaches, and creative thinking to advance the field of targeted protein degradation, and acknowledged their dedication and commitment to this therapeutic approach toward otherwise intractable disease targets with our Global Early Career Researcher Award. We were honored to present the award to Katherine Donovan, Ph.D. of the Dana-Farber Cancer Institute/Harvard Medical School in recognition of her leadership, innovation, and key scientific contributions in the field.

In closing, I want to extend my gratitude to all Arvinas employees for their unwavering commitment to our mission. We are turning targeted protein degradation into one of the most promising areas of medical research and challenging the perceived limits of drug discovery. The Arvinas team is highly motivated and completely focused on developing a new class of medicines with the potential to be transformative for patients, their families, and their health care providers.

I am also grateful to our stockholders, clinical collaborators, and patients participating in our clinical trials. Collectively, their support is a critical piece of our past, current, and future accomplishments.

John Houston, Ph.D.
President & Chief Executive Officer

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2022

OR

☐ **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: 001-38672

ARVINAS, INC.

(Exact name of registrant as specified in its Charter)

Delaware	**47-2566120**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
5 Science Park **395 Winchester Ave.** **New Haven, Connecticut**	**06511**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (203) 535-1456

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, par value $0.001 per share	ARVN	The Nasdaq Global Select Market LLC

Securities registered pursuant to Section 12(g) of the Act:

None

(Title of class)

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

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

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

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

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

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

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

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO x

As of June 30, 2022, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the Common Stock held by non-affiliates of the registrant was approximately $2,175.7 million, based on the closing price of the registrant's Common Stock on such date. The number of shares of registrant's Common Stock, $0.001 par value per share, outstanding as of February 17, 2023 was 53,271,491.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report incorporates by reference information from the definitive Proxy Statement for the registrant's 2023 Annual Meeting of Stockholders, which is expected to be filed with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2022.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND RISK FACTOR SUMMARY

Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "goals," "will," "would," "could," "should," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- the initiation, timing, progress and results of our current and future clinical trials of ARV-471, bavdegalutamide (ARV-110), and ARV-766, including statements regarding the period during which the results of the clinical trials will become available;
- the timing of, and our ability to obtain, marketing approval of ARV-471, bavdegalutamide (ARV-110) and ARV-766, and the ability of ARV-471, bavdegalutamide (ARV-110), ARV-766 and our other product candidates to meet existing or future regulatory standards;
- the potential achievement of milestones and receipt of payments under our collaborations, including our collaboration with Pfizer Inc., or Pfizer, entered into in July 2021, or the ARV-471 Collaboration;
- our plans to pursue research and development of other product candidates;
- our plans to submit Investigational New Drug Applications or Clinical Trial Applications;
- the potential advantages of our platform technology and our product candidates;
- the extent to which our scientific approach and platform technology may potentially address a broad range of diseases and disease targets;
- the potential receipt of revenue from future sales of our product candidates;
- the rate and degree of market acceptance and clinical utility of our product candidates;
- our estimates regarding the potential market opportunity for our product candidates;
- our sales, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for manufacture of our product candidates;
- our ability to enter into additional collaborations with third parties;
- our intellectual property position;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the impact of COVID-19 on our business and operations;
- the impact of government laws and regulations; and
- our competitive position.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the "Risk Factors" section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our future results may differ materially from what we expect. We do not assume any obligation to update any forward-looking statements except as required by applicable law.

This Annual Report on Form 10-K also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. Cross-trial comparisons are not based on head-to-head studies and no direct comparisons can be made.

Throughout this Annual Report on Form 10-K, the "Company," "Arvinas," "we," "us," and "our," except where the context requires otherwise, refer to Arvinas, Inc. and its consolidated subsidiaries, or any one or more of them as the context may require, and "our board of directors" refers to the board of directors of Arvinas, Inc.

The Arvinas name and logo are our trademarks. We also own the service mark and the registered U.S. trademark for PROTAC®. This Annual Report on Form 10-K contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this Annual Report on Form 10-K, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

Risk Factor Summary

Our business is subject to a number of risks that if realized could materially affect our business, prospects, operating results and financial condition. These risks are discussed more fully in the "Risk Factors" section of this Annual Report on Form 10-K. These risks include the following:

- We have incurred significant losses since our inception. We expect to incur losses over at least the next several years and may never achieve or maintain profitability. Our net losses totaled $282.5 million, $191.0 million and $119.3 million for the years ended December 31, 2022, 2021, and 2020, respectively. To date, we have not generated any revenue from product sales and may never be profitable.
- We will need substantial additional funding to continue our operations. If we are unable to raise capital when needed, we may be required to delay, limit, reduce or terminate our research, product development programs or any future commercialization efforts and raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.
- Our approach to the discovery and development of product candidates based on our PROTAC technology platform is unproven, which makes it difficult to predict the time, cost of development and likelihood of successfully developing any products.
- We are early in our development efforts. We are developing ARV-471 for the treatment of patients with locally advanced or metastatic ER+/HER2- breast cancer and bavdegalutamide (ARV-110) and ARV-766 for the treatment of men with metastatic castration-resistant prostate cancer. Additional product candidates are still in preclinical development. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.
- Drug development involves a lengthy and expensive process, with an uncertain outcome. We cannot be certain of the timely completion or outcome of our preclinical testing and clinical trials. and cannot predict if the FDA or similar regulatory authorities outside the United States will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of our programs. The results of preclinical or early clinical studies of our product candidates may not be predictive of the results of later clinical trials. In addition, interim top-line and preliminary data from our clinical trials that we may announce or publish from time to time can change as more patient data becomes available and are subject to audit and

verification procedures that could result in material changes in the final data. If we are unable to obtain, or there are delays in obtaining, required regulatory approvals, we will not be able to successfully commercialize our product candidates and our business will be materially harmed.

- We are developing and may continue to develop our product candidates in combination with other drugs. If the FDA or similar regulatory authorities outside of the United States do not approve these other drugs, or revoke their approval of such drugs, or if safety, efficacy, manufacturing or supply issues arise with the drugs we choose to evaluate in combination with our product candidates, we may be unable to obtain approval of or market our products.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- We currently have, and anticipate in the future seeking additional, third-party collaborators for the research, development, and potential future commercialization of some of our PROTAC programs. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. Further, we may seek to establish additional collaborations. If we are not able to establish collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans.
- We rely, and expect to continue to rely, on third party research organizations to conduct our clinical trials and third party manufacturing organizations for the manufacture of both drug substance and finished drug product for our product candidates for preclinical testing and clinical trials, and we expect to continue to do so for commercialization. If the third party research organizations on which we relay do not perform satisfactorily, including failing to meet deadlines for the completion of trials, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. Further, our reliance on third party manufacturing organizations may increase the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.
- We will need to grow the size of our organization, and we may experience difficulties in managing this growth, which could disrupt our operations. In particular, if we are not able to establish sales and marketing capabilities, we may not be successful in commercializing our product candidates if and when they are approved.
- If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired, and we may not be able to compete effectively in our market.
- Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations

PART I

Item 1. Business.

Overview

We are a clinical-stage biotechnology company dedicated to improving the lives of patients suffering from debilitating and life-threatening diseases through the discovery, development and commercialization of therapies that degrade disease-causing proteins. We use our PROTAC Discovery Engine, our proprietary technology platform to engineer proteolysis targeting chimeras, or PROTAC targeted protein degraders, that are designed to harness the body's own natural protein disposal system to selectively and efficiently degrade and remove disease-causing proteins. We believe that our targeted protein degradation approach is a therapeutic modality that may provide distinct advantages over existing modalities, including traditional small molecule therapies and gene-based medicines. We have a robust preclinical pipeline of PROTAC protein degraders targeting a broad range of intracellular disease targets, including those representing proteins that currently cannot be addressed by existing small molecule therapies, commonly referred to as "undruggable" targets. We are using our PROTAC Discovery Engine to build an extensive pipeline of protein degradation product candidates to target diseases in areas of unmet need, including oncology (including immuno-oncology), neuroscience and other therapeutic areas. We have three investigational clinical stage programs: ARV-471, a novel PROTAC estrogen receptor, or ER, protein degrader for the treatment of patients with locally advanced or metastatic ER positive / human epidermal growth factor receptor 2, or HER2, negative, or ER+/HER2-, breast cancer and bavdegalutamide (ARV-110) and ARV-766, each an oral PROTAC protein degrader that targets the androgen receptor protein, or AR, for the treatment of men with metastatic castration-resistant prostate cancer, or mCRPC.

ARV-471

ARV-471 is an investigational orally bioavailable PROTAC protein degrader designed to target and degrade the ER for the treatment of patients with locally advanced or metastatic ER+/HER2- breast cancer. We are co-developing ARV-471 with Pfizer, Inc., or Pfizer, pursuant to a collaboration agreement that we and Pfizer entered into in July 2021. We granted Pfizer worldwide co-exclusive rights to develop and commercialize ARV-471.

In preclinical studies, ARV-471 demonstrated near-complete ER degradation in tumor cells, induced robust tumor shrinkage when dosed as a single agent in multiple ER-driven xenograft models, and showed superior anti-tumor activity when compared to a standard of care agent, fulvestrant, both as a single agent and in combination with a cyclin-dependent kinase, or CDK, 4/6 inhibitor. In 2019, we initiated a Phase 1 clinical trial of ARV-471 designed to assess the safety, tolerability and pharmacokinetics of ARV-471, which also included measures of anti-tumor activity as secondary endpoints and in the fourth quarter of 2020, we initiated a Phase 1b cohort expansion of ARV-471 in combination with the CDK4/6 inhibitor Ibrance® (palbociclib). In 2021, we initiated VERITAC, the Phase 2 single agent expansion cohort of the ARV-471 clinical trial.

In the third quarter of 2022, we initiated TACTIVE-E, a Phase 1b clinical trial with ARV-471 in combination with everolimus in patients with metastatic breast cancer. Also in the third quarter of 2022, we initiated with Pfizer a Phase 1b trial of ARV-471 as a monotherapy in Japanese patients.

In the fourth quarter of 2022, we presented initial data from VERITAC at the San Antonio Breast Cancer Symposium and we initiated, with Pfizer, the VERITAC-2 Phase 3 trial with ARV-471 as a monotherapy as a second-line and later treatment in patients with ER+/HER2- metastatic breast cancer. Also in the fourth quarter of 2022, we initiated the first of two arms in the ongoing Phase 1b umbrella trial of ARV-471, with ARV-471 in combination with each of the CDK4/6 inhibitors abemaciclib and ribociclib (TACTIVE-U). We initiated the second of two arms in the first quarter of 2023. In addition, in the fourth quarter of 2022, we initiated a Phase 2 clinical trial with ARV-471 as a monotherapy in patients with early breast cancer in the neoadjuvant setting (TACTIVE-N).

In the first quarter of 2023, we and Pfizer requested a meeting with the U.S. Food and Drug Administration, or the FDA, to review the proposed update to the trial protocol for the VERITAC-3 first-line, metastatic ER+ / HER2- breast cancer Phase 3 trial of ARV-471 in combination with IBRANCE® (palbociclib) to determine the optimal dose of palbociclib as part of the trial design. Following correspondence and alignment with the FDA, we and Pfizer determined an approach to the planned Phase 3 trial to enable trial initiation in the second half of 2023, which includes a Phase 3 lead-in to evaluate the optimal dose of palbociclib (100 mg or 75

mg) in combination with 200 mg ARV-471. This approach follows the recent analysis of data from the ongoing Phase 1b combination study of ARV-471 with palbociclib, in which an increase in palbociclib exposure was observed relative to historical palbociclib pharmacokinetic data.

In the first half of 2023, we expect, with Pfizer, to provide an update with preliminary data from the Phase 1b combination trial with palbociclib (Part C of the Phase 1/2 trial) and in the second half of 2023, we expect, with Pfizer, to submit and present data from the Phase 1b combination trial of ARV-471 with palbociclib at a medical congress and. Also in the second half of 2023, we expect, with Pfizer, to initiate a Phase 3 trial with ARV-471 in combination with palbociclib as a first-line treatment in patients with ER+ / HER2- locally advance or metastatic breast cancer. and initiate additional arms of the TACTIVE-U, Phase 1b combination trial with other targeted therapies, during 2023.

Bavdegalutamide (ARV-110)

Bavdegalutamide (ARV-110) is an investigational orally bioavailable PROTAC protein degrader designed to target and degrade the AR, for the treatment of men with mCRPC.

In preclinical studies, bavdegalutamide demonstrated activity of AR mutation or overexpression, both common mechanisms of resistance to currently available AR-targeted therapies. In 2019, we initiated a Phase 1/2 clinical trial of bavdegalutamide designed to assess the safety, tolerability and pharmacokinetics of bavdegalutamide and also included measures of anti-tumor activity as secondary endpoints, including reduction in prostate specific antigen, or PSA, a well-recognized biomarker of prostate cancer progression. In 2019, we also received Fast Track designation for bavdegalutamide for mCRPC. In 2020, we initiated ARDENT, the Phase 2 single agent expansion portion of the bavdegalutamide clinical trial. In 2021, we initiated a Phase 1b clinical trial of bavdegalutamide in combination with abiraterone for the treatment of men with mCRPC.

In the first quarter of 2022, we announced completed Phase 1 and interim ARDENT data for bavdegalutamide at the 2022 American Society of Clinical Oncology Genitourinary (ASCO GU) Cancers Symposium.

We expect to initiate a global Phase 3 trial with a confirmed dose for bavdegalutamide for the treatment of men with mCRPC with AR T878/H875 tumor mutations in the second half of 2023. Also in the second half of 2023, we expect to complete enrollment in the Phase 1b clinical trial with bavdegalutamide in combination with abiraterone.

ARV-766

ARV-766 is an investigational orally bioavailable PROTAC protein degrader designed to target AR with a different profile than bavdegalutamide, as a potential treatment for men with mCRPC.

In preclinical studies, ARV-766 degraded all tested resistance-driving point mutations of AR, including L702H, a mutation associated with treatment with abiraterone and other AR-pathway therapies. In 2021, we initiated a Phase 1/2 clinical trial for ARV-766 designed to assess the safety, tolerability and pharmacokinetics of ARV-766, which trial also includes measures of anti-tumor activity as secondary endpoints, including reduction in PSA. In the second half of 2022, we initiated a Phase 2 expansion trial of ARV-766 for the treatment of men with mCRPC.

We expect to share data from the Phase 1 dose escalation trial of ARV-766 for the treatment of mCRPC in the second quarter of 2023.

We anticipate initiating a Phase 1b or Phase 2 dose escalation trial for either of bavdegalutamide or ARV-766 in patients with AR-dependent tumors who have not previously received novel hormonal agents, or NHA, such as enzalutamide or abiraterone, and who may benefit from bavdegalutamide or ARV-766 therapy, in the second half of 2023.

Each of ARV-471, bavdegalutamide and ARV-766 has demonstrated potent and selective protein degradation in our preclinical studies. We believe favorable clinical trial results in these initial oncology programs could provide validation of our platform as a new therapeutic modality for the potential treatment of diseases caused by dysregulated intracellular proteins regardless of therapeutic area.

We have been a leader in the field of directed protein degradation using chimeric small molecules since our founding in 2013. We have assembled a scientific team with extensive know-how and translational medicine expertise to develop PROTAC targeted protein degraders with features not previously disclosed in published third-party studies. Our management team draws on extensive experience in all phases of drug discovery and development gained at large pharmaceutical and biotechnology companies to continue to advance our product pipeline and expand the capabilities of our platform.

We have designed and optimized our proprietary PROTAC Discovery Engine for the discovery of PROTAC therapeutics to address diseases caused by abnormal proteins or aberrant protein expression. We engineer our PROTAC targeted protein degraders to tag a target protein for degradation through the ubiquitin proteasome system, one of the cell's natural protein disposal systems, and then to iteratively degrade additional target protein molecules. The PROTAC Discovery Engine includes advanced screening capabilities, including in-house high-throughput and deoxyribonucleic acid, or DNA, -encoded library screening abilities that are tailored to the needs of incorporation into PROTAC protein degraders and to optimize their drug-like properties. Following selection and identification, we use tools including predictive computational modeling and privileged linkers that allow the potential for increased potency and selectivity. Finally, we have utilized our own proprietary PROTAC-specific optimization strategies, which we refer to as the Arvinas Rules, to create PROTAC degraders that, for example, are capable of being delivered through multiple routes of administration, including oral delivery, as well as PROTAC targeted protein degraders that are able to penetrate the blood brain barrier.

In addition to our clinical product candidates, we are expanding our pipeline by utilizing our platform to potentially address historically undruggable targets. Unlike existing small molecule inhibitor therapies, our PROTAC targeted protein degraders can degrade proteins using any available binding site, including low-affinity active binding sites or non-functional binding sites, bringing biological utility to ligands that would otherwise be ineffective. While some gene-based medicines are also seeking to address undruggable targets, we believe that our PROTAC targeted protein degraders confer the advantages of traditional small molecule therapies, such as broad tissue distribution, multiple routes of administration, including oral delivery, a well-established development pathway and relative ease of manufacturing.

We are further diversifying our pipeline by developing new PROTAC targeted protein degraders against targets for which we believe protein degradation offers advantages to existing therapeutic modalities, including PROTAC degraders that are designed to reach targets in deep brain regions and are capable of being delivered through multiple routes of administration, including oral delivery. We have engineered PROTAC targeted protein degraders that, in preclinical studies, have successfully achieved blood-brain barrier penetration, a key step in developing drugs with the potential to treat neurodegenerative disease. We believe there are many other indications for which our PROTAC technology may be advantageous.

By year-end 2023, we expect to submit an investigational new drug, or IND, application or clinical trial application, or CTA, for our PROTAC degrader designed to target each of the BCL6 protein, a protein mutated in patients with different forms of Non-Hodgkins Lymphoma, or NHL, including Diffuse Large B-Cell Lymphoma, or DLBCL, and the LRRK2 protein, a protein kinase that has been genetically linked to some forms of Parkinson's Disease, or PD. We also expect to progress at least two additional PROTAC protein degrader programs in IND-enabling or CTA-enabling studies by year-end 2023.

Our Strategy

Our mission is to discover, develop, and commercialize therapies that improve the lives of patients suffering from debilitating and life-threatening diseases. We use our proprietary PROTAC Discovery Engine Platform to engineer PROTAC targeted protein degraders that are designed to harness the body's own natural protein disposal system to selectively and efficiently remove disease-causing proteins. We believe that our proprietary PROTAC technology is a new therapeutic modality with the potential to provide distinct advantages over existing therapies and to address a broad range of targets, including undruggable proteins. The key elements of our strategy are to:

- **Advance clinical development of our lead programs, which address the well-understood oncology targets AR and ER.** Our strategy for our PROTAC platform includes the initial pursuit of oncology targets with well-understood biology, well-characterized disease models and established biomarkers. We have one product candidate in Phase 3 clinical development and two product candidates in Phase 2 clinical development. We are focused on creating potential therapies for patients in both oncology and neuroscience and we believe favorable clinical trial results in these

initial oncology programs would validate the broader therapeutic potential of our PROTAC technology and PROTAC Discovery Engine.

- **Utilize our PROTAC Discovery Engine platform to address historically undruggable and difficult-to-drug targets.** We are applying our platform to develop treatments for diseases associated with historically undruggable targets. Our platform enables us to build PROTAC targeted protein degraders with the potential to degrade these proteins through the cell's natural protein degradation process using any available binding site, including low-affinity active binding sites or non-functional binding sites, bringing biological utility to ligands that would otherwise be inactive. We also believe that many "difficult-to-drug" targets, where prior approaches are inadequate, will also provide opportunities to apply our PROTAC Discovery Engine.
- **Selectively collaborate to realize the full potential of our platform.** We are using our PROTAC Discovery Engine to build an extensive pipeline of product candidates. Our co-development/co-commercialization collaboration with Pfizer has the potential to accelerate and broaden global development and commercialization of ARV-471. In an effort to realize the full potential of our PROTAC technology, our ongoing strategic collaborations with Bayer AG, or Bayer, Genentech, Inc. and F. Hoffman-La Roche Ltd., or Genentech, and Pfizer address targets across multiple therapeutic areas. In addition to these collaborations in human therapeutics, in 2019 we established a joint venture called Oerth Bio LLC, or Oerth Bio, with Bayer to pursue our PROTAC technology in agricultural applications. We have and plan to continue to selectively pursue collaborations with leading biopharmaceutical companies with specialized capabilities or know-how, including global development and commercial expertise and capabilities for those products for which we retain full development and commercialization rights. We believe this selective approach to collaboration will further broaden the therapeutic reach of our PROTAC technology, as well as complement and expand our internal development expertise.
- **Develop new therapeutics with distinct advantages over existing modalities, including gene-based medicines.** We intend to address targets for which we believe protein degradation and the tunable features of our PROTAC targeted protein degraders offer advantages compared to existing therapeutic modalities. For example, unlike gene-based medicines, our PROTAC targeted protein degraders confer the advantages of traditional small molecule therapies, such as broad tissue distribution, multiple routes of administration, including oral delivery, a well-established development pathway and relative ease of manufacturing. In addition, we have engineered PROTAC targeted protein degraders that, in preclinical studies, have successfully achieved blood brain barrier penetration, creating potential opportunities for our PROTAC technology in neurodegenerative diseases. We also believe there are many other indications for which our technology may be advantageous, including autoimmune, anti-infective and inflammatory conditions.
- **Continue to expand the capabilities of our PROTAC Discovery Engine and the breadth of our intellectual property portfolio**. We are investing in our research and development activities to expand the capabilities of our PROTAC Discovery Engine and the breadth of our intellectual property portfolio. This includes: research into novel E3 ligases, key proteins in the ubiquitin proteasome system, that may have tissue-specific or disease-specific features; the discovery of novel binding ligands; the discovery of orally bioavailable and blood brain barrier penetrant PROTAC protein degraders; and improvement of our PROTAC targeted protein degrader design and optimization processes. We have exclusive worldwide rights to our platform technology, as well as issued patents for composition of matter in the United States and other countries for ARV-471 and bavdegalutamide and patent applications pending for composition of matter in the United States and key countries for ARV-766 and patent applications pending for composition of matter in the United States and other key countries for our exploratory programs. We also have patents and pending patent applications for broad platform coverage for other PROTAC targeted protein degraders using specific E3 ligases.

Our Focus

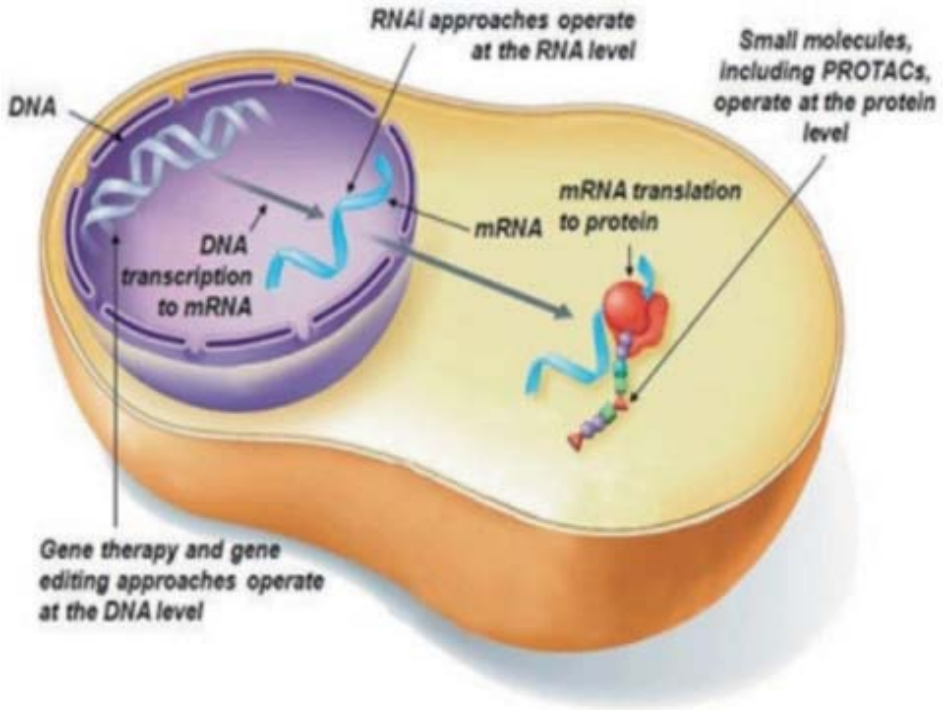
The Role of Proteins in Disease

Human cells produce tens of thousands of different proteins, the entirety of which is referred to as the proteome. Proteins are responsible for many structural, functional and regulatory processes in cells.

Proteins are large, complex biomolecules made through a series of steps based on instructions carried from DNA, the genetic “blueprint” within the cell. Generally, sequences of DNA are converted into messenger ribonucleic acid, or mRNA, during a process called transcription. mRNA provides the template that specifies the assembly of a particular sequence of amino acids into proteins during a process known as translation. The amino acid sequence dictates, among other things, the conformation, or 3-D shape, of the resulting protein. Proteins can have complex shapes, with multiple chains of amino acids folding together in some cases to reach a final form. The final form of the protein, as well as the timing, location and concentration of its expression within the cell, is essential to the protein’s intended function.

In healthy cells, the transcription and translation processes contribute to producing properly folded proteins in the right amounts and at the correct times to ensure normal cell health and function. This balance can be disrupted by a variety of events and factors, such as cellular stress, genetic mutations and transcriptional or translational errors, which can then lead to cellular overexpression, abnormal production rates, misfolding or mutations of proteins. When proteins are overexpressed or mutated, a wide variety of diseases can result. For example, it is well documented that overexpression of androgen receptor, a nuclear hormone receptor, is implicated in prostate cancer. Similarly, overexpression of estrogen receptor is known to be associated with breast cancer. In neurodegenerative diseases, abnormal deposition of misfolded or aggregated proteins in the brain, including the intraneuronal aggregation of the microtubule-associated protein tau, are associated with Alzheimer’s disease. Recent genomic advances continue to implicate the role of specific proteins in many disease states.

There are multiple therapeutic approaches, both approved and in development, to treat diseases caused by abnormal proteins or aberrant protein expression. Each operates at a different point in the lifecycle of the protein, as illustrated in the following graphic:



Small Molecule Inhibitors, Gene Therapy and Gene Editing

Traditional small molecules seek to block or inhibit the expression or function of an errant protein. While there are numerous examples of safe and effective small molecule therapies, their efficacy can be limited by weak or incomplete binding of the therapeutic molecule to the relevant binding site on the protein, the cell’s ability to counteract the inhibitory effect of the drug by producing more of the protein, mutation of the target, or evolution of the cell to rely on alternate pathways. These cellular responses often result in a need for higher dosing levels, which can in turn introduce safety challenges from off-target and toxic effects, or drug resistance.

Gene therapy approaches act by augmenting the errant protein with normal protein by using viral vectors to introduce DNA from an exogenous source that codes for a functional protein. While there have been promising advances in this field, the fundamental approach is limited by delivery, expression efficacy, pre-treatment conditioning, durability and manufacturing challenges that curtail the practical utility of gene therapy.

Gene editing or gene silencing approaches such as CRISPR/Cas9, RNA interference and antisense act by either correcting or inactivating, or knocking out, the gene that would otherwise be transcribed and translated to express the errant protein. By correcting or knocking out the gene, the errant protein is never made, preventing its downstream negative effects. In the case of CRISPR/Cas9, the resulting modification of the gene occurs at the DNA level and is believed to be irreversible. While there are examples of approved therapies in this field that have the potential to correct specific genetic defects, gene editing and gene silencing approaches generally face delivery, stability, biodistribution, specificity and selectivity challenges, in addition to significant manufacturing hurdles.

Protein Degradation

When proteins become old, mutated, misfolded or simply have served their purpose, they are naturally degraded by the body through the ubiquitin proteasome system in which cells mark or tag a particular protein for disposal by attaching several molecules of the small regulatory protein ubiquitin to the protein to be disposed. This process generally proceeds along the following steps in rapid sequence:

- The E1 enzyme activates ubiquitin, which is then transferred to an E2 enzyme.
- An E3 ubiquitin ligase, or E3 ligase, transfers the ubiquitin from the E2 enzyme to a specific target protein.
- Once a chain of at least four ubiquitins are attached to the target protein, the proteasome recognizes the polyubiquinated protein.
- The proteasome breaks down or degrades the protein into its amino acid components.

Several therapeutic approaches work at the protein level by modulating the ubiquitin proteasome system to harness the cell's natural protein disposal system to degrade and remove a protein. Degradation can be induced by inhibiting chaperone molecules such as HSP90, which are known to facilitate correct protein folding, resulting in tagging misfolded proteins for degradation. HSP90 inhibitors, however, have shown limited efficacy in the clinic to date.

Some degraders use an approach that causes a conformational change in a specifically targeted protein, resulting in a misfolded protein, which triggers the cell's innate protein degradation system to dispose of the misfolded protein. Although these compounds have shown efficacy, they only induce the degradation of those proteins able to adopt a non-native state, leaving a wide array of protein targets unaddressed.

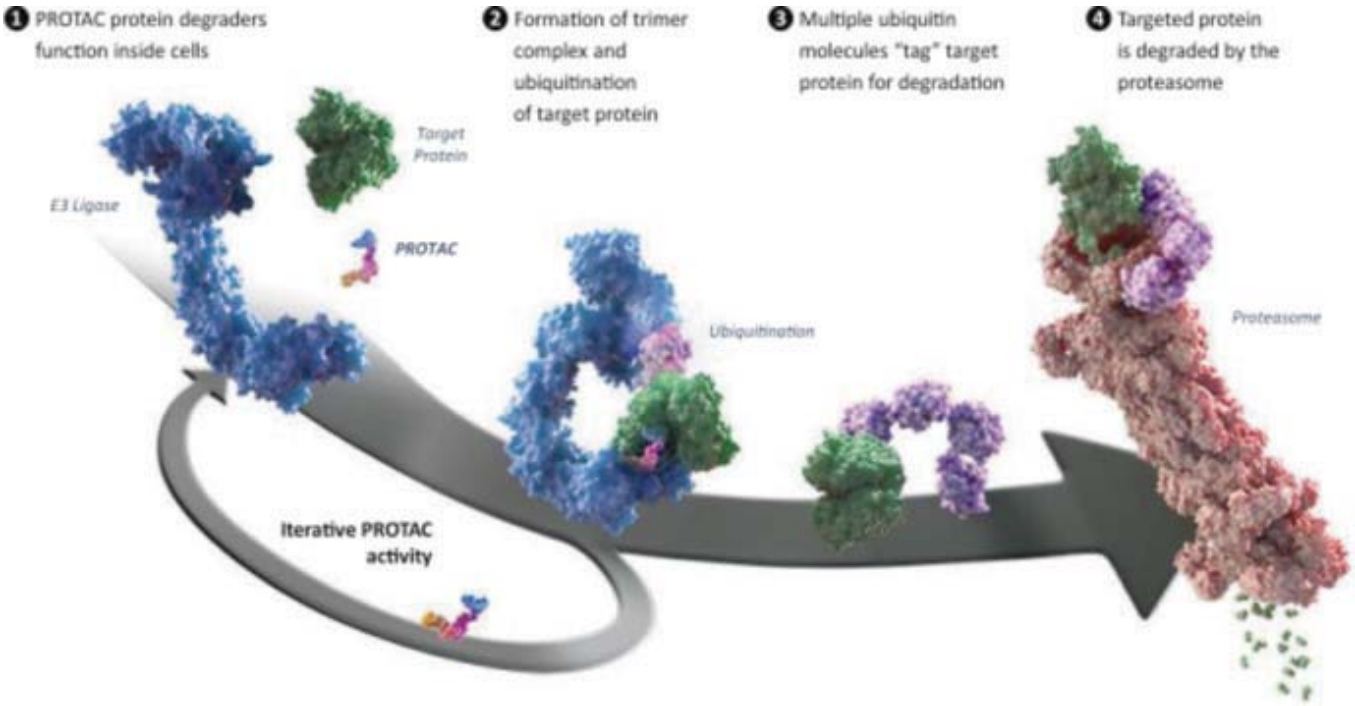
Chimeric small molecules use a different protein degradation approach. Instead of causing improper folding or inhibiting molecules that facilitate proper folding of the target protein, chimeric small molecules directly recruit an E3 ligase to tag specifically targeted proteins with ubiquitin, signaling the proteasome to degrade the targeted protein. Our PROTAC targeted protein degraders take this approach to protein degradation.

PROTAC Targeted Protein Degraders — Our Approach to Protein Degradation

We have engineered our PROTAC targeted protein degraders to utilize the cell's naturally occurring protein disposal system, directing the proteasome to recognize and degrade specific proteins associated with disease. Our PROTAC targeted protein degraders are chimeric small molecules with two operative ends—one, a ligand that binds to the protein targeted for degradation, and the other, a ligand that binds to an E3 ligase. These two ligands are connected by a chemical chain linker. Our PROTAC targeted protein degraders bring the targeted protein and the E3 ligase together into a three-component grouping known as a trimer complex to facilitate the transfer of ubiquitin to the target protein. Once four ubiquitins are attached in a chain to the target protein, the proteasome recognizes and degrades the protein. The entire cycle from the formation of the trimer complex, which can occur in a period of nanoseconds, to degradation of the target protein by the proteasome happens over a period of minutes. After our PROTAC targeted protein degrader facilitates the tagging of a target protein molecule with ubiquitin through formation of the trimer complex, it can move on to another target

protein molecule to conduct the degradation process again, potentially completing this cycle hundreds of times before eventually being metabolized or eliminated from the cell. We refer to this recycling as our PROTAC targeted protein degraders' iterative mechanism of action.

The figure below depicts our PROTAC-induced cycle from E3 ligase binding and target protein recruitment, to trimer formation and ubiquitin transfer, to degradation of the target protein by the proteasome, to the release of ubiquitin and PROTAC targeted protein degrader for further degradation cycles.



Our Discovery Platform — PROTAC Discovery Engine

We have designed and optimized our PROTAC Discovery Engine for the discovery of PROTAC targeted protein degrader therapeutics to address diseases caused by abnormal proteins or aberrant protein expression. The PROTAC Discovery Engine includes advanced screening capabilities, including in-house high-throughput and DNA-encoded library screening abilities that are tailored to the needs of incorporation into PROTAC protein degraders and to optimize their drug-like properties. Following selection and identification, we use tools including predictive computational modeling and privileged linkers that allow the potential for increased potency and selectivity. Finally, we have utilized our own proprietary Arvinas Rules to create PROTAC degraders that, for example, are capable of being delivered through multiple routes of administration, including oral delivery, as well as PROTAC targeted protein degraders that are able to penetrate the blood brain barrier.

Design and Optimization of our PROTAC Targeted Protein Degraders

As genomic knowledge and advances in genome mapping have increased, the understanding of proteins implicated in diseases has similarly increased. We undertake a rigorous evaluation process to prioritize protein targets for which we believe our PROTAC approach can achieve differentiated clinical outcomes for patients over existing modalities. Our PROTAC Discovery Engine is built from over 20 years of experience, know-how, and intellectual property and comprises three stages:

Ligase Selection and Ligand Identification

- **E3 KnowledgeBase** - The human body has more than 600 E3 ligases, and we select ligands for E3 ligases from our proprietary library for incorporation into our PROTAC targeted protein degraders. We continue to research additional E3 ligases that are expressed in specific tissues or diseases, and identify or discover associated binding ligands, to create novel PROTAC protein degraders that recruit E3 ligases with targeted expression patterns, such as tumor or central nervous system-localized E3 ligases, that may be beneficial for the development of targeted cancer and neurologic therapies. To enable targeted protein degradation via alternative E3 ligases, we have discovered and characterized novel small molecule ligands targeting the E3 ligase KLHDC2. We have functionalized these novel KLHDC2-targeting small molecules into robust and potent KLHDC2- PROTAC degraders and demonstrate KLHDC2-dependent degradation of target proteins across cell lines. Furthermore, we have leveraged biochemical studies to understand mechanistic assembly of the KLHDC2 holo-E3 complex together with its cognate adapter proteins in addition to structural studies to show the dynamic tetramer formation of KLHDC2 E3 assemblies induced by small molecule engagement. In doing so, we have expanded the arsenal of E3 ligases that can be targeted by small molecules and may be hijacked for targeted protein degradation. We believe our success with the diverse set of E3 ligases that we are currently employing and the binders of other E3 ligases that we are researching provide us with a competitive advantage as we develop a range of products with different technical characteristics.
- **Advanced Screening Capabilities** - We select ligands for incorporation into our PROTAC targeted protein degraders from a variety of sources. The ligands we select, which target the desired protein for degradation or E3 ligase for incorporation into our PROTAC targeted protein degraders, may include (1) *de novo* ligands discovered through high-throughput screening, biophysical directed binding approaches, virtual or *in silico* computer-based screening, and affinity-based hit identification through our in-house DNA-encoded libraries that that are tailored to the needs of incorporation into PROTAC protein degraders and to optimize their drug-like properties or (2) ligands that are known to bind protein targets but may have faced therapeutic limitations that we believe our PROTAC technology can overcome, such as lack of potency or function, metabolic instability or off-target effects.

Rapid PROTAC Design

- **Zone of Ubiquitination -** Bringing the targeted protein and the E3 ligase together into a trimer complex is necessary but not sufficient for degradation. We use structural and biochemical information to predict precisely which lysine residues on the target protein can be “tagged” with ubiquitin, and we design PROTAC degraders to exploit this knowledge.
- **ANGLE: Arvinas Next Generation Linker Evolution** - We connect the selected protein-targeting ligands and E3 ligase ligands with our privileged chemical linkers. Linker selection is critical for rapid identification of protein degraders and can introduce function and selectivity to a nonfunctional or nonselective binding ligand upon incorporation into a PROTAC targeted protein degrader molecule. Linker composition can also be used to modulate properties of our PROTAC targeted protein degraders, such as membrane permeability, aqueous solubility, metabolic stability and biodistribution. We select from a proprietary library of conformationally privileged linkers to enable the efficient formation of the trimer complex essential to ubiquitin transfer and protein degradation.
- **Predictive Computational Modeling -** We use trimer structure-based computational modeling, sometimes aided by structural biology-generated insights, and design algorithms to rapidly identify potent degraders.
- **Proteomics -** A PROTAC degrader is often more selective than the targeting warhead. We have proteomics capabilities that enable us to understand that specificity in precise detail and iterate quickly to optimize the selectivity of our PROTAC degraders for the protein target.

Turning Degraders into Drugs

- **Arvinas Rules -** Optimization of traditional small molecule agents tends to focus on guidelines that increase the chances of such molecules having sufficient permeability and solubility to make them orally bioavailable. Chimeric small molecules, including our PROTAC targeted protein degraders, are larger than traditional small molecule therapeutics, such that the conventional optimization parameters prevalent in traditional drug discovery do not readily apply. As such we have developed and apply our own proprietary Arvinas Rules for our PROTAC targeted protein degraders. Through our Arvinas Rules, we have made PROTAC targeted protein degraders that are orally bioavailable and that cross the blood brain barrier.
- **Deep knowledge of *in vivo* PK/PD and efficacy relationships -** Our understanding of molecular features that impact PROTAC biodistribution and target degradation, in the body, enables us to create PROTAC degraders with drug-like properties and activities. We can use this understanding to rapidly progress from target identification to PROTAC optimization and development.

Key Features of Our PROTAC Targeted Protein Degraders

In the design, optimization and development of our PROTAC targeted protein degraders, we focus on the following key features that we believe are critical to successfully engineering PROTAC targeted protein degrader therapeutics with potentially robust application across multiple indications and therapeutic areas: potency, selectivity, and deliverability and versatility. We have harnessed these features to successfully target and degrade a wide range of protein classes, including nuclear proteins, transcription factors, epigenetic modulators, membrane proteins, cytosolic proteins and high molecular weight neuroprotein aggregates.

Potency

The potency of our PROTAC technology is driven by two key characteristics: the iterative mechanism of our PROTAC targeted protein degraders and the ability to turn weak binders into potent degraders.

Iterative Mechanism

Our PROTAC targeted protein degraders behave iteratively to repeatedly induce the ubiquitination and subsequent degradation of proteins. As a result, protein degradation may be observed with PROTAC targeted protein degrader concentrations much lower than those required for typical small molecule inhibition, even operating at picomolar concentrations. We expect that the high cellular potency of PROTAC targeted protein degrader could provide the possibility of removal of proteins at levels equivalent to the knock out effect intended by gene-based medicines currently being explored. Our PROTAC targeted protein degraders offer potentially significant therapeutic advantages, including low doses, low drug exposures and practical dosing intervals, potentially mitigating toxicity and tolerability risks.

The iterative mechanism of our PROTAC targeted protein degraders potentially leads to more complete and lasting inactivation of downstream signaling in cells. In oncology, this translates into improved inhibition of tumor cell growth and reduces the likelihood of cell compensation through activation of alternative proteins, a common risk associated with small molecule inhibitors. This enables PROTAC targeted protein degraders to operate in a broad therapeutic space between desired degradation-induced pharmacology and unwanted inhibition-induced effects.

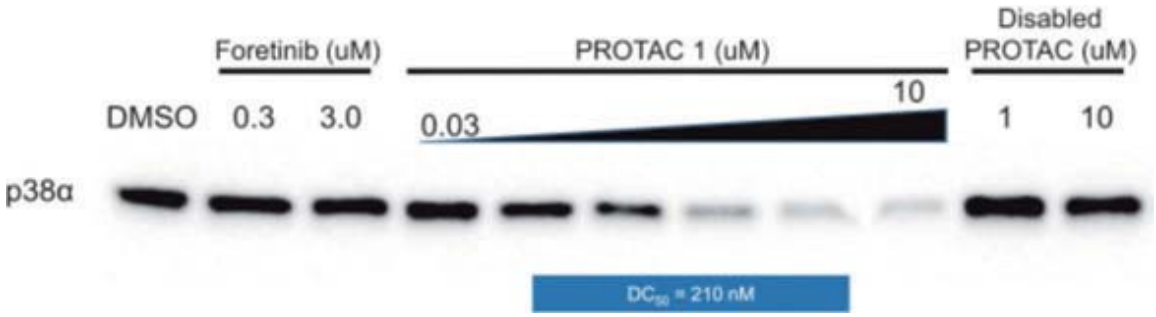
Once the pre-existing reservoir of the targeted protein is depleted, our PROTAC targeted protein degraders only need to degrade newly resynthesized protein to maintain their effect. Depending on the resynthesis rate of the protein, this may be achievable with low tissue concentrations of PROTAC targeted protein degrader, which could lead to safety benefits and opportunities for flexible dosing regimens.

Weak Binders Become Potent Degraders

Using our platform and know-how, we are able to engineer potent PROTAC targeted protein degraders that do not require a high degree of binding strength to their targets. This contrasts with small molecule inhibitors, which require strong binding to a target protein and function by continually occupying the protein's active site. The potency of our PROTAC targeted protein degraders is determined by a number of kinetic

factors: formation of the trimer complex, rapid ubiquitination, trafficking of the ubiquitinated target to the proteasome and release of the PROTAC targeted protein degrader to enter another iterative cycle of degradation. As a result, a PROTAC targeted protein degrader with a low level of target protein occupancy can maintain a deep and prolonged suppression of protein levels, leading to the desired pharmacological effect. This provides opportunities to use our PROTAC technology to repurpose small molecules that only weakly bind to their target to create potent degraders as PROTAC targeted protein degraders.

For example, we have published experiments where we built PROTAC targeted protein degraders from the known protein kinase inhibitor foretinib, which is a relatively weak binder to the protein p38α, a protein implicated in immune disorders and heart disease. We constructed a foretinib-based PROTAC targeted protein degrader we refer to as PROTAC 1, which happened to further weaken the binding affinity to p38α. Binding affinity is measured by K_D, or equilibrium dissociation constant. In this case, we observed that PROTAC 1 exhibited a tenfold reduction in binding affinity relative to foretinib, decreasing from 1 micromolar, or μM, to 11 μM. Despite the significantly weaker binding affinity, PROTAC 1 achieved potent degradation of p38α with a DC_{50}, a concentration that results in half maximal degradation, of 210 nanomolar, or nM, which means that its degradation potency is approximately 50-fold better than its binding strength. The figure below shows a western blot of cells treated with increasing concentrations (left to right) of foretinib, the PROTAC 1, and an inactivated (non-degrading) version of PROTAC 1. The decreasing presence of the p38α protein is depicted by a lighter shade of the p38α band in the western blot as the doses of the PROTAC 1 increase. This demonstrates our ability to use a weak binder to create a potent PROTAC targeted protein degrader. Based on our experience, we believe that with additional medicinal chemistry effort, the degradation potency of this weak-binding PROTAC targeted protein degrader could be further increased.

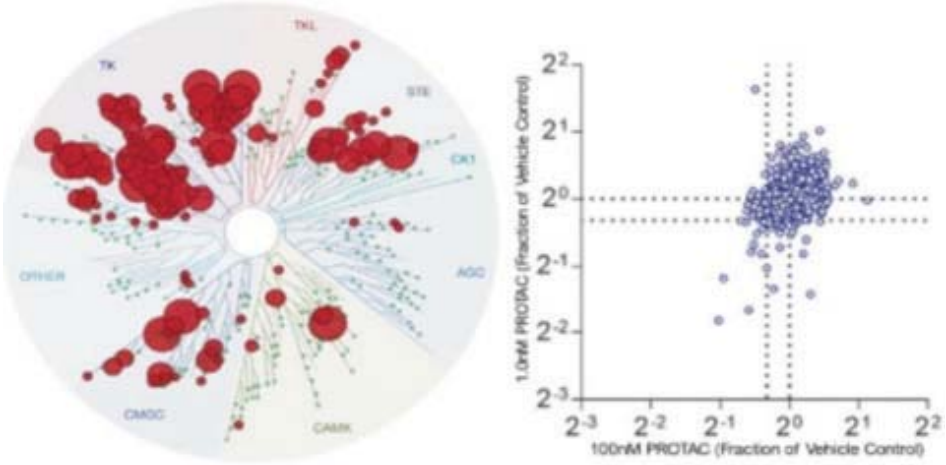


Selectivity

When a ligand is incorporated into a PROTAC targeted protein degrader, the trimer complex initiated by the PROTAC targeted protein degrader often causes the ligand's selectivity to increase, meaning that the degradation profile of a PROTAC targeted protein degrader can be even more selective than the binding profile of the ligand alone. By minimizing the binding of a ligand to off-target proteins and maximizing selectivity for a target protein, our PROTAC targeted protein degraders may reduce the potential for incidental degradation of normal, healthy proteins and unwanted drug effects and toxicity.

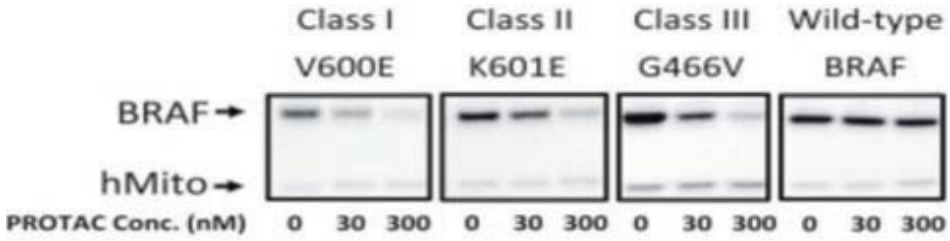
We published experiments in which a ligand binding to 133 kinases degraded fewer than ten proteins when incorporated into a PROTAC targeted protein degrader with limited additional modification. The figure below on the left depicts foretinib binding to 133 protein kinases as measured by a competitive binding assay. The figure on the right depicts cells treated with a foretinib-based PROTAC targeted protein degrader degrading

only a small subset of cellular proteins (lower left quadrant of the graph) as shown by mass spectrometry analysis.



With further modification, and based on our experience, we believe it is possible to engineer promiscuous binders such as this into more selective protein degraders, and when starting with less promiscuous, yet still unselective, binders, identify very selective PROTAC target protein degraders.

This selectivity allows for engineering of PROTAC targeted protein degraders that degrade only the mutated and unwanted protein, while sparing the normal, or wild-type, protein that may be necessary for healthy function. For example, we have demonstrated degradation of abnormal, but not wild-type, forms of the BRAF protein using a PROTAC targeted protein degrader. Wild-type BRAF helps transmit chemical signals from outside the cell to the cell's nucleus and is part of a pathway that regulates cell proliferation, differentiation, migration and apoptosis. Mutations of BRAF, however, have been associated with a number of different cancers. As shown in the figure below, our PROTAC targeted protein degrader degraded BRAF mutants, as depicted by a lighter shade in the columns labeled 300 nM, representative of each of the three classes of BRAF mutations, while not degrading the wild-type BRAF, as depicted by an unchanging shade in each of the columns shown on the western blot.



1hMito is a protein this particular PROTAC targeted protein degrader is not targeted to degrade, and is included as a control to ensure total protein is equivalent in each lane.

Deliverability and Versatility

Our PROTAC targeted protein degraders have the potential for delivery through multiple routes of administration to reach target proteins, and certain of our PROTAC targeted protein degraders are capable of penetrating the blood brain barrier. In addition, the broad expression of the E3 ligases we target and the potential to turn weak binding ligands into potent degraders allows the application of our PROTAC technology to develop treatments for diseases associated with proteins that cannot be addressed by existing small molecule therapies.

Deliverability

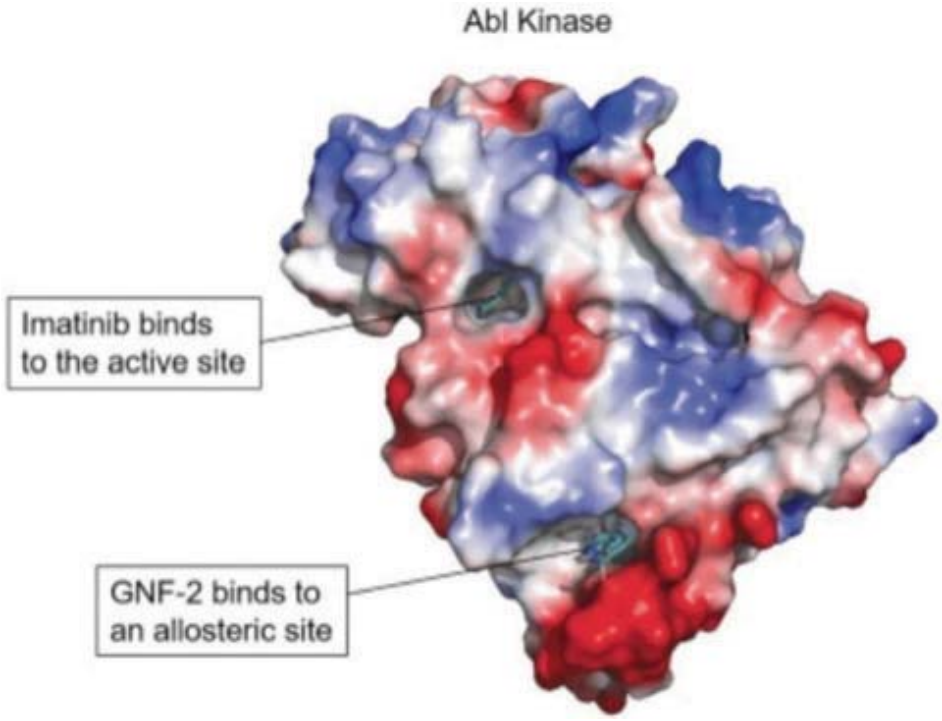
We have developed PROTAC targeted protein degraders that are capable of being delivered orally, intravenously, subcutaneously and intrathecally, among other routes of administration, as well as PROTAC

targeted protein degraders that are able to penetrate the blood brain barrier. The multiple routes of delivery for our PROTAC targeted protein degraders potentially provide many attractive clinical dosing options. For example, oral delivery can offer a differentiating, competitive and commercial advantage over other therapeutic approaches such as gene-based medicines which require parenteral administration. Further, oral administration avoids risks of adverse events associated with intravenous or intramuscular administration, such as the potential for infection and blood clots at the infusion site.

Versatility

We believe our PROTAC targeted protein degraders may have potential application in a wide range of therapeutic areas because the E3 ligases we currently target are expressed widely across tissue types. Ligands that bind to some proteins may be of only weak affinity. However, we believe that our PROTAC technology will allow the degradation of proteins through such low affinity active binding sites or non-functional binding sites. Our ability to design weak binding PROTAC targeted protein degraders that nonetheless initiate rapid ubiquitination and subsequent degradation of targeted proteins has the potential to expand the number of disease-causing proteins targeted for drug development to include undruggable targets. We believe that rendering these targets druggable for the first time represents the true breadth and potential of our PROTAC Discovery Engine.

We conducted an experiment designed to demonstrate that non-functional binding sites, analogous to those that may be present on proteins considered undruggable, can be used to target proteins for degradation by PROTAC targeted protein degraders. The figure below depicts a structural model of the Abl tyrosine kinase. This protein kinase possesses an enzymatic active site that is inhibited by the marketed small molecule, imatinib. The Abl kinase also has a second, non-functional active site, called an allosteric site, in its structure that can bind a different small molecule, named GNF-2, which despite binding allosterically (with a relatively weak K_D of 500 nM), inhibits only the wild type protein (C-Abl), but not BCR-Abl-a mutated form of Abl implicated in chronic myelogenous leukemia.



When GNF-2 is converted into a PROTAC targeted protein degrader and used to treat cells, both BCR-Abl and C-Abl are effectively degraded. The figure below shows western blots of cells treated by increasing concentrations of our PROTAC targeted protein degrader and shows decreasing presence of each of BCR-Abl

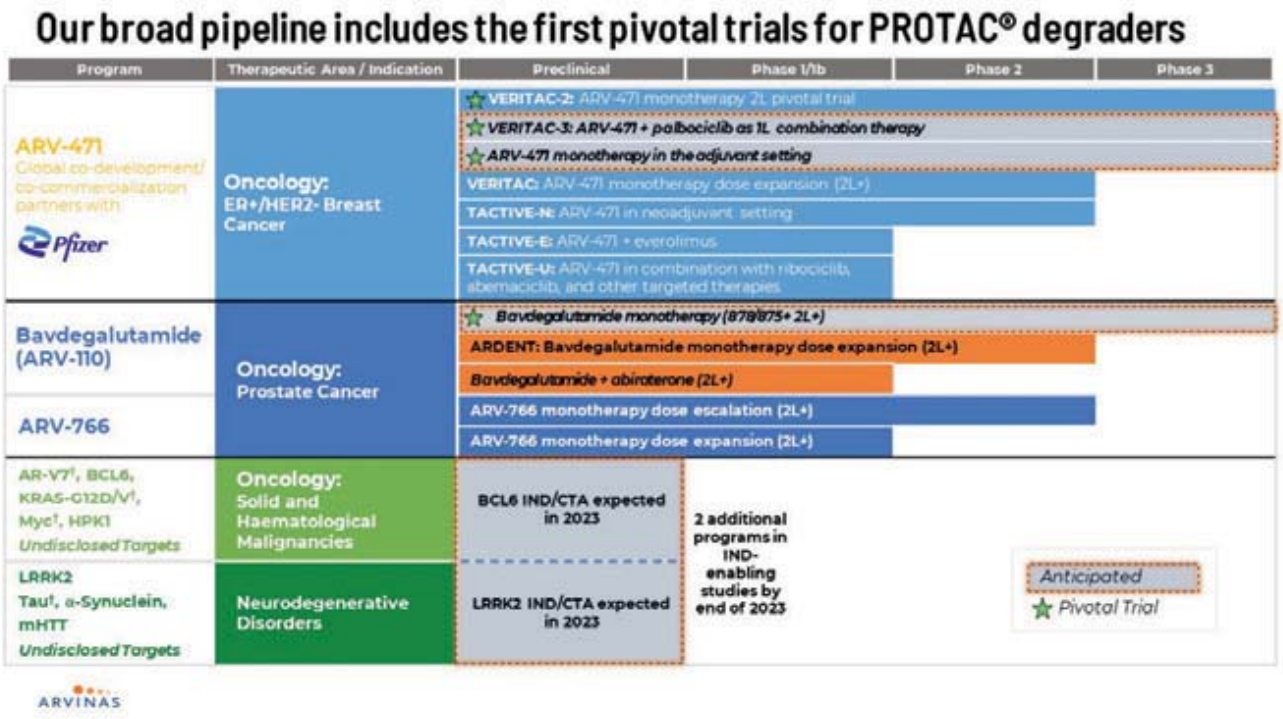
and C-Abl protein (depicted by a lighter shade of the BCR/Abl and C-Abl band in the western blot). Downstream signaling, as denoted by reduction of phosphorylated Stat5 (pStat5), is subsequently inhibited.

1Tubulin is a protein the GNF-2 PROTAC targeted protein degrader is not targeted to degrade, and is included as a control to ensure total protein is equivalent in each lane.

PROTAC-induced degradation may offer a solution for historically undruggable proteins because only binders, not functional inhibitors, are needed to facilitate E3 ligase recruitment and initiation of the degradation process. The probability of finding a suitable ligand using binding-site-agnostic screening is increased because the function of the ligand itself is not required. As a result, there is the potential for PROTAC targeted protein degraders to generate therapeutics from poorly selective ligands, weak-affinity ligands, or ligands that may not be intrinsically biologically active.

Our Product Pipeline and Programs

Our platform has generated several promising degradation product candidates that may be capable of targeting diseases in a wide range of organ systems and tissues. We and our collaborators have initiated programs across multiple therapeutic areas with the goal of developing and delivering life-changing therapies to patients in need. Our lead therapeutic programs are summarized in the table below.



ER+/HER2-, estrogen receptor+/human epidermal growth factor receptor 2-; mCRPC, metastatic castration-resistant prostate cancer; BCL6, B-cell lymphoma 6 protein; KRAS, Kirsten rat sarcoma; HPK1, hematopoietic progenitor kinase 1; mHTT, mutant huntingtin. IND, investigational new drug; CTA, clinical trial application

These agents are currently under investigation. Their safety and effectiveness for these investigational uses have not been established.

† Denotes historically undruggable proteins

In addition to the programs above and our early-stage development collaborations with Pfizer, Genentech, and Bayer, we are conducting exploratory research and development work on multiple other undisclosed targets.

Our Clinical Stage Programs

ARV-471 for the Treatment of Patients with Locally Advanced or Metastatic ER + / HER2 - Breast Cancer

We are developing ARV-471, an orally bioavailable ER degrading PROTAC targeted protein degrader, as an alternative to, and potentially more potent degrader than, the intramuscular injection fulvestrant and other selective ER degraders currently approved or in development for the treatment of patients with locally advanced or metastatic ER+ / HER2- breast cancer. We have chosen ER degradation as a therapeutic focus given the well-documented biology of ER signaling as a principal driver in a high percentage of breast cancers. ARV-471 has demonstrated activity in ER+ breast cancer preclinical models. We are clinically investigating ARV-471 for use as a single agent and in combination with CDK4/6 inhibitors such as palbociclib, abemaciclib and ribociclib, everolimus and other targeted therapies. We believe ARV-471 has the potential to improve clinical outcomes over current standards of care for patients with locally advanced or metastatic ER+ / HER2- breast cancer as well as in earlier treatment settings.

Breast Cancer - Patient Population and Market Opportunity

Breast cancer is the most common cancer diagnosed among women in the United States and the second leading cause of cancer death in women. The American Cancer Society estimates that in 2023 there will be approximately 298,000 women diagnosed with invasive breast cancer in the United States and that one in eight women in the United States will develop breast cancer in her lifetime. Approximately 67% to 80% of all breast cancers are ER+.

Treatment options for breast cancer depend on many different factors, including the stage of the cancer and whether the cancer cells contain hormone receptors. Patients with locally advanced or metastatic breast cancer are treated with systemic therapy, including hormone therapy, chemotherapy and targeted therapy, either as single-agents or in combination. Patients with locally advanced or metastatic ER+ / HER2- breast cancer are often treated with hormone therapy, such as an aromatase inhibitor, sometimes in combination with targeted drugs such as CDK4/6 inhibitors. In patients with aggressive disease or whose disease continues to progress with a hormonal treatment regimen, chemotherapy may be prescribed. Treatment with chemotherapy is generally postponed for as long as possible due to the potential for severe side effects including neuropathies, nausea, diarrhea, decreased mental capacity and increased risk of infections.

A current standard of care for patients with ER+ / HER2- locally advanced or metastatic breast cancer is fulvestrant, an ER degrader administered as a monthly intramuscular injection, either as a single-agent or in combination with another targeted therapy. While fulvestrant has validated the importance of ER degradation as a therapeutic intervention, up to 50% of ER can remain when compared to baseline levels after six months of treatment with fulvestrant, providing an opportunity for more potent ER degraders. In January 2023, the FDA approved the ER degrader elacestrant for postmenopausal women or adult men with ER+ / HER2-, ESR1-mutated advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy.

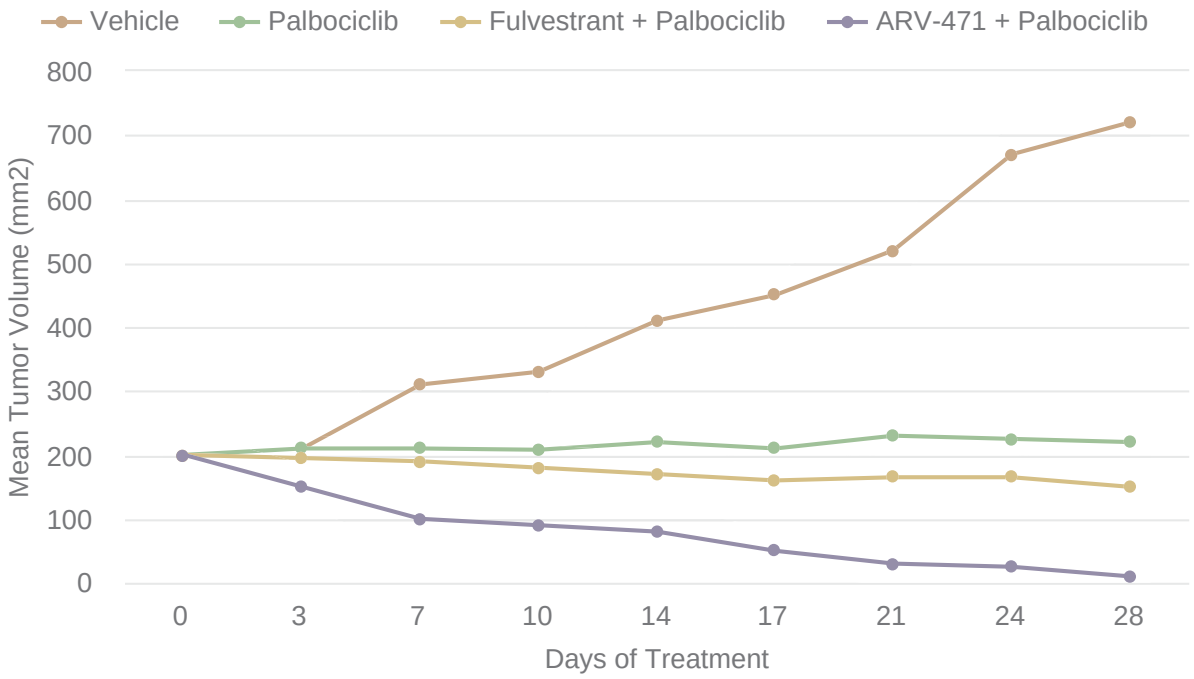
Preclinical Development

We have conducted a comprehensive preclinical program to study ARV-471 as a potential treatment for patients with locally advanced or metastatic ER+ / HER2- breast cancer. In our preclinical studies, ARV-471 demonstrated superior ER degradation compared to fulvestrant. ARV-471 has also demonstrated superior tumor regression when combined with a CDK4/6 inhibitor compared to fulvestrant and the same combination partner.

In *in vitro* models, ARV-471 has induced ER degradation in multiple cell lines typically used in breast cancer research. In *in vivo* experiments ARV-471 has achieved superior tumor growth inhibition and degradation compared to fulvestrant. We have tested ARV-471 for tumor growth inhibitory activity using an industry-standard MCF-7 xenograft mouse model. MCF-7 is a well-characterized estradiol-dependent ER+ / HER2- cell line that forms tumors when implanted in the mammary fat pad of female mice. ARV-471 resulted in very high tumor growth inhibition when dosed daily orally at 10 mpk and more than 80% tumor shrinkage when dosed daily orally at 30 mpk for 28 days. At both doses, ARV-471 demonstrated superior activity compared to a clinically relevant dose of fulvestrant, which is 200 mpk twice per week for two weeks and then once per week for two weeks. After 28 days of dosing in this efficacy study, the MCF-7 tumors were removed from the mice and processed for western blots to observe the level of ER degradation induced by oral dosing of ARV-471. ARV-471 reduced ER by 85%, on average, at 10 mpk as compared to the control tumors and by 89%, on average, at 30 mpk as compared to the control tumors.

We have also conducted preclinical studies to test ARV-471 in a tumor line derived directly from a patient, referred to as a patient derived xenograft, or PDX, model. This model is derived from a tumor with an ESR1 mutation (Y537S), which is a mutation in the ER that occurs in patients who have been treated with standard-of-care agents such as tamoxifen or an aromatase inhibitor, such as letrozole, and has been cited as a mechanism of resistance to those drugs. These studies included a comparison with fulvestrant. In this 28-day dosing study, oral ARV-471 inhibited tumor growth by 99% at the 10 mpk dosing level and by 106% at the 30 mpk dosing level which was observed to be superior at both dosing levels to a clinically relevant dose of 200 mpk of fulvestrant. Further, ARV-471 was shown to reduce ER by 79% and 88% at the 10 mpk and 30 mpk dosing levels, respectively, compared with 63% at the 200 mpk of fulvestrant dosing level.

We have also conducted studies of ARV-471 in combination with palbociclib, a CDK4/6 inhibitor that is standard of care when used together with fulvestrant. In these studies, we have achieved significant tumor shrinkage with ARV-471 in ER+ / HER2- MCF-7 xenograft models. As shown in the figure below, in a 28-day dosing study in MCF-7 xenografts, ARV-471 at 30 mpk daily in combination with palbociclib was superior in shrinking tumors, as compared to either palbociclib as a single agent at 60 mpk daily, or the standard-of-care combination of palbociclib at 60 mpk daily plus fulvestrant at 200 mpk twice per week for two weeks and then once per week for two weeks.



We believe that ARV-471 may also show compelling activity in combination with other targeted agents currently used or in clinical trials for locally advanced or metastatic breast cancer including PI3K and mTOR inhibitors and have tested and plan to continue to test these combinations in preclinical models.

Our Clinical Trials

In 2019, we initiated dosing in a Phase 1 clinical trial for ARV-471. The trial is an open-label dose-escalation study in which we dosed with locally advanced or metastatic ER+ / HER2- breast cancer who had progressed on at least two prior endocrine therapy regimens and a CDK4/6 inhibitor. Eligible patients may have also received up to three prior regimens of cytotoxic chemotherapy.

In 2020, we amended the protocol for our Phase 1 clinical trial for ARV-471, to include the Phase 2 expansion cohort and a Phase 1b cohort expansion of ARV-471 in combination with Ibrance® (palbociclib), respectively. The dose escalation portion of our Phase 1/2 clinical trial of ARV-471 was designed to assess safety, tolerability and pharmacokinetics, or PK, of ARV-471 in patients with locally advanced or metastatic ER+/ HER2- breast cancer, as well as measures of anti-tumor activity as secondary endpoints.

In 2021, we initiated VERITAC, the Phase 2 cohort expansion portion of the ARV-471 clinical trial. We announced initial results from VERITAC in the fourth quarter of 2022. In VERITAC, patients were treated with either 200 mg or 500 mg ARV-471 with a primary endpoint of clinical benefit rate, or CBR, (rate of confirmed complete response, confirmed partial response, or stable disease ≥ 24 weeks). Secondary endpoints included overall response rate, or ORR, duration of response, or DOR, progression free survival, or PFS, and overall survival, or OS, as well as safety and pharmacokinetics.

As of the data cut-off date of June 6, 2022, 71 patients with locally advanced or metastatic ER+/HER2- breast cancer in the VERITAC expansion cohort were treated once-daily with oral doses of ARV-471 at 200 mg (n=35) or 500 mg (n=36). All patients were previously treated with CDK 4/6 inhibitors; 79% of patients were previously treated with fulvestrant; 73% of patients were previously treated with chemotherapy; and 45% received chemotherapy in the metastatic setting. Patients in VERITAC had a median of four lines of prior therapies.

At the time of data cutoff, ARV-471 administered at 200 mg (n=35) and 500 mg (n=36) demonstrated antitumor activity in all CDK4/6 inhibitor-pretreated patients, as measured by a CBR of 38% (total n=71) in all patients, 51.2% in patients with mutant ESR1 tumors (n=41), and 20% in patients with ESR1 wild-type tumors (n=25). At 200 mg, ARV-471 achieved a CBR of 37.1% (n=35) in all patients and 47% in patients with mutant ESR1 tumors (n=19); and at 500 mg, a CBR of 39% (n=36) in all patients and 55% in patients with mutant ESR1 tumors (n=22).

ARV-471 also demonstrated preliminary median progression-free survival, or mPFS, of 3.7 months, a secondary endpoint, in all evaluable patients (n=71) and 5.7 months in patients with mutant ESR1 tumors (n=41) For the 200 mg cohort, ARV-471 demonstrated mPFS of 3.5 months in all evaluable patients (n=35) and 5.5 months in patients with mutant ESR1 tumors (n=19). At the time of the data cutoff, data for the 500 mg cohort were immature and therefore not included in a separate analysis.

ARV-471 was well tolerated across both dose levels. Treatment related adverse events (TRAEs) were primarily Grade 1 and 2, with five patients experiencing Grade 3/4 TRAEs. In the 200 mg cohort, TRAEs were: Grade 1 (n=13): 37%; Grade 2 (n=13): 37%; and Grade 3 or 4 (n=2): 6%. Grade 3/4 TRAEs in the 200 mg cohort were Grade 3 QT prolonged (n=1) and Grade 3 thrombocytopenia and Grade 4 hyperbilirubinemia (n=1). In the 500 mg cohort, TRAEs were: Grade 1 (n=11): 31%; Grade 2 (n=9): 25%; and Grade 3 or 4 (n=3): 8%. Grade 3/4 TRAEs in the 500 mg cohort were Grade 3 fatigue (n=1), Grade 3 decreased appetite (n=1), and Grade 3 neutropenia (n=1).

There was one discontinuation due to a treatment-emergent adverse event, or TEAE, and no dose reductions in the 200 mg cohort. There were two discontinuations and three dose reductions in the 500 mg cohort.

In the third quarter of 2022, we initiated TACTIVE-E, a Phase 1b clinical trial with ARV-471 in combination with everolimus in patients with metastatic breast cancer. Also in the third quarter of 2022, we initiated with Pfizer a Phase 1b trial of ARV-471 as a monotherapy in Japanese patients.

In the fourth quarter of 2022, we and Pfizer initiated the VERITAC-2 Phase 3 trial with ARV-471 as a second-line treatment in patients with ER+ / HER2- metastatic breast cancer, which trial is actively recruiting. In the fourth quarter of 2022, we also initiated with Pfizer TACTIVE-U, the Phase 1b trial with ARV-471 in combination with ribociclib and abemaciclib, in two of the combination arms. In addition, we have initiated sites and are actively recruiting patients for TACTIVE-N, a Phase 2 clinical trial with ARV-471 as a monotherapy in patients with early breast cancer in the neoadjuvant setting in the fourth quarter of 2022.

In the fourth quarter of 2022, we presented initial data from VERITAC at the San Antonio Breast Cancer Symposium and we initiated, with Pfizer, the VERITAC-2 Phase 3 trial with ARV-471 as a monotherapy as a second-line and later treatment in patients with ER+/HER2- metastatic breast cancer. Also in the fourth quarter of 2022, we initiated the first of two arms in the ongoing Phase 1b umbrella trial of ARV-471, with ARV-471 in combination with each of the CDK4/6 inhibitors abemaciclib and ribociclib (TACTIVE-U). We initiated the second of two arms in the first quarter of 2023. In addition, in the fourth quarter of 2022, we initiated a Phase 2 clinical trial with ARV-471 as a monotherapy in patients with early breast cancer in the neoadjuvant setting (TACTIVE-N).

In the first quarter of 2023, we provided an update from the most recent analysis of data from the ongoing Phase 1b trial of ARV-471 in combination with palbociclib. The following were observed:

- An approximate increase of 50% in mean palbociclib exposure (i.e., pharmacokinetic area under the curve and Cmax) in the fed state was observed relative to historical palbociclib pharmacokinetic data in the fasted state.
- Grade 3/4 neutropenia, a known dose-related adverse reaction associated with palbociclib, was 76% for 200 mg ARV-471 with 125 mg palbociclib (n=21).
- As per the U.S. Package Insert, or USPI, the starting dose of palbociclib for patients with ER+ / HER2- metastatic breast cancer is 125 mg. As per the palbociclib USPI, a Grade ≥3 decrease in neutrophil

counts was reported in 66% of patients receiving IBRANCE plus letrozole in Study 1 (PALOMA-2) and 66% of patients receiving IBRANCE plus fulvestrant in Study 2 (PALOMA-3).

- There was no increase in the rate of infection reported in the ARV-471 with palbociclib Phase 1b investigation relative to the rates reported in the registrational Phase 3 studies of palbociclib.
- The neutropenia events in the ARV-471 Phase 1b trial were manageable with standard dose reductions of palbociclib.
- In the arm combining palbociclib with 200 mg ARV-471, one of 21 patients discontinued.

In the first quarter of 2023, we announced updated guidance related to the anticipated initiation of the VERITAC-3 first-line, metastatic ER+ / HER2- breast cancer Phase 3 trial of ARV-471 in combination with IBRANCE® (palbociclib). In the most recent analysis of data from the ongoing Phase 1b combination trial of ARV-471 with palbociclib, an increase in palbociclib exposure was observed relative to historical palbociclib pharmacokinetic data. In light of the recent data analysis, in the first quarter of 2023, we and Pfizer requested a meeting with the U.S. Food and Drug Administration, or the FDA, to review the proposed update to the trial protocol for the VERITAC-3 first-line, metastatic ER+ / HER2- breast cancer Phase 3 trial of ARV-471 in combination with IBRANCE® (palbociclib) to determine the optimal dose of palbociclib as part of the trial design. Following correspondence and alignment with the FDA, we and Pfizer determined an approach to the planned Phase 3 trial to enable trial initiation in the second half of 2023, which includes a Phase 3, lead-in to evaluate the optimal dose of palbociclib (100 mg or 75 mg) in combination with 200 mg ARV-471. Based on this modified approach, we and Pfizer expect to initiate the trial, as anticipated, in the second half of 2023.

In the first half of 2023, we expect, with Pfizer, to provide an update with preliminary data from the Phase 1b combination trial with palbociclib (Part C of the Phase 1/2 trial) and in the second half of 2023, we expect, with Pfizer, to submit and present data from the Phase 1b combination trial of ARV-471 with palbociclib at a medical congress and. Also in the second half of 2023, we expect, with Pfizer, to initiate a Phase 3 trial with ARV-471 in combination with palbociclib as a first-line treatment in patients with ER+ / HER2- locally advance or metastatic breast cancer. and initiate additional arms of the TACTIVE-U, Phase 1b combination trial with other targeted therapies, during 2023.

Bavdegalutamide (ARV-110) and ARV-766 for the Treatment of Men with Metastatic Castration-Resistant Prostate Cancer

We are developing bavdegalutamide (ARV-110) and ARV-766, each an orally bioavailable, AR degrading PROTAC targeted protein degrader, for the treatment of men with mCRPC. Both bavdegalutamide and ARV-766 demonstrated activity in preclinical models of AR overexpression and AR mutations, both common mechanisms of resistance to current standard-of-care agents in men with prostate cancer. We believe that the differentiated PROTAC pharmacology of bavdegalutamide and ARV-766, including their iterative activity, has the potential to translate into significantly improved clinical outcomes over current standard-of-care agents.

Prostate Cancer - Patient Population and Market Opportunity

In the United States, prostate cancer is the second leading cause of cancer death in men. Current estimates predict that one in eight men will be diagnosed with prostate cancer in his lifetime. The American Cancer Society estimates that in 2023 there will be over 288,000 new cases of prostate cancer in the United States and approximately 34,700 deaths from the disease. Men with mCRPC have a poor prognosis and a predicted survival rate of fewer than two years from the initial time of progression.

Treatment options for prostate cancer depend on many different factors, including the stage of the cancer. Castration-resistant prostate cancer is defined by disease progression despite androgen deprivation therapy, or ADT, and is often indicated by rising levels of PSA. In making treatment evaluations, physicians monitor disease burdens in several ways, including changes in PSA levels. Increased PSA blood levels are considered by many physicians as indicative of cancer progression, and alternative treatment options may be considered. Current standard of care for men with castration-resistant prostate cancer provides that patients should initially receive a combination of ADT and either abiraterone, which works by decreasing androgen levels, or enzalutamide, which works by blocking androgen binding to AR. If the disease progresses despite these second-generation hormonal therapies, chemotherapy is considered the next treatment option. Treatment

with chemotherapy is generally postponed for as long as possible due to the potential for severe side effects including neuropathies, nausea, diarrhea, decreased mental capacity and increased risk of infections.

AR remains the principal driver of castration-resistant prostate cancer progression during the transition from localized to metastatic disease, with AR gene amplification occurring in 40% to 60% of patients, amplification of a transcription regulatory region upstream of the AR gene occurring in 70% to 87% of patients, and AR point mutations occurring in approximately 15% of patients. Between 15% to 25% of patients do not respond to either abiraterone or enzalutamide and the vast majority of the responsive patients will ultimately become resistant, resulting in limited survival. There remains meaningful unmet medical need in the treatment paradigm of mCRPC, including a significant underserved set of patients who are or become resistant to current therapies. Based on our preclinical data, we believe our AR-targeting PROTAC protein degraders may overcome these known resistance mechanisms and create meaningful clinical benefit for patients.

Bavdegalutamide Preclinical Development

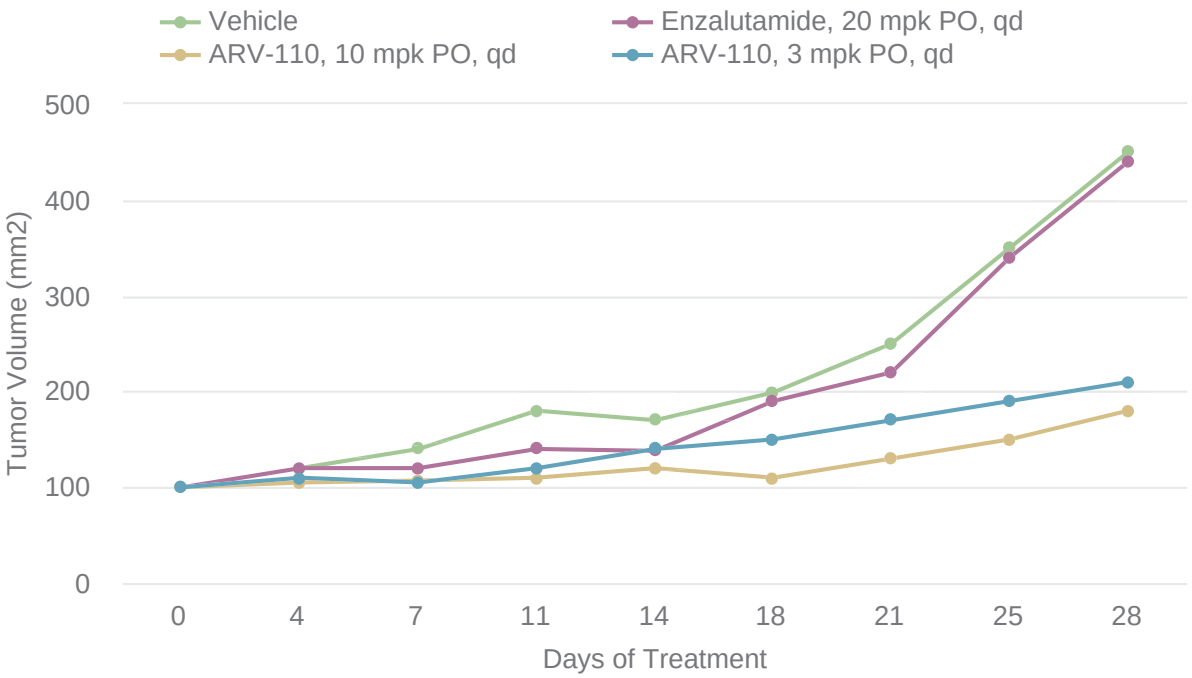
We have conducted a comprehensive preclinical program to study bavdegalutamide as a potential treatment for men with mCRPC. In *in vitro* models, bavdegalutamide degraded 95% to 98% of AR in multiple cell lines typically used in prostate cancer research. Bavdegalutamide is also highly selective for AR. A proteomic analysis of VCaP cells treated *in vitro* with bavdegalutamide at a 10 nM concentration for eight hours demonstrated that only AR was degraded from the nearly 4,000 measured proteins.

Importantly, in addition to AR degradation and selectivity, we have observed in preclinical studies the ability of bavdegalutamide to potently inhibit prostate cancer cell growth and reduce PSA levels. In addition to guiding treatment decisions, reduction in PSA is often an indicator of the effectiveness of treatment in clinical trials, however, it is not recognized as a surrogate endpoint for purposes of regulatory approval. For example, bavdegalutamide demonstrated equivalent reduction in PSA to enzalutamide at ten-fold lower concentration levels in an *in vitro* inhibition study of PSA synthesis in Lymph Node Cancer of the Prostate cells, which are androgen-sensitive human prostate adenocarcinoma cells, that have been engineered to overexpress AR.

In *in vivo* mouse models, bavdegalutamide has inhibited AR-dependent tumor growth in a statistically significant manner. Bavdegalutamide exhibited superior tumor growth inhibition compared to enzalutamide in both castrated and intact (non-castrated) xenograft models derived from VCaP cell lines.

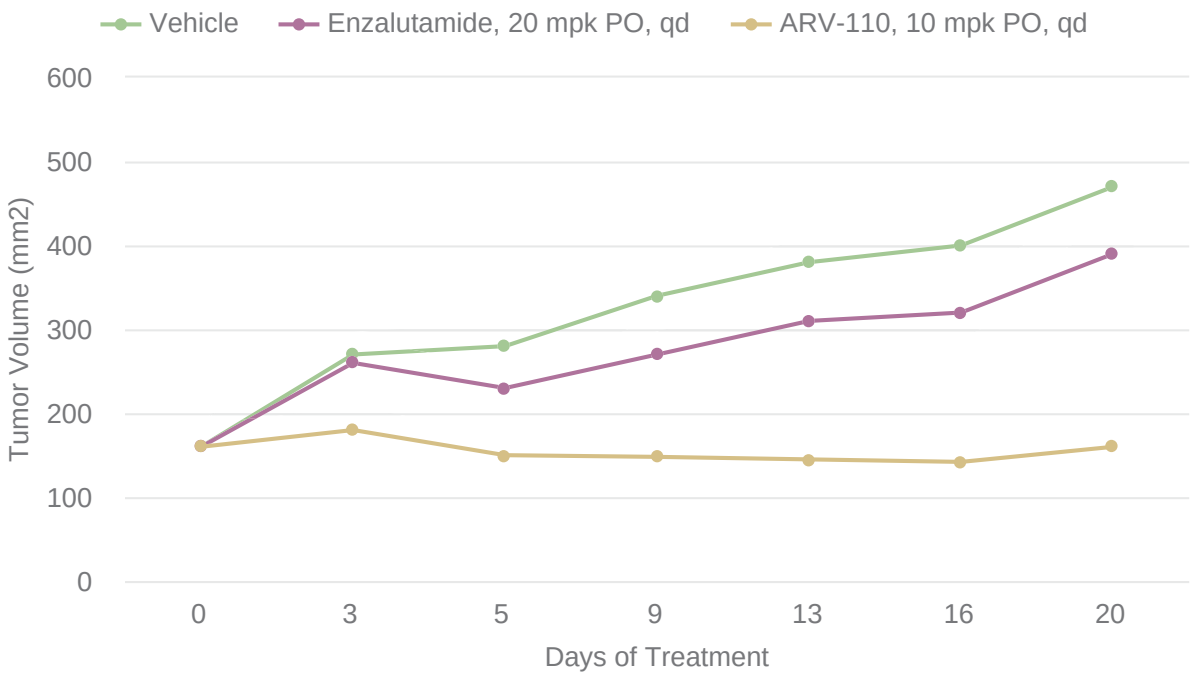
To assess the ability of bavdegalutamide to treat enzalutamide-resistant cancers, we conducted *in vivo* studies of bavdegalutamide in an enzalutamide-resistant VCaP xenograft model. These VCaP tumors acquired resistance to enzalutamide after being continuously propagated in castrated, enzalutamide treated mice for approximately three years. This resistance can be seen in the figure below, as tumors in mice dosed with enzalutamide grew at nearly the same rate as tumors in mice dosed only with the drug vehicle - a control similar

to dosing a placebo. Orally delivered bavdegalutamide significantly inhibited tumor growth, described as tumor growth inhibition, or TGI, in these enzalutamide-resistant VCaP tumors.



We have also conducted preclinical studies of bavdegalutamide for enzalutamide-insensitive tumors. We conducted an *in vivo* study in a PDX model that is derived from a tumor from a patient not treated with enzalutamide but that is insensitive to enzalutamide. This insensitivity can be seen in the figure below, as tumors in mice dosed with enzalutamide grew at only a slightly slower rate than tumors in mice dosed only with the drug vehicle. In contrast, orally delivered bavdegalutamide significantly inhibited tumor growth in these enzalutamide-insensitive tumors, achieving a TGI value of 100%. Further, PSA levels in the plasma of mice

following 20 days of bavdegalutamide dosing significantly decreased in comparison to those dosed with only the drug vehicle or enzalutamide.



We believe the activity of bavdegalutamide in the above VCaP and PDX models may closely reflect enzalutamide resistance or insensitivity in the clinic and shows the potential for treatment of patients whose tumors have become resistant to, or demonstrate intrinsic resistance to, a current standard-of-care agent.

Bavdegalutamide has also reduced the levels of PSA in plasma comparable to levels achieved with enzalutamide in a different VCaP xenograft mouse model but at a lower dosing level.

Bavdegalutamide: Our Clinical Trials

In 2019, we initiated dosing in a Phase 1 clinical trial of bavdegalutamide. Our Phase 1 trial was designed as an open label, dose-escalation study of bavdegalutamide in men with mCRPC whose disease had progressed on at least two prior systemic therapies, one of which must have been enzalutamide or abiraterone. The Phase 1 trial was designed to primarily investigate the safety and tolerability of bavdegalutamide. Secondary endpoints included characterization of bavdegalutamide's pharmacokinetic profile and preliminary assessment of biochemical and clinical activity based on evaluation of PSA levels, and radiographic measurement of evaluable lesions. The anti-tumor effects of bavdegalutamide in measurable lesions were assessed using Response Evaluation Criteria in Solid Tumors, or RECIST, a standardized set of rules for response assessment based on tumor shrinkage which is widely used in oncology clinical trials. We also evaluated exploratory markers of disease burden, such as circulating tumor cell enumeration, as exploratory endpoints of the trial.

A potential drug-drug interaction between bavdegalutamide and rosuvastatin, or ROS, was identified during the trial. One patient receiving 280 mg bavdegalutamide experienced a Grade 4 dose-limiting toxicity of elevated aspartate transaminase/alanine transaminase, or AST/ALT, liver enzymes followed by acute renal failure. A second patient, receiving 70 mg bavdegalutamide, experienced a Grade 3 AST/ALT elevation, which resolved after the removal of ROS, and the patient was retreated with bavdegalutamide. Follow-up exploratory findings indicate that ROS concentrations, but not bavdegalutamide concentrations, were elevated in both patients who had liver function test increases. Subsequent *in vitro* transport pump studies indicated that bavdegalutamide inhibited breast cancer resistant pump transporter, of which ROS is a substrate. Following the initial data that supported a potential interaction with ROS, concomitant use of ROS was precluded.

In 2020, we amended the protocol for our Phase 1 clinical trial for bavdegalutamide to include the addition of a Phase 2 expansion cohort. Based on our observations of a molecularly defined, late-line population with a particularly strong response to bavdegalutamide in the Phase 1 portion of the trial, we designed our Phase 2 dose expansion to assess bavdegalutamide in four specific subgroups: patients with tumors with AR T878X (T878X = T878A or T878S) and/or H875Y mutations but excluding other AR variants; patients with tumors with wild-type AR or AR alterations other than T878X, H875Y, L702H, and AR-V7; patients with tumors with AR-V7 or L702H, which are variants of AR that, preclinically, bavdegalutamide did not degrade, or did not degrade potentaly, respectively; and patients with biomarker agnostic tumors treated with no more than one prior novel hormonal agent, or NHA, such as enzalutamide or abiraterone, and had no prior chemotherapy.

In the fourth quarter of 2020, we initiated the ARDENT Phase 2 expansion portion of the trial at a dose of 420 mg once-daily, the recommended Phase 2 dose, or RP2D.

In February 2022, we announced completed Phase 1 and interim ARDENT data for bavdegalutamide with a data cut-off date of December 20, 2021 at the 2022 American Society of Clinical Oncology Genitourinary (ASCO GU) Cancers Symposium. We reported that bavdegalutamide showed reduced PSA levels of greater than or equal to than 50%, or PSA50, in 46% of the 28 patients with tumors harboring AR T878X/H875Y mutations. These results also demonstrated PSA declines and tumor regressions in patients without tumors harboring AR T878X/H875Y mutations, suggesting an opportunity to develop bavdegalutamide more broadly in prostate cancer.

As of the data cut-off date, 195 patients were enrolled across the Phase 1/2 clinical trial (71 in Phase 1; 124 in Phase 2).

The Phase 1 dose escalation trial evaluated bavdegalutamide at doses ranging from 35–700 mg, once-daily, or 210–420 mg twice-daily, in patients with mCRPC and two or more prior therapies (including abiraterone and/or enzalutamide).

Patients in the ARDENT trial received a median of four prior lines of therapy with 100% receiving at least one NHA (64% abiraterone, 75% enzalutamide or other AR inhibitor, 39% both abiraterone and an AR inhibitor) and 31% receiving at least one chemotherapy regimen.

Efficacy Measures

We presented efficacy measures on a combined basis for patients in both the completed Phase 1 dose escalation trial and the interim analysis from the ongoing ARDENT Phase 2 dose expansion trial. In the biomarker defined (“more pretreated”) subgroups, we observed the following:

- In eight patients with tumors with AR T878X and/or H875Y mutations but excluding other AR variants, PSA50=75%; PSA decline of more than 30%, or PSA30, =75%
- In 44 patients with tumors with wild-type AR or AR alterations other than T878X, H875Y, L702H, or AR-V7, PSA50=11%; PSA30=20%
- In 25 patients with tumors with AR L702H or AR-V7, PSA50=4%; PSA30=20%

In the biomarker agnostic (“less pretreated”) subgroup comprising 27 patients with no more than one prior NHA and no prior chemotherapy, the PSA50 response rate was 22% and the PSA30 response rate was 26%.

In biomarker-evaluable patients treated at or above the RP2D and with tumors harboring AR T878X/H875Y mutations (across all subgroups and thus regardless of prior therapy regimens or other mutations; n=28), the PSA50 response rate was 46% and the PSA30 response rate was 57%.

Of seven RECIST-evaluable patients across the Phase 1 and Phase 2 trials with tumors harboring AR T878X/H875Y mutations, two had confirmed durable partial responses. These patients were on treatment for approximately nine months (ongoing as of the data cut-off) and ten months; the duration of treatment ranged from eight weeks to 44 weeks, with three of the seven patients continuing on treatment as of the data cutoff of December 20, 2021.

Twelve (43%) of the 28 patients with AR T878X/H875Y-positive mutations received bavdegalutamide for 24 weeks or more, with nine patients ongoing as of the data cutoff.

PSA reductions and evidence of anti-tumor activity as measured by RECIST were observed across all subgroups regardless of mutation status, including tumors not harboring AR T878X/875Y mutations.

RECIST responses were seen in patients with tumors lacking AR T878X/H875Y mutations (one confirmed and three unconfirmed RECIST responses).

The “less pretreated” subgroup (n=27) had a similar molecular profile—as assessed by circulating tumor DNA analysis—to the more pretreated, biomarker-defined subgroups in the ARDENT trial. These similarities included both AR variations (point mutations and AR-V7 splice variants) and non-AR mutations frequently associated with poor outcomes (e.g., TP53, BRCA1). Six of the 27 patients (22%) had PSA50 reductions, and this PSA50 rate was similar to that observed collectively in the “more pretreated” subgroups (16%; n=77). Four of the six “less pretreated” patients with PSA50 declines had tumors with AR T878X/H875Y mutations.

Safety and Tolerability

Bavdegalutamide had a manageable tolerability profile at the RP2D. The majority of treatment-related adverse events, or TRAEs, were Grade 1/2 and there were no Grade 4 or greater TRAEs in the 138 patients treated at the RP2D.

TRAEs that occurred in 10% or more of patients treated at the RP2D were nausea (Gr 1: 30%; Gr 2: 16%; Gr 3: 1%), fatigue (Gr 1: 23%; Gr 2: 12%; Gr 3: 1%), vomiting (Gr 1: 20%; Gr 2: 5%; Gr 3: 1%), decreased appetite (Gr 1: 14%; Gr 2: 11%; Gr 3: 1%), diarrhea (Gr 1: 14%; Gr 2: 4%; Gr 3: 2%), alopecia (Gr 1: 13%; Gr 2: 1%; Gr 3: N/A) AST increased (Gr 1: 9%; Gr 2: 3%; Gr 3: 1%), weight decreased (Gr 1: 7%; Gr 2: 5%; Gr 3: 0%), and anemia (Gr 1: 4%; Gr 2: 1%; Gr 3: 5%).

TRAEs at the RP2D led to dose reduction in 11 (8%) patients and discontinuation in 12 (9%) patients.

Our Phase 1b trial of bavdegalutamide in combination with abiraterone for the treatment of men with mCRPC is ongoing. We expect to complete enrollment in the Phase 1b trial in the second half of 2023. Abiraterone is approved, in combination with a corticosteroid, to treat patients with mCRPC or with high-risk castration-sensitive prostate cancer. Up to a third of patients treated with abiraterone develop primary resistance to this drug and nearly all patients experience disease progression. The Phase 1b study evaluates the combination of bavdegalutamide (ARV-110) with abiraterone at the initiation of progression on abiraterone (PSA progression without radiographic progression) to test if the addition of bavdegalutamide will overcome resistance to abiraterone and re-establish the AR pathway blockade in patients with prostate cancer. The primary objectives of the trial are to evaluate the safety and tolerability of bavdegalutamide in combination with abiraterone and determine the RP2D and schedule of this combination (based on the incidence of first-cycle dose-limiting toxicities and the frequency and severity of adverse events and laboratory abnormalities).

We expect to initiate a global Phase 3 trial with a confirmed dose for bavdegalutamide for the treatment of men with mCRPC with AR T878/H875 tumor mutations in the second half of 2023. Also in the second half of 2023, we expect to complete enrollment in the Phase 1b clinical trial with bavdegalutamide in combination with abiraterone.

ARV-766: Our Preclinical and Clinical Development

We are also developing ARV-766, which has a different profile than bavdegalutamide, to target and degrade wild-type and mutated AR including at least one additional, clinically relevant AR point mutation, the L702H point mutation.The L702H point mutation in the ligand-binding domain of AR results in activation of the AR by glucocorticoids and can cause resistance to a standard of care regimen. Recent studies have reported that between approximately 2-9% of patients with mCRPC had an L702H point mutation.

In 2021, we initiated a Phase 1/2 clinical trial for ARV-766 designed to assess the safety, tolerability and pharmacokinetics of ARV-766, which trial also includes measures of anti-tumor activity as secondary endpoints, including reduction in PSA. In the second half of 2022, we initiated a Phase 2 expansion trial of ARV-766 for the treatment of men with mCRPC.

We expect to share data from the Phase 1 dose escalation trial of ARV-766 for the treatment of men with mCRPC in the second quarter of 2023.

We anticipate initiating a Phase 1b or Phase 2 dose escalation trial for either of bavdegalutamide or ARV-766 in patients with AR-dependent tumors who have not previously received novel hormonal agents, or NHA, such as enzalutamide or abiraterone, and who may benefit from bavdegalutamide or ARV-766 therapy, in the second half of 2023.

Next Generation AR Degraders

We are developing additional PROTAC targeted protein degraders capable of degrading certain AR splice variants. We expect that results from our Phase 1/2 clinical trials of bavdegalutamide and ARV-766 will provide further data on the role of androgen receptor splice variant-7, or AR-V7, in prostate cancer. Bavdegalutamide and ARV-766 bind to full-length AR at its ligand-binding domain. AR-V7 is a truncated form of AR that lacks the ligand-binding domain necessary to bind with bavdegalutamide and ARV-766 and which bavdegalutamide and ARV-766 therefore do not degrade. AR functions as a dimer, a complex made up of two individual AR proteins. AR-V7 can form a dimer with a full-length AR, and such non-identical protein dimers are called heterodimers. We believe that bavdegalutamide and ARV-766, by degrading the full-length AR component of the heterodimer, could successfully inactivate AR-V7-directed signaling. Although shown to form a heterodimer preclinically, there is uncertainty as to whether AR-V7 and AR form a heterodimer in patients' tumors. It is also possible that AR-V7 signals through V7-only dimers, which would be unaffected by bavdegalutamide and ARV-766. Although the presence of AR-V7 has been shown to correlate with a lack of response to enzalutamide and abiraterone, a published study demonstrated that approximately 40% of patients with AR-V7 expressing circulating tumor cells show a PSA response to enzalutamide. Given the evolving potential role of AR-V7 in prostate cancer, as a follow-on to bavdegalutamide and ARV-766, we are exploring the identification and development of a PROTAC targeted protein degrader that can degrade AR-V7 directly, as well as other AR splice variants.

Our Preclinical Programs Addressing Other Oncology and Neurodegenerative Disorders

We have active preclinical programs to evaluate additional established targets in oncology for both solid and hematological malignancies and neurodegenerative disorders. In line with our strategy, we assess potential exploratory programs on a target-by-target basis to decide whether our PROTAC targeted protein degraders provide a compelling differentiated approach over standard-of-care or other, existing or potential competing mechanisms of action directed against a specific target. In the case of currently or historically undruggable targets, we assess whether the features of our PROTAC targeted protein degraders, including their potential to degrade proteins via sites other than enzymatic active sites and the ability to initiate the degradation process using only weak binders, offer us opportunities to degrade those targets. In 2023, we expect to submit two IND applications or CTAs for two of our preclinical programs and to have two additional preclinical programs in IND- or CTA-enabling studies.

Oncology

Our exploratory and research activity in oncology includes programs directed to the B-cell lymphoma 6, or BCL6, protein, a transcription factor implicated in B cell lymphomas; Kirsten rat sarcoma, or KRAS, an oncogenic cell growth regulator; Myc, an oncogenic transcription factor driving tumor cell proliferation; and hematopoietic progenitor kinase 1, or HPK1, a suppressor of T cell activation.

In particular, we believe our BCL6 PROTAC degrader has the potential to be a first-in-class potential therapy for the NHL subtype DLBCL and believe additional opportunities for a BCL6 degrader exist in Burkitt's Lymphoma, Follicular Lymphoma, Angioimmunoblastic T-cell lymphoma and solid tumors. BCL6 is genetically mutated in up to 85% of DLBCL, a subset of NHL. More than 18,000 people are diagnosed with DLBCL each year. Treatment for DLBCL is largely devoid of oral options and there are currently no approved BCL6-targeted therapies on the market or in the clinic. BCL6 may also be a clinically relevant therapeutic target in various solid tumors including breast cancer, non-small cell lung cancer and glioblastoma.

Based on our preclinical models, complete tumor stasis, which correlates with 95%-100% degradation of measurable BCL6, was achieved when our oral, BCL6-targeting PROTAC clinical candidate was taken at low, oral daily doses. We saw similar activity in multiple DLBCL models, including for activated B-cell and germinal

center B-cell lymphoma. This program is currently in GLP toxicity studies. We expect to submit an IND application or CTA for our BCL6 PROTAC degrader by year-end 2023.

Neurodegenerative Diseases

Neurodegenerative diseases are generally progressive in nature and result in the degeneration and often death of neurons in the brain, leading to cognitive decline, functional impairment and eventually death. These diseases affect a rapidly growing patient population and represent one of the largest unmet medical needs of our time. Alzheimer's and Parkinson's diseases encompass the largest patient populations among the neurodegenerative diseases. The Alzheimer's Association estimated that 6.5 million Americans aged 65 and older, about one in nine individuals, were living with Alzheimer's disease in 2022, and the Parkinson's Foundation estimated that nearly one million Americans are living with Parkinson's disease, or PD. Alzheimer's disease is marked by the progressive accumulation of aggregated tau protein, while aggregation of alpha-synuclein is thought to cause PD.

Inhibitor-based therapies targeting the proteins thought to be the cause of these neurodegenerative diseases have failed to show clinically meaningful benefit to date. While some existing products provide symptomatic relief to Alzheimer's and Parkinson's patients, they have significant side effect risks and over time gradually lose their effectiveness in treating the symptoms of the disease. Further, there are no approved disease-modifying treatments for Alzheimer's or Parkinson's.

Developing PROTAC Targeted Protein Degraders that Cross the Blood Brain Barrier

Engineering PROTAC degraders that cross the blood-brain barrier is necessary to achieve targeted elimination of disease-causing proteins from the central nervous system. The ability of a targeted therapy to cross the blood-brain barrier is a highly desirable characteristic in developing effective therapeutics for patients with neurodegenerative diseases as compared with therapies delivered directly into the central nervous system, or CNS. Any product candidates for neurodegenerative disease must reach their intended targets in the brain at exposure levels that will provide a therapeutic effect, while having an acceptable safety profile.

Importantly, we have achieved brain penetration in preclinical models following parenteral administration of PROTAC degrader molecules designed to specifically target pathologic oligomers of mutant huntingtin, tau, and α-synuclein, for the treatment of Huntington's disease, Alzheimer's disease (tauopathies) and Parkinson's disease (synucleinopathies), respectively. These PROTAC degrader molecules achieved concentrations in the brain sufficient to induce degradation of the aggregated proteins, widespread penetration into different parts of the brain, and brain/plasma ratios of 0.5 to 5.0, comparable to approved therapeutics with CNS activity.

Developing PROTAC Targeted Protein Degraders that Degrade Proteins Associated with Neurodegenerative Diseases

We have conducted preclinical studies to establish the potential of our PROTAC Discovery Engine in the CNS for the treatment of neurodegenerative diseases, including tauopathies, the largest of which is Alzheimer's disease. We have demonstrated that tau PROTAC protein degrader molecules could be dosed peripherally and degrade pathogenic tau in the brain of a mouse tauopathy model.

In preclinical studies, we have demonstrated that alpha-synuclein PROTAC degraders can specifically degrade aggregated forms of the protein. We have conducted in vitro experiments in cells expressing the A53T mutant form of alpha-synuclein, a mutation that causes aggregation of alpha-synuclein and early-onset Parkinson's diseases in patients. We treated these cells with alpha-synuclein targeting PROTAC degraders at 1 μM for 48 hours.

In addition to our tau and alpha-synuclein programs, our neuroscience pipeline includes a program directed to mutant huntingtin, or mHTT, a key protein target for Huntington's disease. We have identified novel ligands that when incorporated into PROTAC protein degrader molecules induce potent and selective degradation of mutant mHTT protein without impacting wild-type HTT protein in preclinical studies. This selectivity differentiates these ligands from other small molecule splice modulators that reduce both mHTT and wild-type HTT protein.

Parkinson's Disease, or PD, is the second most common neurodegenerative disease, affecting approximately 10 million people world-wide. It is commonly thought of as a movement disorder because patients can experience tremors, slowness of movement, stiffness and difficulty with walking and balance. In addition, Parkinson's patients can have other non-motor type problems such as constipation, depression and memory loss. The disease results from the loss of dopamine-producing cells in the brain and is likely caused by a combination of genetic and environmental risk factors. No disease-modifying therapies have been approved for PD.

Mutations in the LRRK2 gene are one of the most common genetic risk factors for Parkinson's disease. LRRK2 is a multidomain GTPase/ kinase that acts, in part, as a scaffolding protein to interact with components of downstream signaling pathways regulating lysosomal function, mitochondrial processes, neuroinflammation and alpha-synuclein accumulation to negatively impact neuronal survival. Human genetics and preclinical animal model data suggest that a reduction of 50% of LRRK2 protein, but not kinase inhibition, may impact pathology and dysfunction in PD. Therefore, reduction of LRRK2 in the brain may be beneficial for the treatment of PD. We have identified potent, selective, orally bioavailable LRRK2 PROTAC protein degraders that cross the blood-brain barrier in preclinical species and biodistributed to deep brain regions impacted in PD.

Our oral PROTAC LRRK2-targeting protein degrader clinical candidate has been shown preclinically to broadly bio-distribute to deep brain regions in non-human primates and degrades LRRK2 more than 95%. This program is currently in GLP toxicity studies. We expect to submit an IND or CTA for our PROTAC LRRK2 degrader by year end 2023.

Intellectual Property

Our commercial success depends in part upon our ability to secure and maintain patent and other proprietary protection for our platform protein degradation technologies, including our PROTAC targeted protein degrader programs, product candidates, and know-how related to our business, defend and enforce our intellectual property rights, in particular our patent rights, preserve the confidentiality of our trade secrets, and operate without infringing valid and enforceable intellectual property rights of others.

The patent positions for biotechnology companies like us are generally uncertain and can involve complex legal, scientific and factual issues. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that any of our product candidates will be protected or remain protectable by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties.

As of January 30, 2023, our patent estate that we own, co-own and in-license includes 36 issued U.S. patents, 92 granted foreign patents, and 492 pending patent applications (83 domestic and 409 foreign).

PROTAC Patents and Patent Applications

Our PROTAC patent portfolio is generally organized into two categories: PROTAC platform patent filings, and PROTAC product candidate or protein target-specific patent filings.

PROTAC Platform

As of January 30, 2023, our PROTAC platform patent estate that we own, co-own, and in-license, and that covers our various E3 ubiquitin ligase constructs, includes three issued U.S. patents, 32 granted foreign patents, seven pending U.S. patent applications and 63 pending foreign patent applications. This patent estate covers constructs that have ligands for the Von Hippel Lindau, or VHL, E3 ubiquitin ligase, the cereblon, or CRBN, E3 ubiquitin ligase, the inhibitor apoptosis protein, or IAP, E3 ubiquitin ligase, and the human mouse double minute homolog, or MDM2, E3 ubiquitin ligase.

We exclusively license from Yale University, or Yale, a portfolio of patents and patent applications describing composition-of-matter claims encompassing PROTAC targeted protein degrader compounds comprised of ligands for the VHL E3 ubiquitin ligase, as well as claims to associated methods of use. Patents have been granted in Australia, Mexico, Russia, South Korea, and the United States, and patent applications

are pending in Australia, Brazil, Canada, China, Europe, Hong Kong, India, Japan, Mexico, South Korea, Russia and the United States. If all appropriate maintenance fees are paid, each granted patent will expire in 2033 without taking potential patent term extensions into account. We also co-own with Yale patent applications describing composition-of-matter claims encompassing PROTAC targeted protein degrader compounds comprised of ligands for the VHL E3 ligase. Two patents have issued in the United States, three foreign patents have been granted, and patent applications are pending in Australia, Brazil, Canada, China, Europe, Hong Kong, India, Japan, Mexico, Russia, South Korea and the United States. Our rights to this patent and these patent applications are governed by the Yale License Agreement described below under *Licenses and Strategic Collaborations*.

We own one patent family with three pending U.S. patent applications describing composition-of-matter claims covering the CRBN E3 ubiquitin ligase ligand generically, the chemical linker group generically, and a small molecule or peptide ligand that binds to a target protein generically. We own granted patents in Australia, China, Europe, France, Germany, Great Britain, Hungary, India, Italy, Japan, Mexico, the Netherlands, Russia, Spain, Switzerland and South Korea. Patent applications are pending in Australia, Brazil, Canada, China, Europe, Hong Kong, India, Israel, Japan, Mexico, Russia, South Korea and the United States. If all appropriate maintenance fees are paid, each granted patent in these families will expire no earlier than 2035 without taking potential patent term extensions into account.

We own a patent family describing composition-of-matter claims encompassing PROTAC targeted protein degrader compounds comprised of ligands for the IAP E3 ubiquitin ligase as well as claims to associated methods of use. Patent applications in this family are pending in Europe and the United States. If granted, and all appropriate maintenance fees are paid, the expiration of these patents would be in 2036 without taking potential patent term extensions into account.

We own a patent family describing composition-of-matter claims encompassing PROTAC targeted protein degrader compounds comprised of ligands for the MDM2 E3 ubiquitin ligase as well as claims to associated methods of use. Patent applications in this family are pending in Europe and the United States, and granted in Australia. If granted, and all appropriate maintenance fees are paid, the expiration of these patents would be in 2036, without taking potential patent term extensions into account.

PROTAC Product Candidates

Our product or protein-specific patent applications were created to pursue more focused patent exclusivity around PROTAC targeted protein degrader compounds designed to target specific proteins. As of January 30, 2023, our PROTAC product patent portfolio covering AR and ER, and those patents that we co-own and in-license (including protein targets other than AR and ER) includes 20 U.S. issued patents, 92 granted foreign patents, 83 pending U.S. patent applications, 14 pending Patent Cooperation Treaty, or PCT, applications, and 388 pending foreign patent applications.

We own 13 patent families describing composition-of-matter claims encompassing PROTAC targeted protein degrader compounds addressing AR and associated methods of manufacture and methods of treating cancer. The first patent family has three issued U.S. patents, six granted foreign patents, one pending U.S. applications, and 12 pending foreign patent applications describing composition-of-matter, synthetic intermediates, and method of use claims covering bavdegalutamide. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2037 without taking potential patent term extension into account. The second patent family has two issued U.S. patents, two pending applications in the United States, seven granted foreign patents, and 14 pending foreign applications describing alternative composition-of-matter claims. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2036 without taking potential patent term extension into account. The third patent family has two pending U.S. applications and 11 pending foreign applications describing claims directed to additional methods of treating cancer using bavdegalutamide. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2040 without taking potential patent term extension into account. The fourth patent family has one pending U.S. application and 39 pending foreign applications describing composition-of-matter claims directed to ARV-766. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2040 without taking potential patent term extension into account. The fifth patent family has one pending U.S. application and 12 pending foreign applications describing claims directed to additional methods of treating cancer using bavdegalutamide. Any patent granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2041 without taking potential patent term extension into account. The sixth patent family has one pending U.S. application and 31 pending foreign

applications describing claims directed to methods of manufacture, crystalline and ultrapure forms, and dosage forms of bavdegalutamide. Any patent granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2041 without taking potential patent term extension into account. The seventh patent family has one pending U.S. application and one pending PCT application describing claims directed to methods of treating cancer with bavdegalutamide in patients with specific AR mutations. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2041 without taking potential patent term extension into account. The eighth patent family has three pending U.S. applications describing methods of treating cancer with ARV-766. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2043 without taking potential patent term extension into account. The ninth patent family has one pending U.S. application, one granted foreign patent, and 15 pending foreign applications describing alternative AR-based PROTAC compounds and methods of use to treat cancer. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2038 without taking potential patent term extension into account. The tenth patent family has one pending U.S. application describing claims directed towards dosage forms of bavdegalutamide. Any patent granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2044 without taking potential patent term extension into account. The eleventh patent family has one pending U.S. application describing claims directed towards additional methods of treating cancer using bavdegalutamide. Any patent granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2043 without taking potential patent term extension into account. The twelfth patent family has one pending U.S. application and one pending PCT application describing alternative composition-of-matter claims. Any patent granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2041 without taking potential patent term extension into account. The thirteenth patent family has one pending U.S. application and one pending PCT application describing alternative composition-of-matter claims. Any patent granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2041 without taking potential patent term extension into account.

We own 13 patent families describing composition-of-matter claims encompassing PROTAC targeted protein degrader compounds addressing ER and associated methods of treating cancer. The first patent family has three issued U.S. patents, three pending U.S. applications, seven granted foreign patents, and 22 pending foreign patent applications describing composition-of-matter and method of use claims covering ARV-471. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2037 without taking potential patent term extension into account. The second patent family has one pending U.S. application and 23 pending foreign patent applications describing claims directed to methods of treating cancer using ARV-471 as a monotherapy, and combined with an additional anti-cancer agent. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2040 without taking potential patent term extension into account. The third patent family has one pending U.S. application, one pending PCT application, and two pending foreign applications describing claims directed to crystalline forms of ARV-471. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2041 without taking potential patent term extension into account. The fourth patent family has one pending U.S. application, one pending PCT application, and one pending foreign application describing claims directed to methods of treating cancer with ARV-471 in patients with specific ER mutations, and methods of treating cancer with ARV-471 and additional anti-cancer agents. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2041 without taking potential patent term extension into account. The fifth patent family has one pending U.S. patent application describing oral dosage formulations of ARV-471 and methods of preparing such oral dosage formulations of ARV-471. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2042 without taking potential patent term extension into account. The sixth patent family has one issued U.S. patent and three pending foreign applications describing alternative ER-based PROTAC compounds and methods of use to treat cancer. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2037 without taking potential patent term extension into account. The seventh patent family has two issued U.S. patent, one pending U.S. patent application, one issued foreign patent, and 13 pending foreign applications describing alternative ER-based PROTAC compounds and methods of use to treat cancer. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2038 without taking potential patent term extension into account. The eighth patent family has one pending U.S. application and one pending PCT application describing claims directed to methods of manufacture of ARV-471. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2042 without taking potential patent term extension into account. The ninth patent family has one pending U.S. application directed to dosage regimens of ARV-471 as a monotherapy to treat cancer. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2043 without taking potential patent term extension into account. The tenth patent family has one pending U.S. application directed to dosage regimens of ARV-471 combined with an additional anti-cancer

agent to treat cancer. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2043 without taking potential patent term extension into account. The eleventh patent family has one pending U.S. application directed to methods of treating cancer with ARV-471 to reduce any potential drug-drug interactions. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2043 without taking potential patent term extension into account. The twelfth patent family has one U.S. application directed to methods of treating cancer with ARV-471 to reduce any potential drug-drug interactions. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2043 without taking potential patent term extension into account. The thirteenth patent family has one U.S. application directed to a method of treating advanced breast cancer with ARV-471. Any patents granted in this family, assuming all appropriate maintenance fees are paid, will expire in 2043 without taking potential patent term extension into account.

We and Yale co-own five patent families describing composition of matter claims of PROTAC targeted protein degrader compounds addressing certain discovery and other potential protein targets, and associated methods of use. One or more U.S. patents have issued in each of these families and patent applications for four of these families are pending in the United States. In addition, 37 foreign patent applications are pending for two of the families. Patent applications are also pending in the European Patent Office for each of the families. Our rights to these patent applications are governed by the Yale License Agreement described below under *Licenses and Strategic Collaborations* .

We co-own with Genentech two pending U.S. patent applications, two pending PCT applications, and 30 foreign patent applications and one granted foreign patent directed to PROTAC targeted protein degrader compounds addressing a specific protein. Our rights to these patent applications are governed by the Genentech License Agreement described below under *Licenses and Strategic Collaborations*.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, the term of a patent covering a drug approved by the U.S. Food and Drug Administration, or FDA, may be eligible for a patent term extension under the Hatch-Waxman Act as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years beyond the expiration of the patent but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension may be extended. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. It is possible that issued U.S. patents covering bavdegalutamide and ARV-471 may be entitled to patent term extensions. If our product candidates receive FDA approval, we intend to apply for patent term extensions, if available, to extend the term of patents that cover the approved product candidates. We also intend to seek patent term extensions in any jurisdiction where they are available; however, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions.

The United States also offers Patent Term Adjustment, or PTA, whereby a particular patent's term is automatically extended beyond the 20-year term if the United States Patent and Trademark Office caused delays during the underlying patent application's examination. However, potentially available PTA will be reduced by any amount of delay caused by the applicant.

Trade Secrets

We also rely on trade secrets, technical know-how and continuing innovation to develop and maintain our competitive advantage. Our policy requires inventors who are identified on any company-owned patent applications to assign rights to us. We also rely on confidentiality agreements with our employees, consultants and other advisors to protect our proprietary information. Our policy is to require third parties that receive material confidential information to enter into confidentiality agreements with us.

Trademarks

We own a U.S. service mark registration for PROTAC for pharmaceutical products development of new small molecules aimed at degrading disease-causing cellular proteins for treatment in the fields of oncology, immunology, inflammatory diseases, and central nervous system disorders. We also own a U.S. trademark registration for the mark PROTAC for small molecule products aimed at degrading disease-causing cellular

proteins for treatment in the fields of oncology, immunology, inflammatory diseases, and central nervous system disorders.

We also own U.S. trademark and service mark registrations for ARVINAS in word and logo form for pharmaceutical preparations and pharmaceutical products development of cellular proteins for treatment in the fields of oncology, immunology, inflammatory diseases, and central nervous system disorders. The ARVINAS word mark is registered for pharmaceutical products development services in Australia, China, the EU, Japan, Norway, South Korea, and Switzerland, and is pending registration in several other countries. The ARVINAS word mark is also registered for pharmaceutical products in Australia, Brazil, Colombia, the EU, Hong Kong, India, Indonesia, Israel, Japan, Mexico, New Zealand, Norway, Singapore, South Africa, South Korea, Switzerland, Taiwan, and the United Kingdom, and is pending registration in several other countries. The ARVINAS logo mark is registered for pharmaceutical products development services in the EU and the United Kingdom, and is pending registration in several other countries. The ARVINAS logo mark is also registered for pharmaceutical products in the EU, Hong Kong, and the United Kingdom, and is pending registration in several other countries.

We also own U.S. service mark registrations for our “degrading dots” logo mark in both black and white and color form for pharmaceutical products development of new small molecules aimed at degrading disease-causing cellular proteins for treatment in the fields of oncology, immunology, inflammatory diseases, and central nervous system disorders.

Finally, we own pending applications in the U.S. for the PROTAC mark for bi-functional small molecules that mediate targeted protein degradation through the ubiquitin proteasome system for agricultural and pesticide use and agricultural products development services. These applications are licensed for use by Oerth Bio.

Licenses and Strategic Collaborations

Yale University License Agreement

In July 2013, we entered into a license agreement with Yale pursuant to which Yale granted us an exclusive, worldwide license under specified intellectual property rights for the treatment or prevention of any human or animal disease in which a product mediates degradation of one or more target proteins, which we refer to as the Field, subject to certain exceptions. These licensed intellectual property rights arose from the research conducted by Dr. Craig Crews at Yale.

We are obligated to use commercially reasonable efforts to implement a written plan we agreed to with Yale setting forth a description of any research and development, testing, governmental approval and commercialization activities relating to licensed products and our financing plans. We must update this plan on an annual basis to indicate progress to date on the plan and a schedule of major events required to commercialize licensed products.

Pursuant to the license agreement we paid to Yale an upfront payment of $0.1 million. We are responsible for paying Yale an annual license maintenance fee in varying amounts (ranging from the low tens-thousands of dollars to the mid to high tens-thousands of dollars) until the first sale to a third party of any licensed product, which is creditable against our royalty obligations for the given year. As of December 31, 2022, we have paid a total of $0.6 million in license maintenance fees to Yale. We are required to pay Yale, subject to the achievement of specified development and regulatory milestones, payments aggregating up to approximately $3.0 million for the first licensed product and up to approximately $1.5 million for the second licensed product. We are not required to make any milestone payments for any licensed products beyond the first two. While the agreement remains in effect, we are required to pay Yale low single-digit royalties on aggregate worldwide net sales of certain licensed products, which may be subject to reductions. Yale is guaranteed a minimum royalty payment amount (ranging from $0.2 million to $0.5 million) for each year after the first sale of a licensed product that results in net sales. The agreement requires that we must also pay Yale a mid-single digit to mid-double digit percentage of certain consideration we receive from a sublicensee for the first licensed product we sublicense. We are also responsible for costs relating to the prosecution and maintenance of the licensed patents. Finally, subject to certain conditions, all payments made by us to Yale (except patent costs) will be tripled during the pendency of any patent challenge made by us against Yale.

The license agreement remains in effect until (a) for certain products, the date on which the last claim of the licensed patents expires; and (b) for certain products, 10 years after the sale of such products. The

expiration of the last to expire patent right licensed from Yale, if it issues as a patent and all appropriate maintenance fees are paid, is currently expected be in 2039. Either we or Yale may terminate the agreement for the other party's uncured material breach of certain provisions, we may terminate the agreement for convenience upon six months' prior notice, and Yale may terminate the agreement if we fail to make a payment when due, fail to obtain or maintain adequate insurance coverage or fail to achieve specified financing or regulatory milestone events. The agreement will automatically terminate if we become insolvent.

Genentech License Agreement

In September 2015, we entered into an Option and License Agreement with Genentech focused on PROTAC targeted protein degrader discovery and research for target proteins, or Targets, based on our proprietary platform technology, other than excluded Targets as described below. This collaboration was expanded in November 2017 through an Amended and Restated Option, License and Collaboration Agreement, which we refer to as the Restated Genentech Agreement.

The collaboration is managed by a joint research committee and a joint project team, each of which is comprised of representatives from us and Genentech. Decisions of the joint research committee and joint project team are made by consensus, with each party having one vote. If the joint research committee is unable to agree, and the parties' executives are not able to resolve the dispute, then Genentech has final decision-making authority, subject to specified limitations.

Under the Restated Genentech Agreement, Genentech has the right to designate up to ten Targets for further discovery and research utilizing our PROTAC platform technology. Genentech may designate as a Target any protein to which a PROTAC targeted protein degrader, by design, binds, to achieve its mechanism of action, subject to certain exclusions. Genentech also has the right to remove a Target from the collaboration and substitute a different Target that is not an excluded Target at any time prior to us commencing research on such Target or in certain circumstances following commencement of research by us.

Once a Target becomes subject to the collaboration, we are obligated to use diligent efforts to undertake a research program in accordance with a research plan agreed to by the parties for such Target. We are responsible for funding our activities under the research program for each Target up to the amount set forth in the budget for such Target agreed upon by the parties in the research plan. For costs incurred in excess of the budgeted amount, Genentech has the option of either having us continue the work on the Target and reimbursing us for our costs in doing so or terminating the work on such Target.

The research program for each Target contemplates that the discovery and research work will occur in two stages: Stage 1, in which our objective will be to identify a PROTAC targeted protein degrader that demonstrates in vitro protein degradation of the Target; and Stage 2, in which our objective will be to demonstrate certain *in vitro* and *in vivo* research and development activity, but not to complete toxicology studies or other necessary IND-enabling studies. For each Target, at the conclusion of Stage 1, Genentech has the opportunity to continue the research program for such Target or terminate all activities on such Target. At the conclusion of each stage, we are obligated to provide certain deliverables to Genentech, including a data package at the end of Stage 2. Genentech has an option to obtain an exclusive worldwide license to the applicable PROTAC targeted protein degraders directed against the applicable Target, which we refer to as Licensed PROTACs. Each such option must be exercised within a specified time after we deliver the data package for such Licensed PROTAC to Genentech. Once Genentech exercises an option, it is responsible, at its cost, to use diligent efforts to develop and commercialize the Licensed PROTAC through first commercial sale in the United States, the European Union and Japan.

During the term of the Restated Genentech Agreement, we and our affiliates are not permitted, either directly or indirectly, to conduct any activities in the design, identification or discovery of any small molecule pharmacologically active agent directed against a Target included in the collaboration, including certain PROTAC targeted protein degraders whose intended primary mechanism of action is, by design, through induction of proteasomal degradation of such Target.

Under the terms of the Restated Genentech Agreement, we received $11.0 million in 2015 and an additional $34.5 million in 2017 in upfront payments and expansion target payments. We are eligible to receive up to an aggregate of $27.5 million in additional expansion target payments if Genentech exercises its options

for all remaining Targets. We are also eligible to receive payments aggregating up to $44.0 million per Target subject to the achievement of specified development milestones; payments aggregating up to $52.5 million per Target (assuming approval of two indications) subject to the achievement of specified regulatory milestones; and payments aggregating up to $60 million per Licensed PROTAC subject to the achievement of specified sales milestones. These milestone payments are subject to reduction if we do not have a valid patent claim covering the Licensed PROTAC at the time the milestone is achieved. We are also eligible to receive, on net sales of Licensed PROTACs, mid-single digit royalties, which may be subject to reductions.

Unless earlier terminated, the Restated Genentech Agreement will expire upon the expiration of all royalty periods for any Licensed PROTACs. The royalty period for each Licensed PROTAC expires on a country-by-country basis upon either (1) the expiration of the last-to-expire valid patent claim covering such Licensed PROTAC or (2) ten years after the first commercial sale with respect to such Licensed PROTAC, depending on whether the sale of the Licensed PROTAC is covered by an applicable valid claim. The expiration of the last to expire patent right licensed to Genentech, if it issues as a patent and all appropriate maintenance fees are paid, is currently expected be in 2042. We could also obtain rights to additional patents, including through the issuance of pending patent applications, with later expiration dates, or new Licensed PROTACs could be added to the agreement that are subject to additional royalty terms with later expiration dates, which in either case could extend the term of the Restated Genentech Agreement. Genentech has the right to terminate the Restated Genentech Agreement for convenience in its entirety or with respect to a specific Target on 60 days' prior notice. Either we or Genentech may terminate the agreement, in its entirety or with respect to a specific Target, if the other party is in material breach and such breach is not cured within the specified cure period. In addition, either we or Genentech may terminate the agreement in the event of specified insolvency events involving the other party. If Genentech terminates the agreement for convenience or if we terminate the agreement as a result of Genentech's uncured material breach or Genentech's insolvency, all licenses we granted to Genentech terminate (either in its entirety or with respect to a specific Target, as applicable based on the nature of the termination). If Genentech terminates the agreement as a result of our uncured material breach or our insolvency, all licenses that we granted to Genentech terminate (either in its entirety or with respect to a specific Target, as applicable based on the nature of the termination), except that Genentech has the right to elect to retain its licenses, in which case it would no longer be obligated to use diligent efforts to develop and commercialize the applicable Licensed PROTACs and its payment obligations to us would be reduced.

Pfizer Research Collaboration Agreement

In December 2017, we entered into a Research Collaboration and License Agreement with Pfizer setting forth our collaboration to identify or optimize PROTAC targeted protein degraders that mediate for degradation of Targets using our proprietary platform technology that are identified in the agreement or subsequently selected by Pfizer, subject to certain exclusions. We refer to this agreement as the Pfizer Research Collaboration Agreement.

Under the Pfizer Research Collaboration Agreement, Pfizer has designated a number of initial Targets. For each identified Target, we and Pfizer will conduct a separate research program pursuant to a research plan. Pfizer may make substitutions for any of the initial Target candidates, which substitutions are limited subject to the stage of research for such Target.

We and Pfizer are obligated to use commercially reasonable efforts to complete our respective activities set forth in a research plan, including, in our case, the obligation to provide certain deliverables at the end of each stage. Under the research plan, we are required to provide compound formulation and conduct pharmacokinetic/pharmacodynamic and drug safety research and development activities in support of screening and other activities conducted by Pfizer relating to a Target. Following the provision of the deliverables by us for a stage, we will suspend the conduct of any further activities until Pfizer has exercised its right to proceed. If Pfizer does not exercise such right within the applicable time period, we will cease activities for such Target and such Target will no longer be part of the collaboration. Each party will bear its own costs in the conduct of such activities, except that any additional work that we agree with Pfizer to perform outside of the research plan will be paid for by Pfizer.

Pfizer has the right to exercise an option to obtain an exclusive worldwide license with respect to each Target for a specified period of time after receipt of the applicable deliverables for such Target. If Pfizer does not

exercise its option for a Target, such Target is no longer subject to the Pfizer Research Collaboration Agreement. If Pfizer exercises such option, Pfizer will have an exclusive license to develop and commercialize compounds directed against such Target, subject to certain diligence obligations.

During the term of the Pfizer Research Collaboration Agreement, we and our affiliates are not permitted, either directly or indirectly, to develop or commercialize any pharmacologically-active agent whose primary mechanism of action is, by design, directed to a Target, or grant any license, covenant not to sue or other right to any third party for the conduct of such activities. There are no restrictions on Pfizer from developing, manufacturing or commercializing products, programs, technologies or processes that are similar to or may compete with any covered by the Pfizer Research Collaboration Agreement, subject to certain limitations on Pfizer's right to use our confidential information or know-how.

In the year ended December 31, 2018, we received an upfront, non-refundable payment and certain additional payments totaling $28.0 million in exchange for use of our technology license and to fund Pfizer-related research as defined within the Pfizer Research Collaboration Agreement. We are eligible to receive up to an additional $37.5 million in non-refundable option payments if Pfizer exercises its options for all targets under the Pfizer Research Collaboration Agreement. We are also entitled to receive up to $225.0 million in development milestone payments and up to $550.0 million in sales-based milestone payments for all designated targets under the Pfizer Research Collaboration Agreement, as well as mid- to high-single digit tiered royalties, which may be subject to reductions, on net sales of PROTAC targeted protein degrader-related products. In 2021 and 2020, we received payments totaling $1.2 million and $4.4 million, respectively. Pfizer also selected additional targets and initiated additional services totaling $1.0 million and $3.5 million in December 2022 and 2021, respectively, which were included in accounts receivable as of December 31, 2022 and 2021.

In 2022 and 2021, we received payments totaling $3.5 million and $1.2 million, respectively, for addition targets and services. In addition, Pfizer selected an additional target in 2022 totaling $1.0 million which was included in accounts receivable as of December 31, 2022.

Unless earlier terminated, the Pfizer Research Collaboration Agreement will expire upon the expiration of all royalty obligations thereunder. The royalty period for each product developed under the Pfizer Research Collaboration Agreement will expire on a country-by-country basis upon the later of (1) the expiration of the last-to-expire valid patent claim that claims or covers the composition of matter of a compound contained within such product or (2) ten years after the first commercial sale with respect to such product. Pfizer has the right to terminate the Pfizer Research Collaboration Agreement for convenience in its entirety or with respect to a specific target on 60 days' prior notice. Either we or Pfizer may terminate the Pfizer Research Collaboration Agreement, in its entirety or with respect to a specific target, if the other party is in material breach and such breach is not cured within the specified cure period. In addition, either we or Pfizer may terminate the Pfizer Research Collaboration Agreement in the event of specified insolvency events involving the other party. If Pfizer terminates the agreement in its entirety or as a result of our uncured material breach or our insolvency, Pfizer retains its license with respect to Targets for which it has exercised an option (unless Pfizer elects otherwise), subject to reduced payment obligations.

Bayer Collaboration Agreement

In June 2019, we entered into a Collaboration and License Agreement with Bayer setting forth our collaboration to identify or optimize PROTAC targeted protein degraders, that mediate for degradation of Targets using our proprietary platform technology, which Targets will be selected by Bayer, subject to certain exclusions and limitations. We refer to this agreement as the Bayer Collaboration Agreement. The Bayer Collaboration Agreement became effective in July 2019.

For the identified Targets, we and Bayer will conduct a research program pursuant to separate research plans tailored to each Target selected by Bayer. Bayer may make substitutions for any such initial Target candidates, subject to certain conditions and based on the stage of research for such Target.

We and Bayer are obligated to use commercially reasonable efforts to complete our respective activities set forth in each research plan, including, in our case, the obligation to provide certain deliverables at certain stages of the research plans. The joint steering committee established under the collaboration shall determine

whether the research program with respect to a given Target has been completed. In the absence of any such determination by the joint steering committee, and unless otherwise agreed by the parties in writing, for each Target for which research program activities have commenced, if no research funding is allocated to such Target for the 12 month period commencing on July 1, 2019 or any anniversary thereof, and we refer to each as a Research Program Year, the research program with respect to the relevant Target shall be deemed completed as of the end of the last Research Program Year for which funding was allocated to such Target. Bayer shall pay to us research funding payments of $3.0 million dollars per year in each of the first four Research Program Years. If our costs for its research activities under the research plans exceed the research funding provided by Bayer for any Research Program Year before completion of all relevant research program activities in such Research Program Year, and we have complied with its reporting obligations to Bayer with respect to research program costs, we shall not be obligated to carry out further research program activities for the given Research Program Year unless Bayer has agreed in writing to fund such additional activities.

During the term of the Bayer Collaboration Agreement, we and our affiliates are not permitted, either directly or indirectly, to design, identify, discover or develop any small molecule pharmacologically-active agent whose primary mechanism of action is, by design, directed to the inhibition or degradation of any Target selected or reserved by Bayer, or grant any license, covenant not to sue or other right to any third party in the field of human disease under the licensed intellectual property for the conduct of such activities. There are no restrictions on Bayer from developing, manufacturing or commercializing products, programs, technologies or processes that are similar to or may compete with any covered by the Bayer Collaboration Agreement, subject to certain limitations on Bayer's right to use the Arvinas' confidential information or know-how.

Under the terms of the Bayer Collaboration Agreement, we received an aggregate upfront, non-refundable payment of $17.5 million in August 2019. Bayer is committed to fund a total of $12.0 million in research funding payments through 2023, of which $10.5 million was received from inception through December 31, 2022, subject to potential increases if our costs for research activities exceed the research funding payments allocated to a Target and certain conditions are met. We are also eligible to receive up to $197.5 million in development milestones and up to $490.0 million in sales-based milestones for all designated Targets. In addition, we are eligible to receive, on net sales of PROTAC targeted protein degrader-related products, mid-single digit to low-double digit tiered royalties, which may be subject to reductions.

Unless earlier terminated, the Bayer Collaboration Agreement will expire upon the expiration of all royalty obligations thereunder. The royalty period for each product developed under the Bayer Collaboration Agreement will expire on a country-by-country basis upon the later of (1) the expiration of the last-to-expire valid patent claim that covers the manufacture, use or sale of such product or (2) ten years after the first commercial sale with respect to such product. Bayer has the right to terminate the Bayer Collaboration Agreement for convenience in its entirety or with respect to a specific target on 60 days' prior written notice. Either the Company or Bayer may terminate the Bayer Collaboration Agreement, in its entirety or with respect to a specific target, if the other party is in material breach and such breach is not cured within the specified cure period. In addition, either we or Bayer may terminate the Bayer Collaboration Agreement in the event of specified insolvency events involving the other party. If Bayer terminates the agreement in its entirety as a result of our uncured material breach or the Company's insolvency, Bayer may elect in writing to retain its license with respect to any Targets previously identified and delivered to Bayer, subject to reduced payment obligations.

Bayer Joint Venture

In July 2019, we, Bayer and Bayer CropScience LP, or BCS, formed a joint venture, Oerth Bio, a Delaware limited liability company. We and BCS each received an initial ownership interest in Oerth Bio representing 50% of the ownership interests. Oerth Bio was formed for the purpose of researching, developing and commercializing PROTAC targeted protein degraders, or PROTAC Products, for applications in the field of agriculture. A 15% ownership interest of Oerth Bio was reserved for the future grant of incentive units to employees and service providers of Oerth Bio and, as a result, the Company's ownership interest totaled 46.5%, 48.4% and 49.4% as of December 31, 2022, 2021 and 2020, respectively, as a result of vested incentive units.

In exchange for the ownership interests in Oerth Bio, we made an in-kind intellectual property contribution to Oerth Bio and BCS made an in-kind intellectual property contribution to Oerth Bio. In addition, BCS committed and subsequently made cash contributions to Oerth Bio totaling $56.0 million. Under the joint

venture agreement, we have no obligation to provide additional funding and our ownership interest will not be diluted from future contributions from BCS.

Our and BCS's ownership interest in Oerth Bio, and the accompanying rights and obligations as members of Oerth Bio, are governed by an amended and restated limited liability company agreement, or LLC Agreement, by and among us, BCS and Oerth Bio. Oerth Bio is generally governed by a board of managers, or the JV Board, which is comprised of four voting members, two of which have been designated by us and two of which have been designated by BCS. JV Board decisions will generally be made by majority vote of the managers, with each manager having one vote. Certain matters will require the consent of both BCS and the Company or both of their designated managers on the JV Board. As Oerth Bio is jointly controlled by us and BCS, we account for our ownership interest using the equity method of accounting.

We and BCS also entered into separate service agreements, or the Services Agreements. We and BCS will provide services to Oerth Bio as agreed from time to time by us and BCS, as applicable, and set forth in statements of work to be delivered under the applicable Services Agreement.

We and BCS each also entered into respective intellectual property contribution agreements, each, an IP Contribution Agreement, with Oerth Bio. Pursuant to the IP Contribution Agreement by and between us and Oerth Bio, or the Company IP Contribution Agreement, in addition to certain non-exclusive licenses, we granted to Oerth Bio an exclusive, worldwide, fully paid-up, royalty-free license, including certain rights to sublicense, to use certain of our PROTAC technology to research, develop, manufacture, use and commercialize and sell PROTAC Products in the field of agriculture.

Pursuant to the IP Contribution Agreement by and between BCS and Oerth Bio, or the BCS IP Contribution Agreement, in addition to certain non-exclusive licenses, BCS and certain of its affiliates granted to Oerth Bio an exclusive, worldwide, fully paid-up, royalty-free license, including certain rights to sublicense, to use certain of BCS' or its affiliates' intellectual property that covers ubiquitin ligases or moieties that bind ubiquitin ligase complexes, and linkers that attach ubiquitin ligase binding moieties to moieties that bind to a target, to research, develop, manufacture, use and commercialize and sell PROTAC Products in the field of agriculture.

The Company IP Contribution Agreement and the BCS IP Contribution Agreement also contain a non-exclusive, worldwide, fully paid-up, royalty-free license grant from Oerth Bio to each of us and BCS, respectively, under various forms of intellectual property developed by Oerth Bio to research, develop, manufacture, use and commercialize products outside of the field of agriculture, in each case excluding intellectual property licensed by the other contributing party to Oerth Bio.

We, Oerth Bio and BCS also entered into an option agreement, or the Option Agreement, pursuant to which the parties agreed to certain procedures for, and preferential rights relating to, the possible transfer to BCS of PROTAC Product candidates researched, developed and commercialized by Oerth Bio under the joint venture.

In December 2022, we, BCS and Oerth Bio terminated the Option Agreement and the commitment agreement entered into in connection with the formation of Oerth Bio. In addition, we, BCS and Oerth Bio amended and restated the Arvinas IP Contribution Agreement and BCS Contribution Agreement. We and BCS also amended the LLC Agreement.

Pfizer ARV-471 Collaboration Agreement

In July 2021, we entered into a collaboration agreement with Pfizer, or the ARV-471 Collaboration Agreement, pursuant to which we granted Pfizer worldwide co-exclusive rights to develop and commercialize products containing our proprietary compound ARV-471, or the Licensed Products.

Under the ARV-471 Collaboration Agreement, we received an upfront, non-refundable payment of $650 million. In addition, we are eligible to receive up to an additional $1.4 billion in contingent payments based on specified regulatory and sales-based milestones for the Licensed Products. Of the total contingent payments, $400 million in regulatory milestones are related to marketing approvals and $1.0 billion are related to sales-based milestones.

We and Pfizer share equally (50/50) all development costs (including costs for conducting any clinical trials) for the Licensed Products, subject to certain exceptions. Except for certain regions described below, we will also share equally (50/50) all profits and losses in commercialization and medical affairs activities for the Licensed Products in all other countries, subject to certain exceptions.

We will be the marketing authorization holder and, subject to marketing approval, book sales in the United States, while Pfizer will hold marketing authorizations outside the United States. We will determine with Pfizer which, if any, regions within the world will be solely commercialized by one party, and in such region the parties will adjust their share of all profits and losses for the Licensed Products based on the role each party will be performing.

Unless earlier terminated in accordance with its terms, the ARV-471 Collaboration Agreement will expire on a Licensed Product-by-Licensed Product and country-by-country basis when such Licensed Products is no longer commercialized or developed for commercialization in such country. Pfizer may terminate the ARV-471 Collaboration Agreement for convenience in its entirety or on a region-by-region basis subject to certain notice periods. Either party may terminate the ARV-471 Collaboration Agreement for the other party's uncured material breach or insolvency. Subject to applicable terms of the ARV-471 Collaboration Agreement, including certain payments to Pfizer upon termination for our uncured material breach, effective upon termination of the ARV-471 Collaboration Agreement, we are entitled to retain specified licenses to be able to continue to exploit the Licensed Products.

Subject to specified exceptions, we and Pfizer have each agreed not to directly or indirectly research, develop, or commercialize any competing products outside of the ARV-471 Collaboration Agreement anywhere in the world during the term of the ARV-471 Collaboration Agreement.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on intellectual property and proprietary products. While we believe that our technology, expertise, scientific knowledge and intellectual property estate provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization. Not only must we compete with other companies that are focused on protein degradation, but any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. Moreover, our industry is characterized by the existence of large numbers of patents and frequent allegations of patent infringement.

Our platform and product focus is the discovery and development of protein degradation therapies using our small molecule PROTAC targeted protein degraders. Other companies researching chimeric small molecules for protein degradation include Accutar Biotechnology, Inc., C4 Therapeutics, Inc., Cullgen Inc., Foghorn Therapeutics, Inc., Kymera Therapeutics, Inc., Nurix Therapeutics, Inc. and Proteovant Therapeutics, Inc. Further, several large pharmaceutical companies have disclosed preclinical or clinical investments in this field, including AbbVie, Amgen, AstraZeneca plc, Boehringer Ingelheim, Bristol Myers Squibb Company, GlaxoSmithKline plc, Genentech, Novartis International AG and Sanofi SA. Since 2020, some of these biotechnology and pharmaceutical companies have announced the initiation of clinical trials for targeted protein degraders. Additionally, other novel targeting mechanisms could ultimately address similar patient populations, such as CYP11A1 inhibitor (which is being developed by Orion/Merck) and an AR N-Terminal Domain inhibitor (which his being developed by ESSA Pharma) in prostate cancer. In addition to competition from other protein degradation therapies, any products that we develop may also face competition from other types of therapies, such as small molecule, antibody, or gene therapies.

Our lead product candidates target oncologic indications. The most common methods of treating patients in oncologic indications are surgery, radiation and drug therapy, including chemotherapy, hormone therapy and targeted drug therapy. There are a variety of available drug therapies marketed for cancer, including prostate cancer and breast cancer. In many cases, these drugs are administered in combination to enhance efficacy. Some of the currently approved drug therapies are branded and subject to patent protection,

and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors. In general, although there has been considerable progress over the past few decades in the treatment of cancer and the currently marketed therapies provide benefits to many patients, these therapies all are limited to some extent in their efficacy and frequency of adverse events, and none of them are successful in treating all patients. As a result, the level of morbidity and mortality from cancer remains high.

In addition to currently marketed drugs, including the selective estrogen receptor degrader elacestrant, there are also several product candidates in late stage clinical development for the treatment of oncologic indications, including for mCRPC and metastatic ER+ / HER2- breast cancer. These products in development include, in the case of metastatic ER+ / HER2- breast cancer, selective estrogen receptor degraders and may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any of our product candidates for which we obtain market approval.

If any of our product candidates are approved for the indications for which we expect to conduct clinical trials, they will compete with the foregoing therapies and the currently marketed drugs and potentially any drugs in development. It is also possible that we will face competition from other biologic or pharmaceutical approaches as well as from other types of therapies.

Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could 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 any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. There are generic products currently on the market for certain of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our product candidates are approved, we expect that they will be priced at a significant premium over competitive generic products.

The key competitive factors affecting the success of all our programs, if approved, are likely to be their efficacy, safety, convenience, price, level of generic competition and availability of reimbursement.

Commercialization Plans

We have not yet established our own commercial organization or distribution capabilities because our product candidates are still in preclinical and clinical development. Other than our discovery collaboration agreements, we have retained commercialization rights for all of our development programs including global co-commercialization rights for ARV-471 through our collaboration with Pfizer. If any of our product candidates receive marketing approval, we will need to develop a plan to commercialize them in the United States and other key markets. We currently expect that we would build our own focused, specialized sales and marketing organization to support the commercialization of product candidates in the United States for which we receive marketing approval and that can be commercialized with such capabilities and we are beginning that building process, including through the hiring of John Northcott as Chief Commercial Officer in 2022. We expect to utilize a variety of types of collaboration, co-promotion, distribution and other marketing arrangements with one or

more third parties to commercialize our product candidates in markets outside the United States or for situations in which a larger sales and marketing organization is required.

As product candidates advance through our pipeline, our commercial plans may change. In particular, some of our research programs target potentially larger indications. Data, the size of the development programs, the size of the target market, the size of a commercial infrastructure and manufacturing needs may all influence our strategies in the United States, Europe and the rest of the world.

Manufacturing and Supply

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely on and expect to continue to rely on third-party contract manufacturing organizations, or CMOs, for both drug substance and finished drug product as well as for the synthesis of compounds in our preclinical research and development activities. We have engaged third-party manufacturers to supply the drug substances and building blocks for those substances for ARV-471, bavdegalutamide and ARV-766. We have also engaged third-party manufacturers to develop and manufacture finished drug product for ARV-471, bavdegalutamide and ARV-766 that we are using and plan to use in our ongoing and planned Phase 1/2 and pivotal clinical trials. We currently obtain our supplies from these manufacturers on a purchase order basis and do not have long-term supply arrangements in place. Should any of these manufacturers become unavailable to us for any reason, we believe that there are a number of potential replacements, although we may incur some delay in identifying and qualifying such replacements. Under the terms of our collaboration, we expect Pfizer to manufacture commercial supply of ARV-471.

All of our product candidates are organic compounds of low molecular weight, generally called small molecules, but which are larger than traditional small molecule therapeutics. We have selected these compounds not only on the basis of their potential efficacy and safety, but also for their ease of synthesis and reasonable cost of goods. In particular, our lead product candidates are manufactured using reliable and reproducible synthetic processes from readily available starting materials. The chemistry is amenable to scale up and does not require unusual equipment in the manufacturing process. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities or with partners.

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other jurisdictions, such as the European Union, extensively regulate, among other things, the research, development, testing, manufacturing, pricing, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, sales, reimbursement, post-approval monitoring and reporting, and import and export of biopharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign jurisdictions, along with compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Approval and Regulation of Drugs in the United States

In the United States, drug products are regulated under the Federal Food, Drug, and Cosmetic Act, or FDCA, and applicable implementing regulations and guidance. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products, and for their regulatory approval, is typically referred to as a sponsor. The failure of a sponsor to comply with the applicable regulatory requirements at any time during the product development process, including nonclinical testing, clinical testing, the approval process or post-approval process, may result in delays to the conduct of a study, regulatory review and approval and/or administrative or judicial sanctions.

A sponsor seeking approval to market and distribute a new drug in the United States generally must satisfactorily complete each of the following steps before the product candidate will be approved by the FDA:

- preclinical testing including laboratory tests, animal studies and formulation studies, which must be performed in accordance with the FDA's good laboratory practice, or GLP, regulations and standards;
- completion of the manufacture, under current Good Manufacturing Practices, or cGMP, conditions, of the drug substance and drug product that the sponsor intends to use in human clinical trials along with required analytical and stability testing;
- design of a clinical protocol and submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for each proposed indication, in accordance with good clinical practices, or GCP;
- preparation and submission to the FDA of a new drug application, or NDA, for a drug product which includes not only the results of the clinical trials, but also, detailed information on the chemistry, manufacture and quality controls for the product candidate and proposed labeling for one or more proposed indication(s);
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities, including those of third parties, at which the product candidate or components thereof are manufactured to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of any FDA audits of the clinical trial sites to assure compliance with GCP and the integrity of clinical data in support of the NDA;
- payment of user fees and securing FDA approval of the NDA to allow marketing of the new drug product; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategies, or REMS, and the potential requirement to conduct any post-approval studies required by the FDA.

Preclinical Studies

Before a sponsor begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage, including *in vitro* and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish rationale for therapeutic use. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. These studies are typically referred to as IND-enabling studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards and the United States Department of Agriculture's Animal Welfare Act, if applicable. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved NDA. In support of a request for an IND, sponsors must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials,

among other things, must be submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin or recommence.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. The FDA imposes clinical holds whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, nonclinical, and/or chemistry, manufacturing, and controls, or CMC. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, such studies must be conducted in accordance with GCP including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee, or DSMB. This group provides authorization as to whether or not a trial may move forward at designated check points based on certain available data from the study to which only the DSMB may access. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-

size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

There is no obligation for a sponsor to make its drug products available for expanded access. However, if a sponsor has a policy regarding how it responds to expanded access requests, it must make that policy available. This provision requires drug and biologic companies to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy. We received Fast Track designation for bavdegalutamide for mCRPC in 2019.

In addition, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without needing FDA approval under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients under the Right to Try Act.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product candidate to human subjects under the supervision of a qualified investigator in accordance with GCP requirements which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written clinical trial protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may also be required after approval.

Phase 1 clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion and pharmacodynamics in healthy humans or in patients. During Phase 1 clinical trials, information about the investigational drug product's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid Phase 2 clinical trials.

Phase 2 clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials. Phase 2 clinical trials are well controlled, closely monitored and conducted in a limited patient population.

Phase 3 clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 clinical trial may be designed to deliver

the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a drug: such Phase 3 studies are referred to as “pivotal.”

A clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A company’s designation of a clinical trial as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. Moreover, as noted above, a pivotal trial is a clinical trial that is believed to satisfy FDA requirements for the evaluation of a product candidate’s safety and efficacy such that it can be used, alone or with other pivotal or non-pivotal trials, to support regulatory approval. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

In some cases, the FDA may approve an NDA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate’s safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional experience from the treatment of a larger number of patients in the intended treatment group and to further document a clinical benefit in the case of drugs approved under accelerated approval regulations. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

In March 2022, the FDA finalized guidance entitled “Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics,” which outlines how sponsors can utilize an adaptive trial design in the early stages of oncology product development (i.e., the first-in-human clinical trial) to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts are included in IND applications and assessed by FDA. Expansion cohort trials can potentially bring efficiency to product development and reduce developmental costs and time.

In December 2022, with the passage of Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other “pivotal study” of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, actions plans must include the sponsor’s goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk to humans exposed to the product; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. The FDA will typically inspect one or more clinical sites to assure compliance with GCPs and the integrity of the clinical data submitted.

Finally, sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. The failure to submit clinical trial information to clinicaltrials.gov is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues. Although the FDA has historically not enforced these reporting requirements due to the Department of Health and Human Services’, or HHS’s, long delay in issuing final implementing regulations, those regulations have now been issued and the FDA has issued several Notices of Noncompliance to manufacturers since April 2021.

Manufacturing and Other Regulatory Requirements

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Specifically, the FDA's regulations require that pharmaceutical products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. Manufacturers and other entities involved in the manufacture and distribution of approved pharmaceuticals are required to register their establishments with the FDA and some state agencies, and they are subject to periodic unannounced inspections by the FDA for compliance with cGMPs and other requirements. Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated. Changes to the manufacturing process, specifications or container closure system for an approved product are strictly regulated and often require prior FDA approval before being implemented. The FDA's regulations also require, among other things, the investigation and correction of any deviations from cGMP and the imposition of reporting and documentation requirements upon the sponsor and any third-party manufacturers involved in producing the approved product.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, or PREA, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The sponsor, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time.

For drugs intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of a sponsor, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, the FDA will meet early in the development process to discuss pediatric study plans with sponsors and the FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety (90) days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The law requires the FDA to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. It further requires the FDA to publicly post the PREA Non-Compliance letter and sponsor's response. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although FDA has recently taken steps to limit what it considers abuse of this statutory exemption.

The FDA Reauthorization Act of 2017 established new requirements to govern certain molecularly targeted cancer indications. Any company that submits an NDA three years after the date of enactment of that statute must submit pediatric assessments with the NDA if the drug is intended for the treatment of an adult cancer and is directed at a molecular target that FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. The investigation must be designed to yield clinically meaningful pediatric study data regarding the dosing, safety and preliminary efficacy to inform pediatric labeling for the product.

Review and Approval of an NDA

In order to obtain approval to market a drug product in the United States, a marketing application must be submitted to the FDA that provides sufficient data establishing the safety and efficacy of the proposed drug product for its intended indication. The application includes all relevant data available from pertinent preclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the drug product to the satisfaction of the FDA.

The NDA is a vehicle through which sponsors formally propose that the FDA approve a new product for marketing and sale in the United States for one or more indications. Every new drug product candidate must be the subject of an approved NDA before it may be commercialized in the United States. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2023 is approximately $3.25 million for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual prescription drug product program fee, which for federal fiscal year 2023 is approximately $394,000. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation, an exception from the program fee when the program does not engage in manufacturing the drug during a particular fiscal year and a waiver for certain small businesses.

Following submission of an NDA, the FDA conducts a preliminary review of the application within 60 calendar days of its receipt and it must inform the sponsor by that time or before whether the application is sufficiently complete to permit substantive review. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File, or RTF, determination to the sponsor. The FDA may request additional information rather than accept the application for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which the FDA accepts the application for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of products that are not NMEs, the ten-month and six-month review periods run from the date that the FDA receives the application. The review process and the Prescription Drug User Fee Act, or PDUFA, target action date may be extended by the FDA for three additional months to consider new information or clarification provided by the sponsor to address an outstanding deficiency identified by the FDA following the original submission.

In connection with its review of an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including component manufacturing, finished product manufacturing and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.

Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Under the FDA Reauthorization Act of 2017, the FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain applications, including applications for products in shortage or those for which approval is dependent on remediation of conditions identified in the inspection report. Moreover, with passage of FDORA, Congress clarified FDA's authority to conduct inspections by expressly permitting inspection of facilities involved in the preparation, conduct, or analysis of clinical and non-clinical studies submitted to FDA as well as other persons holding study records or involved in the study process.

In addition, as a condition of approval, the FDA may require a sponsor to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events and whether the product is a new molecular entity.

The FDA may refer an application for a novel product to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA is authorized to expedite the review of applications in several ways. Under the Fast Track program, the sponsor of a product candidate may request the FDA to designate the product for a specific indication as a Fast Track product concurrent with or after the filing of the IND. Candidate products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. In addition to other benefits, such as the ability to have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track application before the application is complete, a process known as rolling review.

Any product candidate submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as breakthrough therapy designation, priority review and accelerated approval.

- *Breakthrough therapy designation.* To qualify for the breakthrough therapy program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives intensive guidance on an efficient development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review and rolling review.

- *Priority review.* A product candidate is eligible for priority review if it treats a serious condition and, if approved, it would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention compared to marketed products. FDA aims to complete its review of priority review applications within six months as opposed to 10 months for standard review.

- *Accelerated approval.* Drug products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval. Accelerated approval means that a product candidate may be approved on the basis of adequate and well controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity and prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug product candidate receiving accelerated approval perform adequate and well controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials. With the passage of FDORA in December 2022, Congress modified

certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to: require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded, require a sponsor of a product granted accelerated approval to submit progress reports on its post-approval studies to FDA every six months (until the study is completed); and use expedited procedures to withdraw accelerated approval of an NDA or BLA after the confirmatory trial fails to verify the product's clinical benefit. Further, FDORA requires the agency to publish on its website "the rationale for why a post-approval study is not appropriate or necessary" whenever it decides not to require such a study upon granting accelerated approval.

- *Regenerative advanced therapy.* With passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

None of these expedited programs changes the standards for approval but they may help expedite the development or approval process of product candidates.

The FDA's Decision on an NDA

After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either a Complete Response Letter, or CRL, or an approval letter. To reach this determination, the FDA must determine that the drug is effective and that its expected benefits outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the product's safety and efficacy in the NDA. This assessment is also informed by other factors, including: the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks. In connection with this assessment, the FDA review team will assemble all individual reviews and other documents into an "action package," which becomes the record for FDA review. The review team then issues a recommendation, and a senior FDA official makes a decision.

A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. The CRL may require additional clinical or other data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time- consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the sponsor will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the sponsor an additional six month extension to respond. The FDA has committed to reviewing resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. The FDA has taken the position that a CRL is not final agency action making the determination subject to judicial review.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. That is, the approval will be limited to the conditions of use (e.g., patient population, indication) described in the FDA-approved labeling. Further, depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, require that post-approval trials, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution and use restrictions or other risk

management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing trials or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA may have imposed as part of the approval process. The sponsor will be required to report, among other things, certain adverse reactions and manufacturing problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or withdrawal of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product.

It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product. Further, with passage of the Pre-Approval Information

Exchange Act in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. Previously, such communications were permitted under FDA guidance but the new legislation explicitly provides protection to sponsors who convey certain information about products in development to payors, including unapproved uses of approved products.

Violations of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the HHS, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product for the proposed use. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the sponsor to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the sponsor for approval of the application "were not conducted by or for the sponsor and for which the sponsor has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Section 505(b)(2) thus authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the sponsor. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) sponsor can establish that reliance on the FDA's previous approval is scientifically appropriate, the sponsor may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) sponsor.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, a sponsor must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the

rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug." Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. This interpretation was confirmed with enactment of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the sponsor may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight (8) months for a drug that has three (3) or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The FDA is also authorized to expedite review of "competitor generic therapies" or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the sponsor's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. The FDA's regulations governing patient listings were largely codified into law with enactment of the Orange Book Modernization Act in January 2021. When an ANDA sponsor files its application with the FDA, the sponsor is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA sponsor is not seeking approval. To the extent that the Section 505(b)(2) sponsor is relying on studies conducted for an already approved product, the sponsor is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA sponsor would.

Specifically, the sponsor must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the sponsor does not

challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the sponsor is not seeking approval).

If the ANDA sponsor has provided a Paragraph IV certification to the FDA, the sponsor must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA sponsor.

To the extent that the Section 505(b)(2) sponsor is relying on studies conducted for an already approved product, the sponsor is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA sponsor would. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) sponsor.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of regulatory exclusivity to the term of any patent or existing regulatory exclusivity, including orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an “orphan drug” if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must seek orphan drug designation before submitting an NDA for the candidate product. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor’s marketing application for the same drug for the same condition for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different conditions. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

The period of market exclusivity begins on the date that the marketing application is approved by the FDA and applies only to the disease or condition for which the product has been designated. Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if the company with

orphan drug exclusivity is not able to meet market demand or the subsequent product is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan drug exclusivity regardless of a showing of clinical superiority. Under Omnibus legislation signed by President Trump on December 27, 2020, the requirement for a product to show clinical superiority applies to drug products that received orphan drug designation before enactment of amendments to the FDCA in 2017 but have not yet been approved by FDA.

In September 2021, the Court of Appeals for the 11th Circuit held that, for the purpose of determining the scope of market exclusivity, the term "same disease or condition" in the statute means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, FDA announced that, in matters beyond the scope of that court order, FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved.

Patent Term Restoration and Extension

A patent claiming a new drug product, its method of use or its method of manufacture may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of the IND for the clinical investigation is begun and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The United States Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Health Care Law and Regulation

Health care providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable state and federal fraud and abuse laws and regulations (including anti-kickback and false claims laws), patient privacy laws and regulations, and other health care laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state health care laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchasing, ordering, leasing, arranging for, or recommending the purchasing, ordering, or leasing of, any good or service for which payment may be made, in whole or in part, under a federal health care program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and Civil Monetary Penalties Law, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, false or fraudulent claims for payment or knowingly making, using or causing to made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any health care benefit program or making false statements relating to health care matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and the regulations promulgated thereunder, including 45 C.F.R. Parts 160 and 164, imposing rules regarding privacy, security, and data breach notifications;
- the Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;
- the federal physician transparency requirements known as the Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, or the ACA, which requires manufacturers of drugs, medical devices, biological and medical supplies covered by Medicare, Medicaid, or State Children's Health Insurance Program to report annually to the Centers for Medicare & Medicaid Services, or CMS, within HHS, information related to payments and other transfers of value made by that entity to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to health care items or services that are reimbursed by non-government third-party payors, including private insurers.

Further, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pharmaceutical Insurance Coverage and Health Care Reform

In the United States and other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated health care costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of health care costs also has become a priority of federal, state and foreign governments and the prices of products 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 further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the United States.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2030 under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. These Medicare sequester reductions were suspended and reduced through June 2022, with the full 2% cut resuming thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court heard this case on November 10, 2020 and, on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden rescinded those orders and issued a new executive order that directs federal agencies to reconsider rules and other policies that limit access to healthcare, and consider actions that will protect and strengthen that access. Under this order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and under the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders

intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which has been delayed until January 1, 2026 by the Infrastructure Investment and Jobs Act.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Order directs HHS to create a plan within 45 days to combat “excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging.” On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

More recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of enrolling in a plan providing outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 additional Part D drugs in 2027, 15 additional Part B or Part D drugs in 2028, and 20 additional Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated “maximum fair price” under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law

also caps Medicare beneficiaries' out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

At the state level, individual states are increasingly aggressive 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. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription pharmaceutical and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Review and Approval of Medicinal Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, a sponsor will need to obtain the necessary approvals by the comparable non-U.S. regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others. Specifically, however, the process governing approval of medicinal products in the European Union, or EU, generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application, or MAA, and granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU.

Clinical Trial Approval

On January 31, 2022, the Clinical Trials Regulation (EU) No 536/2014 became effective in the European Union and replaced the prior Clinical Trials Directive 2001/20/EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one Member State of the European Union, or EU Member State, is only required to submit a single application for approval. The submission is made through the Clinical Trials Information System, a new clinical trials portal overseen by the European Medicines Agency, or EMA, and available to clinical trial sponsors, competent authorities of the EU Member States and the public.

Specifically, the main characteristics of the new regulation include: a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

The new regulation did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific study site after the applicable ethics committee has issued a favorable opinion.

Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the EU at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation in the EU

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the Committee for Human Medicinal Products, or CHMP, or Committee for Advanced Therapies, or CAT, are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Pediatric Studies

Prior to obtaining a marketing authorization in the European Union, sponsors must demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are laid down in Regulation (EC) No 1901/2006, the so-called Paediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Paediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine for children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine for children is not needed or is not appropriate, such as for diseases that only affect the elderly population. Before an MAA can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.

Marketing Authorization

To obtain a marketing authorization for a product under EU regulatory systems, a sponsor must submit an MAA either under a centralized procedure administered by the EMA, or one of the procedures administered by competent authorities in the EU Member States (decentralized procedure or mutual recognition procedure). A marketing authorization may be granted only to a sponsor established in the EU. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the EU, sponsors have to demonstrate compliance with all measures included in an EMA-approved PIP covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid across the European Economic Area (i.e. the EU as well as Iceland, Liechtenstein and Norway). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products and products with a new active substance

indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. The centralized procedure may at the request of the applicant also be used in certain other cases.

Under the centralized procedure, the CHMP is responsible for conducting the initial assessment of a product and for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 15 calendar days of receipt of a final opinion from the CHMP, the European Commission must prepare a draft decision concerning an application for marketing authorization. This draft decision must take the opinion and any relevant provisions of EU law into account. Before arriving at a final decision on an application for centralized authorization of a medicinal product the European Commission must consult the Standing Committee on Medicinal Products for Human Use. The Standing Committee is composed of representatives of the EU Member States and chaired by a non-voting European Commission representative. The European Parliament also has a related “droit de regard.” The European Parliament’s role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse to grant a marketing authorization.

The European Commission may grant a so-called “marketing authorization under exceptional circumstances.” Such authorization is intended for products for which the sponsor can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the sponsor cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the sponsor must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;
- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radiopharmaceutical, by an authorized person; and
- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

A marketing authorization under exceptional circumstances is subject to annual review to reassess the risk-benefit balance in an annual reassessment procedure. Continuation of the authorization is linked to the annual reassessment and a negative assessment could potentially result in the marketing authorization being suspended or revoked. The renewal of a marketing authorization of a medicinal product under exceptional circumstances, however, follows the same rules as a “normal” marketing authorization. Thus, a marketing authorization under exceptional circumstances is granted for an initial five years, after which the authorization will become valid indefinitely, unless the EMA decides that safety grounds merit one additional five-year renewal.

The European Commission may also grant a so-called “conditional marketing authorization” prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional marketing authorizations may be granted for product candidates (including medicines designated as orphan medicinal products), if (i) the risk-benefit balance of the product candidate is positive, (ii) it is likely that the sponsor will be in a position to provide the required comprehensive clinical trial data, (iii) the product fulfills an unmet medical need and (iv) the benefit to public health of the immediate availability on the market of the

medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

The EU medicines rules expressly permit the EU Member States to adopt national legislation prohibiting or restricting the sale, supply or use of any medicinal product containing, consisting of or derived from a specific type of human or animal cell, such as embryonic stem cells. While the products we have in development do not make use of embryonic stem cells, it is possible that the national laws in certain EU Member States may prohibit or restrict us from commercializing our products, even if they have been granted an EU marketing authorization.

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU Member States.

The mutual recognition procedure similarly is based on the acceptance by the competent authorities of the EU Member States of the marketing authorization of a medicinal product by the competent authorities of other EU Member States. The holder of a national marketing authorization may submit an application to the competent authority of an EU Member State requesting that this authority recognize the marketing authorization delivered by the competent authority of another EU Member State.

Regulatory Data Protection in the EU

In the EU, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance the centralized authorization procedure. Data exclusivity prevents sponsors for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. The European Commission or the competent authorities of the EU Member States may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (in case of centralized procedure) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Pediatric Exclusivity

If a sponsor obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the centralized procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate, or SPC.

Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a drug can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment. For either of these conditions, the sponsor must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to 10 years of market exclusivity in all EU Member States and in addition a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the 10-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Patent Term Extensions in the European Union and Other Jurisdictions

The European Union also provides for patent term extension through SPCs. The rules and requirements for obtaining a SPC are similar to those in the United States. An SPC may extend the term of a patent for up to five years after its originally scheduled expiration date and can provide up to a maximum of fifteen years of marketing exclusivity for a drug. These periods can be extended for six additional months if pediatric exclusivity is obtained, which is described in detail below. Although SPCs are available throughout the European Union, sponsors must apply on a country-by-country basis. Similar patent term extension rights exist in certain other foreign jurisdictions outside the European Union.

Regulatory Requirements after a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the EU's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.
- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU.
- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the EU notably under Directive 2001/83EC, as amended, and are also subject to EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom's withdrawal from the EU took place on January 31, 2020. The EU and the United Kingdom reached an agreement on their new partnership in the Trade and Cooperation Agreement, or the Agreement, which was applied provisionally beginning on January 1, 2021 and which entered into force on May 1, 2021. The Agreement focuses primarily on free trade by ensuring no tariffs or quotas on trade in goods, including healthcare products such as medicinal products. Thereafter, the EU and the United Kingdom will form two separate markets governed by two distinct regulatory and legal regimes. As such, the Agreement seeks to minimize barriers to trade in goods while accepting that border checks will become inevitable as a consequence that the United Kingdom is no longer part of the single market. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law whereas Northern Ireland continues to be subject to EU rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law the body of EU law instruments governing medicinal products that pre-existed prior to the United Kingdom's withdrawal from the EU.

Since a significant proportion of the regulatory framework for pharmaceutical products in the U.K. covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit may have a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the U.K. For example, the U.K. is no longer covered by the centralized procedures for obtaining EU-wide marketing authorization from the EMA, and a separate marketing authorization will be required to market our product candidates in the U.K. Until December 31, 2023, it is possible for the MHRA to rely on a decision taken by the European Commission on the approval of a new marketing authorization via the centralized procedure.

Furthermore, while the Data Protection Act of 2018 in the United Kingdom that "implements" and complements the European Union's General Data Protection Regulation, or GDPR, has achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is still unclear whether transfer of data from the European Economic Area, or EEA, to the United Kingdom will remain lawful under GDPR. The United Kingdom has already determined that it considers all of the EU 27 and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the EU/EEA remain unaffected.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the GDPR which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

In October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield. The EU initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022. It is unclear if and when the framework will be finalized and whether it will be challenged in court. The uncertainty around this issue may further impact our business operations in the EU.

Pricing Decisions for Approved Products

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, EU Member States have the option to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU Member States allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced EU Member States, can further reduce prices. 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 products, if approved in those countries.

Employees and Human Capital Management

As of December 31, 2022, we had approximately 415 full-time employees. Of these full-time employees, approximately 330 employees were engaged in research and development activities, with 300 employees possessing advanced degrees, and approximately 85 employees were engaged in general and administrative activities. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We believe that we maintain good relations with our employees.

We recognize that identifying, attracting, incentivizing, integrating, retaining and promoting talented employees is vital to our success, particularly as we continue to grow. We aim to create an equitable, inclusive and empowering environment in which our employees can grow and advance their careers, with the overall goal of developing, expanding and retaining our workforce to support our current pipeline and future business goals. Our efforts to recruit and retain a diverse and passionate workforce include providing competitive compensation,

including equity incentive compensation, and comprehensive benefits that provide resources to help employees manage their health, finances and life outside of work. As of December 31, 2022, and for the last several years, our company turnover rate was and has been lower than the industry market average.

Training and educating our employees is key to our organizational success. We endeavor to provide in person and virtual trainings, as well as experiential learning through cross-functional exposure via presentations or shadowing opportunities. In addition, we value our employee's opinions and thoughts and provide virtual and onsite forums where our employees can provide feedback on corporate initiatives, recognize each other's contributions and accomplishments, and provide other suggestions for improving our evolving workplace. We prioritize employee feedback, and conduct an employee survey to measure employee engagement and to inform future talent initiatives. Similarly, we have introduced technology that enables employees to provide anonymous real-time feedback.

In addition, we are committed to our employees' health, safety and well-being. In March 2020, in response to the COVID-19 pandemic, we adjusted our workplace policies to allow employees to work from home and we remodeled our work paradigm to one that is flexible and designed to accommodate a range of work profiles from office based to hybrid to fully remote, allowing us to maximize productivity and performance. We leveraged remote hiring supported by virtual processes through which we provided a high level of interpersonal engagement and continued to expand our robust onboarding program to ensure all new hires are grounded in our business and culture.

We are also committed to diversity, equality and inclusion and we are committed to increasing representation of under-represented populations at our company, particularly in leadership roles. Over the last two years we have made conscious hiring decisions to significantly grow the number of women and diverse employees, particularly in positions of Director or above. In addition, as of December 31, 2022, five members of our board of directors identify as female and/or from a diverse racial and ethnic group.

With the goal of ensuring every employee is included, supported, and treated equitably, our employees formed a committee to support and guide us as a diverse, inclusive, and culturally intelligent workplace. This committee is comprised of a mix of employees from various functions and positions. Since its launch in 2021, the committee has worked to identify areas for growth and education in order to develop processes, systems and actions that will enable us to continue to build an inclusive workplace and a diverse workforce.

We also believe in the importance of our employees engaging in our community. In 2022, we hosted our first ever IMPACT day, a company-wide community service day benefiting organizations in the Greater New Haven area. Giving back to the communities in which we work and live is an integral part of our corporate values and over half of our employees participated in person or virtually. The activities selected support important priorities for Arvinas, including science, technology, engineering, and math (STEM) initiatives, and the Greater New Haven and patient communities.

Available Information

Our principal executive offices are located at 5 Science Park, New Haven, Connecticut 06511. Our telephone number is (203) 535-1456. Our website address is www.arvinas.com.

We make available, through our website and free of charge, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the U.S. Securities and Exchange Commission, or the SEC. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investors & Media," as a source of information about us. The information on our website is not incorporated by reference into this Annual Report on Form 10-K and should not be considered to be a part of this Annual Report on Form 10-K.

Item 1A. Risk Factors.

We face a variety of risks and uncertainties in our business and investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K, before deciding to invest in our common stock. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also become important factors that affect our business. If any of the following risks actually occur, our business, prospects, operating results and financial condition could suffer materially. In such event, the trading price of our common stock could decline and you might lose all or part of your investment.

Risks Related to Our Financial Position and Need For Additional Capital

We have incurred significant losses since our inception. We expect to incur losses over at least the next several years and may never achieve or maintain profitability.

Our net losses totaled $282.5 million, $191.0 million and $119.3 million for the years ended December 31, 2022, 2021, and 2020, respectively. As of December 31, 2022, we had an accumulated deficit of $965.4 million. To date, we have not generated any revenue from product sales and have financed our operations primarily through sales of our equity interests, proceeds from our collaborations, grant funding and debt financing. We are still in the early stages of development of our product candidates, and we have not completed development of any product candidates. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We anticipate that our expenses will increase substantially if and as we:

- continue a Phase 1/2 clinical trial of our product candidate ARV-471, a Phase 1b clinical trial of ARV-471 in combination with palbociclib, a Phase 1b cohort expansion in combination with a standard of care agent, and a Phase 3 trial with ARV-471 as a second-line treatment, and initiate a Phase 3 trial of ARV-471 in combination with palbociclib, each in patients with locally advanced or metastatic ER+ / HER2-breast cancer;
- continue a Phase 1/2 clinical trial of our product candidate bavdegalutamide (ARV-110) and a Phase 1b clinical trial of bavdegalutamide in combination with abiraterone for the treatment of men with metastatic castration-resistant prostate cancer, or mCRPC, and initiate one or more additional Phase 1b cohort expansions of bavdegalutamide in combination with standard of care agents and a Phase 3 clinical trial, in men with mCRPC;
- continue a Phase 1/2 clinical trial of our product candidate ARV-766 in men with mCRPC;
- apply our PROTAC Discovery Engine to advance additional product candidates into preclinical and clinical development;
- expand the capabilities of our PROTAC Discovery Engine;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any products for which we may obtain marketing approval;
- expand, maintain and protect our intellectual property portfolio;
- hire additional development, including clinical and regulatory, and scientific personnel; and
- add operational, financial and management information systems and personnel to support our research, product development and future commercialization efforts and support our operations as a public company.

Our expenses could increase beyond our expectations if we are required by the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or other regulatory authorities to perform trials in addition to those that we currently expect or anticipate, or if there are any delays in establishing appropriate manufacturing arrangements for or in completing our clinical trials or the development of any of our current or future product candidates.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we will incur or when, if ever, we will be able to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

We have never generated revenue from product sales and may never be profitable.

We have never generated revenue from product sales. Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with collaboration partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, product candidates we may identify for development. We do not anticipate generating revenues from product sales for the next several years, if ever. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. To become and remain profitable, we must succeed in developing, obtaining marketing approval for and commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, establishing arrangements with third parties for the manufacture of clinical supplies of our product candidates, obtaining marketing approval for our product candidates and manufacturing, marketing and selling any products for which we may obtain marketing approval.

If one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

We will need substantial additional funding to continue our operations. If we are unable to raise capital when needed, we may be required to delay, limit, reduce or terminate our research or product development programs or future commercialization efforts.

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we continue our ongoing and initiate our planned clinical trials of bavdegalutamide, ARV-471 and ARV-766, advance our other oncology and neurodegenerative programs and continue research and development and initiate additional clinical trials of and potentially seek marketing approval for our lead programs and our other product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. We continue to incur significant costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on acceptable terms or not at all, we may be required to delay, limit, reduce or terminate our research, product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We had cash, cash equivalents, restricted cash and marketable securities of approximately $1.2 billion as of December 31, 2022. We believe that our cash, cash equivalents, restricted cash and marketable securities as of December 31, 2022 will enable us to fund our planned operating expenses and capital expenditure requirements into 2026. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the progress, costs and results of our ongoing clinical trials for ARV-471, bavdegalutamide and ARV-766 and any future clinical development of ARV-471, bavdegalutamide and ARV-766;
- the scope, progress, costs and results of preclinical and clinical development for our other product candidates and development programs;
- the number of, and development requirements for, other product candidates that we pursue, including our other oncology and neurodegenerative research programs;

- the success of our collaborations with Pfizer, Inc., or Pfizer; Genentech, Inc. and F. Hoffman LaRoche Ltd., collectively referred to as Genentech; and Bayer AG, or Bayer;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- our ability to establish additional collaboration arrangements with other biotechnology or pharmaceutical companies on favorable terms, if at all, for the development or commercialization of our product candidates.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives. Adequate additional funds may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial revenue from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. Although we may receive potential future payments under our collaborations with Pfizer, Genentech and Bayer, we do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights as common stockholders. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making acquisitions or capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be acceptable or favorable to us.

Our limited operating history may make it difficult for our stockholders to evaluate the success of our business to date and to assess our future viability.

Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, conducting discovery and research activities, filing patent applications, identifying potential product candidates, undertaking preclinical studies, establishing arrangements with third parties for the manufacture of initial quantities of our product candidates and conducting Phase 1, Phase 2 and Phase 3 clinical trials for our product candidates. However, we have not yet demonstrated our ability to successfully complete any clinical trials, obtain marketing approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions stockholders make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a young business with limited operating experience and no history of revenue-generating commercial activity, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Changes in tax law may adversely affect our business or financial condition. The Tax Cuts and Jobs Act of 2017, commonly referred to as the TCJA, as amended by the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, significantly revises the U.S. Internal Revenue Code of 1986, as amended, or the Code. The TCJA contains, among other things, significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21% and the limitation of the deduction for net operating losses to 80% of current-year taxable income for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely). In addition, beginning in 2022, the TCJA eliminates the option to deduct research and development expenditures currently and requires corporations to capitalize and amortize them over five years.

In addition to the CARES Act, as part of Congress's response to the COVID-19 pandemic, economic relief legislation has been enacted in 2020 and 2021 containing tax provisions. The Inflation Reduction Act, or IRA, was also signed into law in August 2022. The IRA introduced new tax provisions, including a 1% excise tax imposed on certain stock repurchases by publicly traded corporations. The 1% excise tax generally applies to any acquisition by the publicly traded corporation (or certain of its affiliates) of stock of the publicly traded corporation in exchange for money or other property (other than stock of the corporation itself), subject to a de minimis exception. Thus, the excise tax could apply to certain transactions that are not traditional stock repurchases. Regulatory guidance under the TCJA, the IRA, and such additional legislation is and continues to be forthcoming, and such guidance could ultimately increase or lessen the impact of these laws on our business and financial condition. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the IRA, and additional tax legislation.

In the future, we might not be able to utilize a significant portion of any net operating loss carryforwards and research and development tax credit carryforwards we may have.

As of December 31, 2022, we had no federal net operating loss carryforwards, $63.4 million of state and local net operating loss carryforwards, no federal research and development tax credit carryforwards and $1.9 million of state research and development tax credit carryforwards. During the year ended December 31, 2022, we fully utilized our previously held net federal operating loss and credit carryforwards due to taxable income resulting from revenue recognition for tax purposes from our ARV-471 Collaboration Agreement and the mandatory capitalization of qualified research and development expenses incurred on or after January 1, 2022 under the TCJA. We expect in to incur net operating losses in future periods as a result of additional product development. To the extent net operating loss and tax credit carryforwards expire unused, they will not be available to offset our future income tax liabilities.

In addition, under Section 382 of the Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership by certain stockholders over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We believe our federal net operating losses are subject to an annual limitation as a result of changes in the Company's ownership, as defined by Code Section 382, in July 2018 and December 2020. Notwithstanding the limitations, we expect the federal net operating losses to be fully available under Section 382, subject to any other limitations under the Code. In addition, we may experience ownership changes in the future as a result of subsequent changes in our stock ownership, some of which may be outside of our control. If we determine that an ownership change has occurred and our ability to use our historical net operating loss and tax credit

carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

There is also a risk that due to regulatory changes, such as suspensions on the use of net operating losses, or other unforeseen reasons, our existing any future net operating losses could expire or otherwise become unavailable to offset future income tax liabilities. As described above in "Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition," the TCJA, as amended by the CARES Act, includes changes to U.S. federal tax rates and the rules governing net operating loss carryforwards that may significantly impact our ability to utilize our net operating losses to offset taxable income in the future. In addition, state net operating losses generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our net operating losses and other tax attributes.

Risks Related to the Discovery and Development of Our Product Candidates

Our approach to the discovery and development of product candidates based on our PROTAC technology platform is unproven, which makes it difficult to predict the time, cost of development and likelihood of successfully developing any products.

Our PROTAC technology platform is a relatively new technology. Our future success depends on the successful development of this novel therapeutic approach. Prior to the initiation of our Phase 1 clinical trial for bavdegalutamide in 2019, no product candidates that use a chimeric small molecule approach to protein degradation, such as our PROTAC targeted protein degraders, had been tested in humans. No product candidates of this type have been approved in the United States or Europe, and the data underlying the feasibility of developing chimeric small molecule-based therapeutic products is both preliminary and limited. We have not yet succeeded and may not succeed in demonstrating the efficacy and safety of any of our product candidates in clinical trials or in obtaining marketing approval thereafter. We have not yet completed a clinical trial of any product candidate and we have not yet completed assessment of the safety of any product candidate in humans. As such, there may be adverse effects from treatment with any of our current or future product candidates that we cannot predict at this time.

As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our PROTAC Discovery Engine, or any similar or competitive protein degradation platforms, will result in the development, and marketing approval of any products. Any development problems we experience in the future related to our PROTAC Discovery Engine or any of our research programs may cause significant delays or unanticipated costs or may prevent the development of a commercially viable product. Any of these factors may prevent us from completing our current or future preclinical studies or clinical trials or from commercializing any product candidates we may develop on a timely or profitable basis, if at all.

We are early in our development efforts. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

All of our product candidates are in development. We are developing ARV-471 for the treatment of patients with locally advanced or metastatic ER+/HER2- breast cancer and bavdegalutamide and ARV-766 for the treatment of men with metastatic castration-resistant prostate cancer. Additional product candidates are still in preclinical development. Our ability to generate revenue from product sales, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. The success of our product candidates will depend on several factors, including the following:

- successfully completing preclinical studies and clinical trials;
- receipt and related terms of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our product candidates;

- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- obtaining and maintaining third-party coverage and adequate reimbursement;
- maintaining a continued acceptable safety profile of the products following approval; and
- effectively competing with other therapies.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

Drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

We have product candidates in clinical development and preclinical development. The risk of failure for each of our product candidates is high. We are unable to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support our planned INDs in the United States or similar applications in other jurisdictions. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or similar regulatory authorities outside the United States will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of our programs.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to the outcome. A failure of one or more clinical trials can occur at any stage of testing. We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical trials for various reasons, including noncompliance with regulatory requirements;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials;
- unforeseen global instability, including political instability or instability from an outbreak of pandemic or contagious disease, such as the COVID-19 pandemic, in or around the countries in which we

conduct our clinical trials, could delay the commencement or timing of completion of our clinical trials;

- the cost of clinical trials of our product candidates may be greater than we anticipate and could be exacerbated by macroeconomic conditions such as inflation; and
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate, or their cost could increase dramatically making them financially infeasible.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in preclinical studies or clinical trials or in obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Further, cancer therapies are sometimes characterized as first-line, second-line, or third-line, and the FDA often approves new therapies initially only for third-line use. When cancer is detected early enough, first-line therapy, usually hormone therapy, surgery, radiation therapy or a combination of these, is sometimes adequate to cure the cancer or prolong life without a cure. Second- and third-line therapies are administered to patients when prior therapy is not effective. Our current clinical trials for bavdegalutamide, ARV-471 and ARV-766 are in patients who have received prior treatments. Subsequently, for those products that prove to be sufficiently beneficial, if any, we would expect to seek approval potentially as a first-line therapy, but any product candidates we develop, even if approved, may not be approved for first-line therapy, and, prior to any such approvals, we may have to conduct additional clinical trials.

If serious adverse events, undesirable side effects, or unexpected characteristics are identified during the development of any product candidates we may develop, we may need to abandon or limit our further clinical development of those product candidates.

If any product candidates we develop are associated with serious adverse events, or undesirable side effects, or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the adverse events, undesirable side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk-benefit perspective, any of which would have a material adverse effect on our business, financial condition, results of operations, and prospects. Many product candidates that initially showed promise in early-stage testing for treating cancer or other diseases have later been found to cause side effects that prevented further clinical development of the product candidates or limited their competitiveness in the market. It is impossible to predict when or if any product candidates we may develop will prove safe in humans. There can be no assurance that our PROTAC technology will not cause undesirable side effects.

A potential risk in any protein degradation product is that healthy proteins or proteins not targeted for degradation will be degraded or that the degradation of the targeted protein in itself could cause adverse

events, undesirable side effects, or unexpected characteristics. It is possible that healthy proteins or proteins not targeted for degradation could be degraded using our PROTAC technology in any of our ongoing, planned or future clinical studies. There is also the potential risk of delayed adverse events following treatment using our PROTAC technology.

Positive data from preclinical or early clinical studies of our product candidates are not necessarily predictive of the results of later clinical studies and any future clinical trials of our product candidates. If we cannot replicate the positive data from our preclinical or early clinical studies of our product candidates in our future clinical trials, we will be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.

The results of preclinical studies may not be predictive of the results of clinical trials, and the results of early-stage clinical trials may not be predictive of the results of the later-stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. In particular, the small number of patients in our ongoing early clinical trials may make the results of these trials less predictive of the outcome of later clinical trials. For example, even if successful, the results of the clinical trials of ARV-471, bavdegalutamide and and ARV-766 may not be predictive of the results of further clinical trials of these product candidates or any of our other product candidates. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Our current or future clinical trials may not ultimately be successful or support further clinical development of any of our product candidates. There is a high failure rate for product candidates proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving encouraging results in earlier studies. Any such setbacks in our clinical development could materially harm our business and results of operations.

Interim top-line and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we have published and may in the future publish interim top-line or preliminary data from our clinical trials. Interim data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. For example, the initial safety, tolerability, pharmacokinetic and efficacy data that we have disclosed in connection with our ongoing Phase 1/2 clinical trials of ARV-471 and bavdegalutamide (ARV-110) may not be indicative of the full results of those trials obtained upon completion. Preliminary or top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our reputation and business prospects.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary marketing approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. In particular, we are conducting several clinical trials, including a Phase 1/2 clinical trial and Phase 3 clinical trial with ARV-471 as a second-line treatment,of ARV-471 for patients with locally advanced or metastatic ER+ / HER2- breast cancer, a Phase 1/2 clinical trial of bavdegalutamide for men with mCRPC, and a Phase 1/2 clinical trial of ARV-766 for men with mCRPC. We cannot predict how difficult it will be to enroll patients for trials in these indications. Therefore, our ability to identify and enroll eligible patients for ARV-471, bavdegalutamide, and ARV-766 clinical trials may be limited or may result in slower enrollment than we anticipate. In addition, some of our competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates, and patients who would

otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. Patient enrollment is affected by other factors including:

- the severity of the disease under investigation;
- the eligibility criteria for the trial in question;
- the perceived risks and benefits of the product candidates under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the availability of competing therapies;
- the patient referral practices of physicians;
- the burden on patients due to inconvenient procedures;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

In April 2020, we announced that, as a result of the COVID-19 pandemic, two trial sites for our ongoing Phase 1/2 clinical trial of bavdegalutamide had publicly announced pauses in patient enrollment for clinical trials, including our trials. In addition, one trial site for our ongoing Phase 1/2 clinical trial of ARV-471 had a pause in patient enrollment for clinical trials, including our trial. While the pauses at each of the trial sites have been lifted, we may nonetheless face difficulties recruiting or retaining patients in our ongoing and planned clinical trials if patients are affected by the virus or are fearful of traveling to, or are unable to travel to, our clinical trial sites because of the outbreak. For example, we experienced a short delay in the enrollment for one cohort of our ARV-471 trial as a result of screening slowdowns attributable to COVID-19. In addition, we may engage in conversations with regulators regarding clinical trial protocols, which could result in delays to our anticipated timing to enroll patients in our studies.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We are developing and may continue to develop our product candidates in combination with other drugs. If the FDA or similar regulatory authorities outside of the United States do not approve these other drugs, or revoke their approval of such drugs, or if safety, efficacy, manufacturing or supply issues arise with the drugs we choose to evaluate in combination with our product candidates, we may be unable to obtain approval of or market our products.

We are currently conducting clinical trials of ARV-471, bavdegalutamide and ARV-766 and intend to conduct other clinical trials for each of ARV-471, bavdegalutamide and ARV-766 and potentially other product candidates, in combination with other therapies. We did not develop or obtain marketing approval for, nor do we manufacture or sell, any of the currently approved drugs that we are or may study in combination with ARV-471, bavdegalutamide or ARV-766. If the FDA or similar regulatory authorities outside of the United States revoke

their approval of the drug or drugs in combination with which we determine to develop ARV-471, bavdegalutamide or ARV-766 we will not be able to market ARV-471, bavdegalutamide or ARV-766 in combination with such revoked drugs.

If safety or efficacy issues arise with any of these drugs, we could experience significant regulatory delays, and the FDA or similar regulatory authorities outside of the United States may require us to redesign or terminate the applicable clinical trials. If the drugs we use are replaced as the standard of care for the indications we choose for bavdegalutamide or ARV-471, the FDA or similar regulatory authorities outside of the United States may require us to conduct additional clinical trials. In addition, if manufacturing or other issues result in a shortage of supply of the drugs with which we determine to combine with bavdegalutamide or ARV-471, we may not be able to complete clinical development of bavdegalutamide or ARV-471 on our current timeline or at all.

Even if bavdegalutamide or ARV-471 were to receive marketing approval or be commercialized for use in combination with other existing drugs, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the United States could revoke approval of the drug used in combination with bavdegalutamide or ARV-471 or that safety, efficacy, manufacturing or supply issues could arise with these existing drugs. Combination therapies are commonly used for the treatment of cancer, and we would be subject to similar risks if we develop any of our other product candidates for use in combination with other drugs or for indications other than cancer. This could result in our own products being removed from the market or being less successful commercially.

We plan to conduct clinical trials for our product candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations.

We plan to conduct clinical trials of our product candidates outside the United States, including our planned global Phase 3 trial for bavdegalutamide for the treatment of men with mCRPC with AR T878/H875 tumor mutations . Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and be performed by qualified investigators in accordance with ethical principles. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U.S. laws and regulations. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and could delay or permanently halt our development of the applicable product candidates.

In addition, there are risks inherent in conducting clinical trials in multiple jurisdictions, inside and outside of the United States, such as:

- regulatory and administrative requirements of the jurisdiction where the trial is conducted that could burden or limit our ability to conduct our clinical trials;
- foreign exchange rate fluctuations;
- manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research; and
- the risk that the patient populations in such trials are not considered representative as compared to the patient population in the target markets where approval is being sought.

We may not be successful in our efforts to identify or discover additional potential product candidates.

A key element of our strategy is to apply our PROTAC Discovery Engine to address a broad array of targets and new therapeutic areas. The therapeutic discovery activities that we are conducting may not be successful in identifying product candidates that are useful in treating cancer or other diseases. Our research

programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval or achieve market acceptance; or
- potential product candidates may not be effective in treating their targeted diseases.

Research programs to identify new product candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. If we are unable to identify suitable product candidates for preclinical and clinical development, we will not be able to obtain revenues from sale of products in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face and will continue to face competition from third parties that use protein degradation, antibody therapy, inhibitory nucleic acid, gene editing or gene therapy development platforms and from companies focused on more traditional therapeutic modalities, such as small molecule inhibitors. The competition is likely to come from multiple sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, government agencies and public and private research institutions.

We are aware of several biotechnology companies focused on developing chimeric small molecules for protein degradation including Accutar Biotechnology, Inc., C4 Therapeutics, Inc., Cullgen Inc., Foghorn Therapeutics, Inc., Kymera Therapeutics, Inc., Nurix Therapeutics, Inc. and Proteovant Therapeutics, Inc. Further, several large pharmaceutical companies have disclosed preclinical investments in this field, including AbbVie, Amgen Inc., AstraZeneca plc, Boehringer Ingelheim, Bristol Myers Squibb Company, GlaxoSmithKline plc, Genentech, Novartis International AG and Sanofi SA. Since 2020, some of these biotechnology and pharmaceutical companies have announced the initiation of clinical trials for targeted protein degraders. Additionally, other novel targeting mechanisms could ultimately address similar patient populations, such as CYP11A1 inhibitor (which is being developed by Orion/Merck) and an AR N-Terminal Domain inhibitor (which is being developed by ESSA Pharma) in Prostate Cancer.

Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could 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 any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. There are generic products currently on the market for certain of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our product candidates are approved, we expect that they will be priced at a significant premium over competitive generic products.

Risks Related to Dependence on Third Parties

If our collaboration with Pfizer is not successful, we may not be able to capitalize on the market potential of ARV-471.

In July 2021, we entered into a collaboration agreement with Pfizer, or the ARV-471 Collaboration Agreement, pursuant to which we granted Pfizer worldwide co-exclusive rights to develop and commercialize products containing our proprietary compound ARV-471, or the Licensed Products. Although pursuant to the terms of the ARV-471 Collaboration Agreement, we and Pfizer share equally (50/50) all development costs, including costs for conducting clinical trials, for the Licensed Products, subject to certain exceptions, our control over the amount and timing of resources that Pfizer dedicates to the development or commercialization of the Licensed Products is limited. Our ability to generate revenues from the ARV-471 Collaboration Agreement will depend, in part, on Pfizer's ability to successfully perform the functions assigned to it in such agreement. We cannot predict the success of this collaboration with Pfizer, and we cannot guarantee that this collaboration will lead to development or commercialization of the Licensed Products in the most efficient manner or at all.

If this collaboration with Pfizer does not result in the successful development and commercialization of Licensed Products, or if Pfizer terminates the ARV-471 Collaboration Agreement, which it may do for convenience subject to certain notice periods, we may not receive any of the $1.4 billion in contingent payments based on specified regulatory and sales-based milestones for the Licensed Products under the ARV-471 Collaboration Agreement.

We currently depend, and expect to continue to depend, on collaborations with third parties for the research, development, and the potential future commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to capitalize on the market potential of those product candidates.

We currently have, and anticipate in the future seeking additional, third-party collaborators for the research, development, and potential future commercialization of some of our PROTAC programs. For example, in September 2015 we entered into a research collaboration with Genentech, which we amended and restated in November 2017; in December 2017 we entered into a research collaboration with Pfizer; in July 2019 we entered into a research collaboration with Bayer; and in July 2021 we entered into a development and commercialization collaboration with Pfizer. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies and biotechnology companies. Any such arrangements with third parties will likely limit our control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of any product candidates we may seek to develop with them. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Any collaborations involving our research programs or any product candidates we may develop, including our current collaborations with Pfizer, Genentech and Bayer, pose the following risks to us:

- Collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations. For example, our collaboration with Genentech is managed by a joint research committee and joint project team, which is composed of representatives from us and Genentech, with Genentech having final decision-making authority. Similarly, our research collaborations with Pfizer and Bayer are managed by joint research committees composed of an equal number of representatives from us and our respective collaborative partners, with the collaborative partner having final decision-making authority.
- Collaborators may not pursue development and commercialization of any product candidates we may develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition or business combination that diverts resources or creates competing priorities.
- Genentech, Pfizer and Bayer have broad rights to select any target for protein degradation development on an exclusive basis, even as to us, so long as not excluded by us under the terms of each collaboration and may select targets we are considering but have not taken sufficient action to exclude under the collaboration.

- Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing.
- Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.
- Collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products.
- Collaborators may not properly obtain, maintain, enforce, or defend our intellectual property or proprietary rights or may use our proprietary information in such a way that could jeopardize or invalidate our proprietary information or expose us to potential litigation. For example, Pfizer, Genentech and Bayer have the first right to enforce or defend certain intellectual property rights under the applicable collaboration arrangement with respect to particular licensed programs, and although we may have the right to assume the enforcement and defense of such intellectual property rights if the collaborator does not, our ability to do so may be compromised by their actions.
- Disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources.
- We may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control.
- Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates. For example, each of Genentech, Pfizer and Bayer can terminate its agreement with us in its entirety or with respect to a specific target for convenience subject to specified notice periods, in certain cases as short as 60 days, or in connection with a material breach of the agreement by us that remains uncured for a specified period of time.
- Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished, or terminated.

If our collaborations do not result in the successful development and commercialization of products, or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of product candidates could be delayed, and we may need additional resources to develop product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, marketing approval, and commercialization described in this Annual Report on Form 10-K apply to the activities of our collaborators.

We may in the future decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of any product candidates we may develop. These relationships, or those like them, may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators, and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement will depend, among other things, upon our assessment of the collaborator’s resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator’s evaluation of several factors. If we license rights to any product candidates we or our collaborators may develop, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

We may seek to establish additional collaborations. If we are not able to establish collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans.

To realize the full potential of our PROTAC Discovery Engine and accelerate the development of additional PROTAC programs, we plan to continue to selectively pursue collaborations with leading biopharmaceutical companies with particular experience, including development and commercial expertise and capabilities. We face significant competition in attracting appropriate collaborators to advance the development of any product candidates for which we may seek a collaboration. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or other regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, the terms of any existing collaboration agreements, and industry and market conditions generally. The collaborator may also have the opportunity to collaborate on other product candidates or technologies for similar indications and will have to evaluate whether such a collaboration could be more attractive than one with us.

Collaborations are complex and time-consuming to negotiate, document and execute. In addition, consolidation among large pharmaceutical companies has reduced the number of potential future collaborators. Our existing collaboration agreements limit our ability to enter into future agreements on certain terms with potential collaborators. For example, we have granted exclusive rights to Genentech, Pfizer and Bayer for the discovery, development and commercialization of PROTAC targeted protein degraders directed to certain protein targets, and during the terms of those agreements, we will be restricted from granting rights to other parties to use our PROTAC technology for those targets. Any collaboration we enter into may limit our ability to enter into future agreements on particular terms or covering similar target indications with other potential collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate revenue from product sales, which could have an adverse effect on our business, prospects, financial condition and results of operations.

We rely and expect to continue to rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We currently rely and expect to continue to rely on third-party CROs to conduct our ongoing and planned clinical trials. We currently do not plan to independently conduct any clinical trials of bavdegalutamide, ARV-471 and ARV-766 or of our other product candidates. Agreements with these third parties might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, that would delay our product development activities.

Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols in the applicable IND. Moreover, the FDA requires compliance with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected.

Furthermore, these third parties may have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines

or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We rely on third-party CMOs for the manufacture of both drug substance and finished drug product for our product candidates for preclinical testing and clinical trials and expect to continue to do so for commercialization. This reliance on third parties may increase the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely on and expect to continue to rely on third-party CMOs for both drug substance and finished drug product as well as the building blocks used to manufacture drug substance. This reliance on third parties may increase the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We may be unable to establish agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory, compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

We have only limited technology transfer agreements in place with respect to our product candidates, and these arrangements do not extend to commercial supply. We acquire many key materials on a purchase order basis. As a result, we do not have long term committed arrangements with respect to our product candidates and other materials. If we receive marketing approval for any of our product candidates, we will need to establish an agreement for commercial manufacture with a third party.

Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. As a result, we may not obtain access to these facilities on a priority basis or at all. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. Some of our manufacturers are based outside of the United States, including the manufacturers of the building blocks for our drug substances which are based in China and India. As a result of the COVID-19 pandemic, there has been an increased risk of supply interruption with our manufacturers and, in the first quarter of 2020, the production of certain building blocks for the drug substance used in the manufacture of ARV-471 was delayed at one of our China-based manufacturers. While this production delay did not delay the overall clinical development of our product candidates, other delays in the manufacture of building blocks, drug substance or drug products for our product candidates could arise, which could have a material adverse effect on our clinical development.

If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could

manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement manufacturer or be unable to reach agreement with any alternative manufacturer.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

Risks Related to the Commercialization of Our Product Candidates

Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current cancer treatments, such as chemotherapy and radiation therapy, are well established in the medical community, and doctors may continue to rely on these treatments. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant revenue from product sales and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including, but not limited to:

- the efficacy and potential advantages as compared to alternative treatments;
- the prevalence and severity of any side effects of our product candidates, in particular as compared to alternative treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing, sales and distribution support;
- the availability of third-party coverage and adequate reimbursement;
- the timing of any marketing approval in relation to other product approvals;
- support from patient advocacy groups; and
- any restrictions on the use of our products together with other medications.

If we are unable to establish sales and marketing capabilities, we may not be successful in commercializing our product candidates if and when they are approved.

We do not currently have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of biopharmaceutical products. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish sales, marketing and distribution capabilities, either ourselves or through collaboration or other arrangements with third parties.

We currently expect that we would build our own focused, specialized sales and marketing organization to support the commercialization of product candidates in the United States for which we receive marketing approval and that can be commercialized with such capabilities. There are risks involved with establishing our own sales and marketing capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective, knowledgeable and experienced sales and marketing personnel;
- the inability of such sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales and marketing capabilities or enter into arrangements with third parties to perform these services, our revenue from product sales and our profitability, if any, are likely to be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to market and sell our product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of these third parties may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues, if any, we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize any product candidates successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government healthcare programs, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, government authorities and third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the FDA or similar regulatory authorities approve the drug outside of the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- termination of clinical trials;
- withdrawal of any marketing approval, recall, restriction on the approval or a “black box” warning or contraindication for an approved drug;
- failure to enroll clinical trial participants or withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- injury to our reputation and significant negative media attention;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

We currently hold $10.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $10.0 million, which may not be adequate to cover all liabilities that we may incur. We will need to increase product liability insurance coverage as we expand our clinical trials and if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired, and we may not be able to compete effectively in our market.

Our commercial success depends in part on our ability to obtain and maintain patent and other proprietary protection in the United States and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing patent applications in the United States and other jurisdictions related to our novel technologies and product candidates. Any disclosure to or misappropriation by

third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. Moreover, the patent applications we own, co-own or license may fail to result in issued patents in the United States or in other foreign countries.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or at all. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has, in recent years, been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned, co-owned or licensed patents or pending patent applications, or that we were the first inventors to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Moreover, we may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or the USPTO, or in addition to interference proceedings, may become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or other post-grant proceedings challenging our or our licensors' patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Our owned, co-owned and licensed patent estate includes patent applications, many of which are at an early stage of prosecution. Even if our owned, co-owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned, co-owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned, co-owned and licensed patents may be challenged in the courts or patent offices in the United States and other jurisdictions. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned, co-owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Changes in patent laws or patent jurisprudence could diminish the value of our patents in general, thereby impairing our ability to protect our product candidates.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The USPTO developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first-inventor-to-file provisions, became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition. Furthermore, for applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications.

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years limiting where a patentee may file a patent infringement suit, narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations, and there are other open questions under patent law that courts have yet to decisively address. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained.

Depending on decisions by Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways and could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution, but the complexity and uncertainty of European patent laws has also increased in recent years. Complying with these laws and regulations could limit our ability to obtain new patents in the future that may be important for our business.

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

Competitors may infringe our issued patents, the patents of our licensors, or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive, time-consuming and unpredictable. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours or our licensors is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Even if we successfully assert our patents, a court may not award remedies that sufficiently compensate us for our losses.

We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms or at all.

A third party may hold intellectual property, including patent rights, that are important or necessary to the development of our products. It may be necessary for us to use the patented or proprietary technology of a third party to commercialize our own technology or products, in which case we would be required to obtain a license from such third party. A license to such intellectual property may not be available or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition.

The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or

attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. We may not be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, reexamination, and *inter partes* review proceedings before the USPTO and oppositions and other comparable proceedings in foreign jurisdictions.

We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference, derivation, reexamination or *inter partes* review proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. There may be third-party patents of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents.

If we are found by a court of competent jurisdiction to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. In addition, even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

If we fail to comply with our obligations in our current and future intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

We are party to a license agreement with Yale that provides us with the foundational intellectual property rights for our PROTAC targeted protein degradation technology. This license agreement imposes diligence, development and commercialization timelines and milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations, including achieving specified milestone events, Yale may have the right to terminate this license, in which event we might not be able to develop, manufacture or market any product that is covered by the intellectual property we in-license from Yale and may face other penalties. Such an occurrence would materially adversely affect our business prospects. For a variety of purposes, we will likely enter into additional licensing and funding arrangements with third parties that may also impose similar obligations on us.

Termination of any of our current or future in-licenses would reduce or eliminate our rights under these agreements and may result in our having to negotiate new or reinstated agreements with less favorable terms or cause us to lose our rights under these agreements, including our rights to important intellectual property or

technology. Any of the foregoing could prevent us from commercializing our other product candidates, which could have a material adverse effect on our operating results and overall financial condition.

In addition to the above risks, intellectual property rights that we license in the future may include sublicenses under intellectual property owned by third parties, in some cases through multiple tiers. The actions of our licensors may therefore affect our rights to use our sublicensed intellectual property, even if we are in compliance with all of the obligations under our license agreements. Should our licensors or any of the upstream licensors fail to comply with their obligations under the agreements pursuant to which they obtain the rights that are sublicensed to us, or should such agreements be terminated or amended, our ability to develop and commercialize our product candidates may be materially harmed.

Further, we do not have the right to control the prosecution, maintenance and enforcement of all of our licensed and sublicensed intellectual property, and even when we do have such rights, we may require the cooperation of our licensors and upstream licensors, which may not be forthcoming. For example, under the Yale license, any patent applications and issued patents under the agreement remain the property of Yale, and Yale has the right to choose patent counsel. Our business could be adversely affected if we or our licensors are unable to prosecute, maintain and enforce our licensed and sublicensed intellectual property effectively.

We may be subject to claims by third parties asserting that our employees, consultants, contractors or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

We employ individuals who were previously employed at universities as well as other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We have received confidential and proprietary information from collaborators, prospective licensees and other third parties. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. We may not be successful in defending these claims, and if we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful, litigation could result in substantial cost and reputational loss and be a distraction to our management and other employees.

In addition, while it is our policy to require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Such assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by governmental patent offices, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and patent offices in foreign countries in several stages over the lifetime of the patent. The USPTO and patent offices in foreign countries require compliance with a number of procedural, documentary, fee payment and other requirements during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of a patent or patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside of the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

If we are not able to obtain patent term extensions in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of our marketing exclusivity for our product candidates, our business may be impaired.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one of the U.S. patents covering each of such product candidates or the use thereof may be eligible for a patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch-Waxman Act. The period of extension may be up to five years beyond the expiration date of a patent but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA-approved product. Similar patent term extension also may be available in certain foreign countries upon regulatory approval of our product candidates. Nevertheless, we may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request.

If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product may be shortened and our competitors may obtain approval of competing products following our patent expiration sooner, and our revenue could be reduced, possibly materially.

We only have limited geographical protection with respect to certain patents and we may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In-licensing patents covering our product candidates in all countries throughout the world may similarly be prohibitively expensive, if such opportunities are available at all. And in-licensing or filing, prosecuting and defending patents even in only those jurisdictions in which we develop or commercialize our product candidates may be prohibitively expensive or impractical. Competitors may use our and our licensors' technologies in jurisdictions where we have not obtained patent protection or licensed patents to develop their own products and, further, may export otherwise infringing products to territories where we and our licensors have patent protection, but enforcement is not as strong as that in the United States or the European Union. These products may compete with our product candidates, and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

In addition, we may decide to abandon national and regional patent applications while they are still pending. The grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications may be rejected by the relevant patent office, while substantively similar applications are granted by others. For example, relative to other countries, China has a heightened detailed description requirement for patentability. Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy and costly litigation or other proceedings. Generic drug manufacturers may develop, seek approval for and launch generic versions of our products. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or regulations in the United States and the European Union, and many companies have encountered significant difficulties in protecting and defending proprietary rights in such jurisdictions. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets or other forms of intellectual property, which could make it difficult for us to prevent competitors in some jurisdictions from marketing competing products in violation of our proprietary rights generally.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, are likely to result in substantial costs and divert our efforts and attention from other aspects of our business, and additionally could put our or our licensors' patents at risk of being invalidated or interpreted narrowly, could increase the risk of our or our licensors' patent applications not issuing, or could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, while damages or other remedies may be awarded to the adverse party, which may be commercially significant. If we prevail, damages or other remedies awarded to us, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition in those jurisdictions.

In some jurisdictions, compulsory licensing laws compel patent owners to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties under patents relevant to our business, or if we or our licensors are prevented from enforcing patent rights against third parties, our competitive position may be substantially impaired in such jurisdictions.

Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal and Compliance Matters

The regulatory approval process of the FDA is lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to obtain marketing approval for our product candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained marketing approval for any product candidate to date and it is possible that none of our existing product candidates, or any product candidates we may seek to develop in the future, will ever obtain marketing approval.

Our product candidates could fail to receive marketing approval for many reasons, including the following:

- the FDA may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA that a product candidate is safe and effective for its proposed indication;
- results of clinical trials may not meet the level of statistical significance required by the FDA for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA may disagree with our interpretation of data from preclinical studies or clinical trials;
- data collected from clinical trials of our product candidates may not be sufficient to support the submission of a New Drug Application, or NDA, to the FDA or other submission or to obtain marketing approval in the United States;
- the FDA may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA may significantly change in a manner rendering our clinical data insufficient for approval.

The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations and prospects. The FDA has substantial discretion in the approval process, and determining when or whether regulatory approval will be obtained for any of our product candidates. Even if we believe the data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of any or all of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval,

advertising, promotion, sale and distribution, export and import are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and similar regulatory authorities outside of the United States. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction.

As a company, we do not have experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party clinical research organizations or other third-party consultants or vendors to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. New oncology drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed.

The process of obtaining marketing approvals, both in the United States and in other jurisdictions, is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may increase costs or cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed outside of the United States and may limit our ability to generate revenue from product sales.

In order to market and sell our products in the European Union and in other jurisdictions outside of the United States, we, and any collaborators, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. We, and any collaborators, may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA.

In many countries outside the United States, a product candidate must also be approved for reimbursement before it can be sold in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval. Obtaining non-U.S. regulatory approvals and compliance with non-U.S. regulatory requirements could result in significant delays, difficulties and costs for us and any collaborators and could delay or prevent the introduction of our product candidates in certain countries. In addition, if we or any collaborators fail to obtain the non-U.S. approvals required to market our product candidates outside the United States or if we or any collaborators fail to comply with applicable non-U.S. regulatory requirements, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business, financial condition, results of operations and prospects may be adversely affected.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the withdrawal of the United Kingdom from the EU, commonly referred to as Brexit. The United Kingdom is no longer part of the European Single Market and European Union Customs Union. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to European Union rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has been incorporated into the domestic law of the body of European Union law instruments governing medicinal products that pre-existed prior to the United Kingdom's withdrawal from the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling outside of the United States; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, and, as a result, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, in response to the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. As of May 26, 2021, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, the FDA may not be able to continue its current pace and review timelines could be extended, thus, the FDA may be unable to complete such required inspections during the review period. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future

shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

Even if we, or any collaborators, obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any collaborators, must therefore comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we, and any collaborators will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our third-party manufacturers, any collaborators and their third-party manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or any collaborators, receive marketing approval for one or more of our product candidates, we, and any collaborators, and our respective third-party manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and any collaborators, are not able to comply with post-approval regulatory requirements, we, and any collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or any collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

We may seek certain designations for our product candidates, including Breakthrough Therapy, Fast Track and Priority Review designations in the United States, but we might not receive such designations, and even if we do, such designations may not lead to a faster development or regulatory review or approval process.

We may seek certain designations for one or more of our product candidates that could expedite review and approval by the FDA. A Breakthrough Therapy product is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

The FDA may also designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective.

We may also seek a priority review designation for one or more of our product candidates. If the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no

adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months.

These designations are within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. Further, even if we receive a designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA, including the Fast Track designation we received in May 2019 for bavdegalutamide for mCRPC. In addition, even if one or more of our product candidates qualifies for these designations, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Any product candidate for which we, or any collaborators, obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market and we, or any collaborators, may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our products when and if any of them are approved.

Any product candidate for which we, or any collaborators, obtain marketing approval, as well as the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA, EMA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a risk evaluation and mitigation strategy. New cancer drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug in this way, which could limit sales of the product.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product, including the adoption and implementation of risk evaluation and mitigation strategies. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown side effects or other problems with our products or their manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions and warnings on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;

- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; or
- litigation involving patients using our products.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs applicable to drug manufacturers or quality assurance standards applicable to medical device manufacturers, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, and any contract manufacturers we may engage in the future, our collaborators and their contract manufacturers will also be subject to other regulatory requirements, including submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements regarding the distribution of samples to clinicians, recordkeeping, and costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product such as the requirement to implement a risk evaluation and mitigation strategy.

Similar restrictions apply to the approval of our products in the EU. The holder of a marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include: compliance with the EU's stringent pharmacovigilance or safety reporting rules, which can impose post-authorization studies and additional monitoring obligations; the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory; and the marketing and promotion of authorized drugs, which are strictly regulated in the EU and are also subject to EU Member State laws.

Our relationships with health care providers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other health care laws and regulations, which could expose us to civil, criminal and administrative sanctions, contractual damages, reputational harm and diminished future profits and earnings.

Health care providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any drugs for which we obtain marketing approval. Our future arrangements with third-party payors, health care providers and physicians may expose us to broadly applicable state and federal fraud and abuse and other health care laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drugs for which we obtain marketing approval. These include the following:

- *Anti-Kickback Statute,* which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchasing, ordering, leasing, arranging for, or recommending the purchasing, ordering, or leasing of, any good or service for which payment may be made, in whole or in part, under a federal health care program such as Medicare or Medicaid;
- *False Claims Act* - the federal civil and criminal false claims laws, including the civil False Claims Act, and Civil Monetary Penalties Law, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, false or fraudulent claims for payment or knowingly making, using or causing to made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government;

- *HIPAA* - the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit, among other things, executing a scheme to defraud any health care benefit program or making false statements relating to health care matters, and apply regardless of the payor (e.g., public or private);
- *HIPAA and HITECH* - HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which impose obligations on HIPAA covered entities and their business associates, including mandatory contractual terms and required implementation of administrative, physical and technical safeguards to maintain the privacy and security of individually identifiable health information;
- *Transparency Requirements* - the federal physician transparency requirements known as the Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the ACA, which requires manufacturers of drugs, medical devices, biological and medical supplies covered by Medicare, Medicaid, or State Children's Health Insurance Program to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- *Analogous State, Local and Foreign Laws* - analogous state, local and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, which may be broader than similar federal laws, can apply to claims involving health care items or services regardless of payor, and are enforced by many different federal and state agencies as well as through private actions.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to payments and other transfers of value to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable health care laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other health care laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and/or administrative penalties, damages, fines, individual imprisonment, disgorgement, exclusion from government funded health care programs, such as Medicare and Medicaid, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. If any of the physicians or other health care providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded health care programs.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of European Union Member States. In addition, payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information, including comprehensive regulatory systems in the U.S., EU and UK. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws and regulations could result in enforcement action against us, including fines, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to HIPAA establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. These obligations may be applicable to some or all of our business activities now or in the future.

If we are unable to properly protect the privacy and security of protected health information, we could be found to have breached our contracts. Further, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

In 2018, California passed into law the California Consumer Privacy Act, or the CCPA, which took effect on January 1, 2020 and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the General Data Protection Regulation, or the GDPR, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act, or the CPRA, which went into effect on January 1, 2023 and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities. In addition, other states, including Virginia, Colorado, Utah, and Connecticut already have passed state privacy laws. Virginia's privacy law also went into effect on January 1, 2023, and the laws in the other three states will go into effect later in the year. Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Similar to the laws in the U.S., there are significant privacy and data security laws that apply in Europe and other countries. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in EEA, and the processing of personal data that takes place in the EEA, is regulated by the GDPR, which went into effect in May 2018 and which imposes obligations on companies that operate in our industry with respect to the processing of personal data and the cross-border transfer of such data. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. If our or our partners' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill.

The GDPR places restrictions on the cross-border transfer of personal data from the EU to countries that have not been found by the EU to offer adequate data protection legislation, such as the U.S. There are ongoing concerns about the ability of companies to transfer personal data from the EU to other countries. In July 2020, the Court of Justice of the European Union, or the CJEU, invalidated the EU-U.S. Privacy Shield, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U.S. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the U.S. While we were not self-certified under the Privacy Shield, this CJEU decision may lead to increased scrutiny on data transfers from the EEA to the U.S. generally and increase our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners.

Additionally, in October 2022, President Joe Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield. The EU initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022. It is unclear if and when the framework will be finalized and whether it will be challenged in court. The uncertainty around this issue may further impact our business operations in the EU.

Following the withdrawal of the UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. In relation to data transfers, both the UK and the EU have determined, through separate "adequacy" decisions, that data transfers between the two jurisdictions are in compliance with the UK Data Protection Act and the GDPR, respectively. Any changes or updates to these adequacy decisions have the potential to impact our business.

Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow GDPR as a model, other laws contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and the sale and distribution of commercial products, through increased compliance costs, costs associated with contracting and potential enforcement actions.

While we continue to address the implications of the recent changes to data privacy regulations, data privacy remains an evolving landscape at both the domestic and international level, with new regulations coming into effect and continued legal challenges, and our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities in the EEA and elsewhere and carries with it the potential for significant penalties if we are found to be non-compliant. Similarly, failure to comply with federal and state laws in the U.S. regarding privacy and security of personal information could expose us to penalties under such laws. Any such failure to comply with data protection and privacy laws could result in government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

Current and future legislation may increase the difficulty and cost for us and any collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by legislative initiatives. Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any FDA approved product.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for prescription drugs purchased through a pharmacy by the elderly and disabled and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this statute provides authority for limiting the number of drugs that will be covered in any therapeutic class, subject to certain exceptions. Cost reduction initiatives and other provisions of this statute could decrease the coverage and price that we receive for any approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors. In March 2010, then-President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. These Medicare sequester reductions were reduced and suspended through June 2022 with the full 2% cut resuming thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts for Jobs Act, or TCJA, in 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court heard this case on November 10, 2020 and on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden rescinded those orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents. This Executive Order also directs HHS to create a special enrollment period for the Health Insurance Marketplace in response to the COVID-19 pandemic.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we obtain for our drug products, if and when approved.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have been delayed until January 1, 2026 by the Infrastructure Investment and Jobs Act.

More recently, on August 16, 2022, the IRA was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of enrolling in a plan providing outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 additional Part D drugs in 2027, 15 additional Part B or Part D drugs in 2028, and 20 additional Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated “maximum fair price” under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare beneficiaries' out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological 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. In addition, health care organizations 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 health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

In other jurisdictions, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we, or our collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our drug to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the FCPA, the Bribery Act, and other anticorruption laws that apply in countries where we do business and may do business in the future. The FCPA, the Bribery Act, and these other laws generally prohibit us, our officers and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to

obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential FCPA or Bribery Act violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the FCPA, the Bribery Act, or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United States, United Kingdom, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, which we collectively refer to as Trade Control Laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA, the Bribery Act, or other legal requirements, including Trade Control Laws. If we are not in compliance with the FCPA, the Bribery Act, and other anti-corruption laws or Trade Control Laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges, including the Nasdaq Stock Market, for violations of the FCPA's accounting provisions. Likewise, any investigation of any potential violations of the FCPA, the Bribery Act, other anti-corruption laws or Trade Control Laws by U.S., U.K. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could significantly harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Although we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain key executives and to attract, train, retain and motivate qualified personnel.

We are highly dependent on the research, development and clinical expertise of our management and scientific teams. Although we have offer letters or employment agreements with each of our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain marketing approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms or at all given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategies. These consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract, train, retain and motivate high quality personnel, our ability to pursue our corporate growth strategy will be limited.

We will need to grow the size of our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, manufacturing, regulatory and medical affairs and compliance and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Any future growth will impose significant added responsibilities on members of management, including, but not limited to:

- identifying, recruiting, training, integrating, retaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and FDA review process for bavdegalutamide, ARV-471, ARV-766 and any product candidate we develop, while complying with our contractual obligations to contractors and other third parties, including our partners and collaborators; and
- improving our managerial, operational and financial controls, reporting systems and procedures.

Our future financial performance and our ability to advance the development of and, if approved, commercialize bavdegalutamide, ARV-471, ARV-766 and any other product candidate we develop will depend, in part, on our ability to effectively manage any future growth. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our internal computer systems, or those of any collaborators, contractors, consultants or other third parties that we work with, may fail or suffer security breaches, which could damage the integrity of our clinical trials, impact our regulatory filings, compromise our ability to protect our intellectual property, and subject us to regulatory actions that could result in significant fines or other penalties.

Our internal computer systems and those of any collaborators, contractors, consultants or other third parties that we work with, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyber-attacks by malicious third parties. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult, time consuming and costly to detect and we have experienced certain attacks, though minor, related to third party vendors. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the

confidentiality, integrity and availability of information. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

While we have not experienced any material system failure, accident or security breach to date, if such an event were to occur, it could result in diversion of management's attention and a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be materially harmed and the further development and commercialization of our product candidates could be delayed.

Our employees, independent contractors, vendors, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading laws, which could materially harm our business.

We are exposed to the risk that our employees, independent contractors, vendors, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include:

- intentional, reckless or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA or similar foreign regulatory authorities;
- healthcare fraud and abuse laws and regulations in the United States and in other jurisdictions;
- violations of U.S. federal securities laws, including those related to trading in our common stock; and
- failures to report financial information or data accurately.

In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations regulate a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Other forms of misconduct could involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could, among other things, result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct and implement other internal controls applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third parties. In addition, 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 comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any legal, regulatory or administrative actions or proceedings are instituted against us, and we are not successful in defending ourselves or asserting our rights, such actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diversion of management attention, general costs of litigation or proceedings, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Related to Our Common Stock

The price of our common stock is volatile and may fluctuate substantially, which could result in the loss of all or part of our stockholders' investment.

Our stock price has been and likely will continue to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

- the degree of success of any competitive products or technologies;
- results of or developments in preclinical studies and clinical trials of our product candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional technologies or product candidates;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems in the United States and other jurisdictions;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

If any of the foregoing factors were to occur, or if our operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially.

In addition, in the past, companies that have experienced volatility in the market price of their stock have frequently been the subject of securities class action and shareholder derivative litigation. Such litigation, if instituted against us, whether successful or not, could cause us to incur substantial costs to defend such claims and divert management's attention and resources, which could seriously harm our business, financial condition, results of operations and prospects.

Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to significantly influence or control all matters submitted to stockholders for approval.

Our executive officers and directors, combined with our stockholders who own more than 5% of our outstanding common stock, in the aggregate, beneficially own shares representing approximately 53% of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence or control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could significantly influence or control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and the board of directors; or
- impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

Provisions in our organizational documents and under Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- provide for a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- provide for advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue "blank check" preferred stock, which could be issued without stockholder approval, may contain voting, liquidation, dividend and other rights superior to our common stock, and could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our trials or operating results fail to meet the expectations of analysts, our stock price will likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

If a significant portion of our total outstanding shares are sold into the market, the market price of our common stock could drop significantly, even if our business is doing well.

Most of our outstanding common stock can be traded without restriction at any time. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Holders of a significant portion of our common stock have rights, subject to

specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.

In July 2019, we issued 1,346,313 shares of our common stock to Bayer. On October 1, 2019, we filed a registration statement on Form S-3 covering the resale of these shares.

In September 2021, we issued 3,457,815 shares of our common stock to Pfizer.

We have a significant number of shares that are subject to outstanding options and restricted stock units, and in the future we may issue additional options, restricted stock units, or other derivative securities convertible into our common stock under our equity compensation plans. The exercise or vesting of any such options, restricted stock units, or other derivative securities, and the subsequent sale of the underlying common stock, could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. Such sales of our common stock could result in higher than average trading volume and may cause the market price for our common stock to decline.

We currently have on file with the SEC universal shelf registration statements on Form S-3 which allow us to offer and sell registered common stock, preferred stock, debt securities, depositary shares, units and/or warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. In October 2019, we entered into an Equity Distribution Agreement, or the Distribution Agreement, with Piper Sandler & Co. (formerly Piper Jaffray & Co.), or Piper Sandler, pursuant to which we sold 2,593,637 shares of common stock in at-the-market offerings for aggregate net proceeds of $64.1 million. We terminated the Distribution Agreement in August 2021.

In August 2021, we entered into an Equity Distribution Agreement with Piper Sandler & Company, or Piper Sandler, and Cantor Fitzgerald & Co., or Cantor, as agents, pursuant to which we may offer and sell from time to time, through the agents, up to $300.0 million of the common stock registered under the universal shelf registration statement pursuant to one or more "at-the-market" offerings. During the year ended December 31, 2022, no shares were issued under this agreement.

Sales of substantial amounts of shares of our common stock or other securities by our stockholders under our universal shelf registration statement, including pursuant to our "at-the-market" offering program, or otherwise could also dilute our stockholders.

We will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market and other applicable securities rules and regulations, including those promulgated by the SEC, impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly.

Pursuant to Section 404 of Sarbanes-Oxley, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. To achieve compliance with Section 404, we are engaged in a process to document and evaluate our internal control over financial reporting and internal controls, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and carry out a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in harm to our reputation or an

adverse reaction in the financial markets and it could restrict our future access to the capital markets due to a loss of confidence in the reliability of our consolidated financial statements which would materially harm our business.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders. Our certificate of incorporation further provides that the federal district courts of the United States are the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended. These choice of forum provisions could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or other stockholders.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty owed by our directors, officers, other employees or stockholders to the company or our stockholders, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law or as to which the Delaware General Corporation Law confers jurisdiction on the Court of Chancery of the State of Delaware, or any action asserting a claim arising pursuant to our certificate of incorporation or our bylaws or governed by the internal affairs doctrine. Our certificate of incorporation further provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended. These choice of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers, other employees or other stockholders, which may discourage such lawsuits against us and our directors, officers, other employees or other stockholders. Alternatively, if a court were to find this provision in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition. Neither of these choice of forum provisions would affect suits brought to enforce any liability or duty created by the Exchange Act or the rules and regulations thereunder, jurisdiction over which is exclusively vested by statute in the United States federal courts, or any other claim for which United States federal courts have exclusive jurisdiction.

Because we have never paid and do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be our stockholders' sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends in respect of our common stock in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects, then applicable contractual restrictions and any other factors deemed relevant by our board of directors. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

We lease approximately 63,000 square feet of office and laboratory space in New Haven, Connecticut under leases, as amended, that expire in December 2024. In May 2021, we entered into a lease, which was amended in August 2022, for approximately 160,000 square feet of office and laboratory space in New Haven, Connecticut which we expect to begin occupying in 2024. We believe that our facilities are sufficient to meet our current needs and that suitable additional or alternative space will be available as and when needed on commercially reasonable terms for our future growth.

Item 3. Legal Proceedings.

From time to time, we may become involved in litigation or other legal proceedings arising in the ordinary course of business and regardless of outcome, litigation can have an adverse impact on our business, financial condition, results of operations and prospects because of defense and settlement costs, diversion of management resources and other factors. We are not currently a party to any material litigation or legal proceedings.

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 has been publicly traded on the Nasdaq Global Select Market under the symbol "ARVN" since September 27, 2018 in connection with our initial public offering, or IPO. Prior to that time, there was no public market for our common stock.

Holders

As of February 17, 2023, there were approximately 24 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends in respect of our common stock in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects, then applicable contractual restrictions and any other factors deemed relevant by our board of directors.

Recent Sales of Unregistered Securities

We did not issue any securities that were not registered under the Securities Act of 1933, as amended, or the Securities Act, during the year ended December 31, 2022.

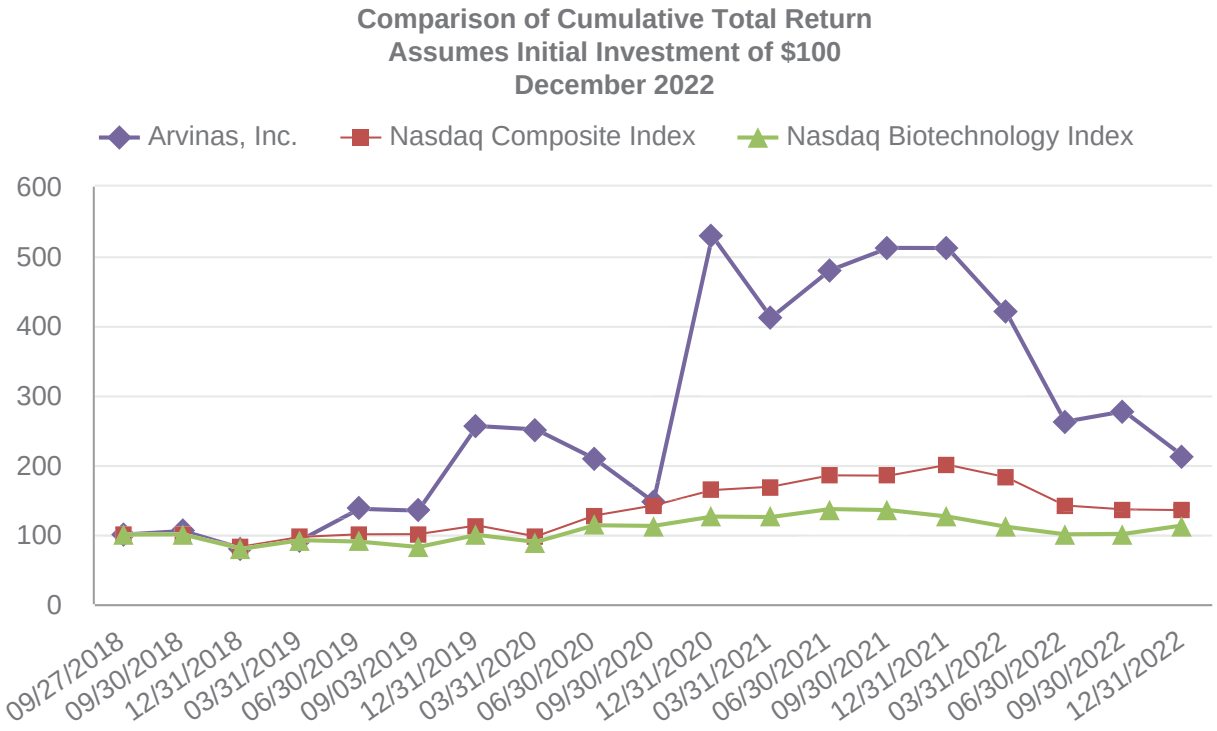
Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Performance Graph

The performance graph shown below compares the quarterly change in cumulative total shareholder return on our common shares with the Nasdaq Composite Index and the Nasdaq Biotechnology Index from September 27, 2018 (the first date on which shares of our common stock were publicly traded) through the quarter ended December 31, 2022. The graph assumes an investment of $100 on September 27, 2018 in our common shares, the Nasdaq Composite Index and the Nasdaq Biotechnology Index and assumes that any dividends are reinvested. All index values are weighted by the capitalization of the companies included in the index. The comparisons shown in the graph below are based upon historical data. The stock price performance included in this graph is not necessarily indicative of future stock price performance. The following performance graph and related information shall not be deemed to be "soliciting material" or to be "filed" with the Securities and Exchange Commission, or SEC, for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, nor shall such information be incorporated by reference into any future filing

under the Exchange Act or Securities Act, except to the extent that we specifically incorporate it by reference into such filing.



Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis is meant to provide material information relevant to an assessment of the financial condition and results of operations of our company, including an evaluation of the amount and certainty of cash flows from operations and from outside sources, so as to allow investors to better view our company from management's perspective. You should read the following discussion and analysis of financial condition and results of operations together with our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties. As a result of many factors, such as those set forth in the section titled "Risk Factors" and elsewhere in this Annual Report on Form 10-K, our actual results may differ materially from those anticipated in or implied by these forward-looking statements.

Overview

Our Business

We are a clinical-stage biotechnology company dedicated to improving the lives of patients suffering from debilitating and life-threatening diseases through the discovery, development and commercialization of therapies that degrade disease-causing proteins. We use our PROTAC Discovery Engine, our proprietary technology platform to engineer proteolysis targeting chimeras, or PROTAC targeted protein degraders, that are designed to harness the body's own natural protein disposal system to selectively and efficiently degrade and remove disease-causing proteins. We believe that our targeted protein degradation approach is a therapeutic modality that may provide distinct advantages over existing modalities, including traditional small molecule therapies and gene-based medicines. We have a robust preclinical pipeline of PROTAC protein degraders targeting a broad range of intracellular disease targets, including those representing proteins that currently cannot be addressed by existing small molecule therapies, commonly referred to as "undruggable" targets. We

are using our PROTAC Discovery Engine to build an extensive pipeline of protein degradation product candidates to target diseases in areas of unmet need, including oncology (including immuno-oncology), neuroscience and other therapeutic areas. We have three investigational clinical stage programs: ARV-471, a novel PROTAC estrogen receptor, or ER, protein degrader for the treatment of patients with locally advanced or metastatic ER positive / human epidermal growth factor receptor 2, or HER2, negative, or ER+/HER2-, breast cancer and bavdegalutamide (ARV-110) and ARV-766, each an oral PROTAC protein degrader that targets the androgen receptor protein, or AR, for the treatment of men with metastatic castration-resistant prostate cancer, or mCRPC.

ARV-471

ARV-471 is an investigational orally bioavailable PROTAC protein degrader designed to target and degrade the ER for the treatment of patients with locally advanced or metastatic ER+/HER2- breast cancer. We are co-developing ARV-471 with Pfizer, Inc., or Pfizer, pursuant to a collaboration agreement that we and Pfizer entered into in July 2021. We granted Pfizer worldwide co-exclusive rights to develop and commercialize ARV-471.

In preclinical studies, ARV-471 demonstrated near-complete ER degradation in tumor cells, induced robust tumor shrinkage when dosed as a single agent in multiple ER-driven xenograft models, and showed superior anti-tumor activity when compared to a standard of care agent, fulvestrant, both as a single agent and in combination with a cyclin-dependent kinase, or CDK, 4/6 inhibitor. In 2019, we initiated a Phase 1 clinical trial of ARV-471 designed to assess the safety, tolerability and pharmacokinetics of ARV-471, which also included measures of anti-tumor activity as secondary endpoints and in the fourth quarter of 2020, we initiated a Phase 1b cohort expansion of ARV-471 in combination with the CDK4/6 inhibitor Ibrance® (palbociclib). In 2021, we initiated VERITAC, the Phase 2 single agent expansion cohort of the ARV-471 clinical trial.

In the third quarter of 2022, we initiated TACTIVE-E, a Phase 1b clinical trial with ARV-471 in combination with everolimus in patients with metastatic breast cancer. Also in the third quarter of 2022, we initiated with Pfizer a Phase 1b trial of ARV-471 as a monotherapy in Japanese patients.

In the fourth quarter of 2022, we presented initial data from VERITAC at the San Antonio Breast Cancer Symposium and we initiated, with Pfizer, the VERITAC-2 Phase 3 trial with ARV-471 as a monotherapy as a second-line and later treatment in patients with ER+/HER2- metastatic breast cancer. Also in the fourth quarter of 2022, we initiated the first of two arms in the ongoing Phase 1b umbrella trial of ARV-471, with ARV-471 in combination with each of the CDK4/6 inhibitors abemaciclib and ribociclib (TACTIVE-U). We initiated the second of two arms in the first quarter of 2023. In addition, in the fourth quarter of 2022, we initiated a Phase 2 clinical trial with ARV-471 as a monotherapy in patients with early breast cancer in the neoadjuvant setting (TACTIVE-N).

In the first quarter of 2023, we and Pfizer requested a meeting with the U.S. Food and Drug Administration, or the FDA, to review the proposed update to the trial protocol for the VERITAC-3 first-line, metastatic ER+ / HER2- breast cancer Phase 3 trial of ARV-471 in combination with IBRANCE® (palbociclib) to determine the optimal dose of palbociclib as part of the trial design. Following correspondence and alignment with the FDA, we and Pfizer determined an approach to the planned Phase 3 trial to enable trial initiation in the second half of 2023, which includes a Phase 3 lead-in to evaluate the optimal dose of palbociclib (100 mg or 75 mg) in combination with 200 mg ARV-471. This approach follows the recent analysis of data from the ongoing Phase 1b combination study of ARV-471 with palbociclib, in which an increase in palbociclib exposure was observed relative to historical palbociclib pharmacokinetic data.

In the first half of 2023, we expect, with Pfizer, to provide an update with preliminary data from the Phase 1b combination trial with palbociclib (Part C of the Phase 1/2 trial) and in the second half of 2023, we expect, with Pfizer, to submit and present data from the Phase 1b combination trial of ARV-471 with palbociclib at a medical congress and. Also in the second half of 2023, we expect, with Pfizer, to initiate a Phase 3 trial with ARV-471 in combination with palbociclib as a first-line treatment in patients with ER+ / HER2- locally advance or metastatic breast cancer. and initiate additional arms of the TACTIVE-U, Phase 1b combination trial with other targeted therapies, during 2023.

Bavdegalutamide (ARV-110)

Bavdegalutamide (ARV-110) is an investigational orally bioavailable PROTAC protein degrader designed to target and degrade the AR for the treatment of men with mCRPC.

In preclinical studies, bavdegalutamide demonstrated activity of AR mutation or overexpression, both common mechanisms of resistance to currently available AR-targeted therapies. In 2019, we initiated a Phase 1/2 clinical trial of bavdegalutamide designed to assess the safety, tolerability and pharmacokinetics of bavdegalutamide and which trial also included measures of anti-tumor activity as secondary endpoints, including reduction in prostate specific antigen, or PSA, a well-recognized biomarker of prostate cancer progression. In 2019, we also received Fast Track designation for bavdegalutamide for mCRPC. In 2020, we initiated ARDENT, the Phase 2 single agent expansion portion of the bavdegalutamide clinical trial. In 2021, we initiated a Phase 1b clinical trial of bavdegalutamide in combination with abiraterone for the treatment of men with mCRPC.

In the first quarter of 2022, we announced completed Phase 1 and interim ARDENT data for bavdegalutamide at the 2022 American Society of Clinical Oncology Genitourinary (ASCO GU) Cancers Symposium.

We expect to initiate a global Phase 3 trial with a confirmed dose for bavdegalutamide for the treatment of men with mCRPC with AR T878/H875 tumor mutations in the second half of 2023. Also in the second half of 2023, we expect to complete enrollment in the Phase 1b clinical trial with bavdegalutamide in combination with abiraterone.

ARV-766

ARV-766 is an investigational orally bioavailable PROTAC protein degrader designed to target AR with a different profile than bavdegalutamide, as a potential treatment for men with mCRPC.

In preclinical studies, ARV-766 degraded all tested resistance-driving point mutations of AR, including L702H, a mutation associated with treatment with abiraterone and other AR-pathway therapies. In 2021, we initiated a Phase 1/2 clinical trial for ARV-766 designed to assess the safety, tolerability and pharmacokinetics of ARV-766, which trial also includes measures of anti-tumor activity as secondary endpoints, including reduction in PSA. In the second half of 2022, we initiated a Phase 2 expansion trial of ARV-766 for the treatment of men with mCRPC.

We expect to share data from the Phase 1 dose escalation trial of ARV-766 for the treatment of men with metastatic castration-resistant prostate cancer in the second quarter of 2023.

We anticipate initiating a Phase 1b or Phase 2 dose escalation trial for either of bavdegalutamide or ARV-766 in patients with AR-dependent tumors who have not previously received novel hormonal agents, or NHA, such as enzalutamide or abiraterone, and who may benefit from bavdegalutamide or ARV-766 therapy, in the second half of 2023.

We are further diversifying our pipeline by developing new PROTAC targeted protein degraders against targets for which we believe protein degradation offers advantages to existing therapeutic modalities, including PROTAC degraders that are designed to reach targets in deep brain regions and are capable of being delivered through multiple routes of administration, including oral delivery. We have engineered PROTAC targeted protein degraders that, in preclinical studies, have successfully achieved blood-brain barrier penetration, a key step in developing drugs with the potential to treat neurodegenerative diseases. We believe there are many other indications for which our PROTAC technology may be advantageous.

By year-end 2023, we expect to submit an investigational new drug, or IND, application or clinical trial application, or CTA, for our PROTAC degrader designed to target each of the BCL6 protein, a protein mutated in patients with different forms of Non-Hodgkins Lymphoma, or NHL, including Diffuse Large B-Cell Lymphoma, or DLBCL, and the LRRK2 protein, a protein kinase that has been genetically linked to some forms of Parkinson's Disease, or PD. We also expect to progress at least two additional PROTAC protein degrader programs in IND-enabling or CTA-enabling studies by year-end 2023.

Our Operations

We commenced operations in 2013. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, conducting discovery and research activities, filing patent applications, identifying potential product candidates, undertaking preclinical studies and clinical trials and establishing arrangements with third parties for the manufacture of initial quantities of our product candidates. To date, we have not generated any revenue from product sales and have financed our operations primarily through sales of our equity interests, proceeds from our collaborations, grant funding and debt financing. Since inception through December 31, 2022, we raised approximately $1.3 billion in gross proceeds from the sale of equity instruments and the exercise of stock options, and had received an aggregate of $780.5 million in payments primarily from collaboration partners.

We are a clinical-stage company. ARV-471, bavdegalutamide (ARV-110) and ARV-766 are each in Phase 1/2 clinical trials and ARV-471 is in a Phase 3 clinical trial, and our other drug discovery activities are at the research and preclinical development stages. Our ability to generate revenue from product sales sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. Since inception, we have incurred significant operating losses and expect to incur increasing operating losses for at least the next several years due to costs associated with our ongoing and anticipated clinical activities for ARV-471, bavdegalutamide and ARV-766, development activities associated with our other product candidates, research activities in oncology, neurological and other disease areas to expand our pipeline, hiring additional personnel in research, clinical trials, quality and other functional areas, increased expenses incurred with CMOs to supply us with product for our preclinical and clinical studies and CROs for the synthesis of compounds in our preclinical development activities, as well as other associated costs including the management of our intellectual property portfolio.

We do not expect to generate revenue from sales of any product for many years, if ever. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research or product development programs or any future commercialization efforts, or to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future. Our revenues to date have been generated through research collaboration and license agreements. Revenue is recognized ratably over our expected performance period under each agreement. We expect that any revenue for the next several years will be derived primarily from our current collaboration agreements and any additional collaborations that we may enter into in the future. To date, we have not received any sales-based milestone payments or royalties under any of the collaboration agreements.

Genentech License Agreement

In September 2015, we entered into an Option and License Agreement with Genentech, Inc. and F. Hoffmann-La Roche Ltd, collectively referred to as Genentech, focused on PROTAC targeted protein degrader discovery and research for target proteins, or Targets, based on our proprietary platform technology, other than excluded Targets as described below. This collaboration was expanded in November 2017 through an Amended and Restated Option, License and Collaboration Agreement, which we refer to as the Restated Genentech Agreement.

Under the Restated Genentech Agreement, Genentech has the right to designate up to ten Targets for further discovery and research utilizing our PROTAC platform technology. Genentech may designate as a Target any protein to which a PROTAC targeted protein degrader, by design, binds to achieve its mechanism of action, subject to certain exclusions. Genentech also has the right to remove a Target from the collaboration and substitute a different Target that is not an excluded Target at any time prior to us commencing research on such Target or in certain circumstances following commencement of research by us.

At the time we entered into the original agreement with Genentech, we received an upfront payment of $11.0 million, and, at the time we entered into the Restated Genentech Agreement, we received an additional $34.5 million in upfront and expansion target payments. We are eligible to receive up to an aggregate of $27.5 million in additional expansion target payments if Genentech exercises its options for all remaining Targets. We are also eligible to receive payments aggregating up to $44.0 million per Target upon the achievement of specified development milestones; payments aggregating up to $52.5 million per Target (assuming approval of two indications) subject to the achievement of specified regulatory milestones; and payments aggregating up to $60.0 million per PROTAC targeted protein degrader directed against the applicable Target, subject to the achievement of specified sales milestones. These milestone payments are subject to reduction if we do not have a valid patent claim covering the licensed PROTAC targeted protein degrader at the time the milestone is achieved. We are also eligible to receive, on net sales of licensed PROTAC targeted protein degraders, mid-single digit royalties, which may be subject to reductions.

Pfizer Research Collaboration Agreement

In December 2017, we entered into a Research Collaboration and License Agreement with Pfizer, setting forth our collaboration to identify or optimize PROTAC targeted protein degraders that mediate for degradation of Targets, using our proprietary platform technology that are identified in the agreement or subsequently selected by Pfizer, subject to certain exclusions. We refer to this agreement as the Pfizer Research Collaboration Agreement.

Under the Pfizer Research Collaboration Agreement, Pfizer has designated a number of initial Targets. For each identified Target, we and Pfizer will conduct a separate research program pursuant to a research plan. Pfizer may make substitutions for any of the initial Target candidates, subject to the stage of research for such Target.

In the year ended December 31, 2018, we received an upfront, non-refundable payment and certain additional payments totaling $28.0 million in exchange for use of the technology license and to fund Pfizer-related research, as defined within the Pfizer Research Collaboration Agreement. We are eligible to receive up to an additional $37.5 million in non-refundable option payments if Pfizer exercises its options for all targets under the Pfizer Research Collaboration Agreement. We are also entitled to receive up to $225.0 million in development milestone payments and up to $550.0 million in sales-based milestone payments for all designated targets under the Pfizer Research Collaboration Agreement, as well as mid- to high-single digit tiered royalties, which may be subject to reductions, on net sales of PROTAC targeted protein degrader-related products. In 2021 and 2020, we received payments totaling $1.2 million and $4.4 million, respectively. Pfizer selected additional targets and initiated additional services totaling $1.0 million and $3.5 million in December 2022 and 2021, respectively, which were included in accounts receivable as of December 31, 2022 and 2021.

Bayer Collaboration Agreement

In June 2019, we entered into a Collaboration and License Agreement, or the Bayer Collaboration Agreement, with Bayer AG, or, together with its controlled affiliates, Bayer, setting forth our collaboration to identify or optimize PROTAC targeted protein degraders that mediate for degradation of Targets, using our proprietary platform technology, that are selected by Bayer, subject to certain exclusions and limitations. The Bayer Collaboration Agreement became effective in July 2019.

Under the Bayer Collaboration Agreement, we and Bayer conduct a research program pursuant to separate research plans mutually agreed to by us and Bayer and tailored to each Target selected by Bayer. Bayer may make substitutions for any such initial Target candidates, subject to certain conditions and based on the stage of research for such Target. During the term of the Bayer Collaboration Agreement, we are not permitted, either directly or indirectly, to design, identify, discover or develop any small molecule pharmacologically-active agent whose primary mechanism of action is, by design, directed to the inhibition or degradation of any Target selected or reserved by Bayer, or grant any license, covenant not to sue or other right to any third party in the field of human disease under the licensed intellectual property for the conduct of such activities.

Under the terms of the Bayer Collaboration Agreement, we received an aggregate upfront, non-refundable payment of $17.5 million. Bayer is committed to fund a total of $12.0 million in research funding

payments through 2023, of which $10.5 million was received from inception through December 31, 2022, subject to potential increases if our costs for research activities exceed the research funding payments allocated to a Target and certain conditions are met. We are also eligible to receive up to $197.5 million in development milestone payments and up to $490.0 million in sales-based milestone payments for all designated Targets. In addition, we are eligible to receive, on net sales of PROTAC targeted protein degrader-related products, mid-single digit to low-double digit tiered royalties, which may be subject to reductions.

Pfizer ARV-471 Collaboration Agreement

In July 2021, we entered into the ARV-471 Collaboration Agreement with Pfizer, pursuant to which we granted Pfizer worldwide co-exclusive rights to develop and commercialize products containing our proprietary compound ARV-471, or the Licensed Products.

Under the ARV-471 Collaboration Agreement, we received an upfront, non-refundable payment of $650 million. In addition, we are eligible to receive up to an additional $1.4 billion in contingent payments based on specified regulatory and sales-based milestones for the Licensed Products. Of the total contingent payments, $400 million in regulatory milestones are related to marketing approvals and $1.0 billion are related to sales-based milestones.

We and Pfizer share equally (50/50) all development costs (including costs for conducting any clinical trials) for the Licensed Products, subject to certain exceptions. Except for certain regions described below, we will also share equally (50/50) all profits and losses in commercialization and medical affairs activities for the Licensed Products in all other countries, subject to certain exceptions.

We will be the marketing authorization holder and, subject to marketing approval, book sales in the United States, while Pfizer will hold marketing authorizations outside the United States. We will determine with Pfizer which, if any, regions within the world will be solely commercialized by one party, and in such region the parties will adjust their share of all profits and losses for the Licensed Products based on the role each party will be performing.

Unless earlier terminated in accordance with its terms, the ARV-471 Collaboration Agreement will expire on a Licensed Product-by-Licensed Product and country-by-country basis when such Licensed Products are no longer commercialized or developed for commercialization in such country. Pfizer may terminate the ARV-471 Collaboration Agreement for convenience in its entirety or on a region-by-region basis subject to certain notice periods. Either party may terminate the ARV-471 Collaboration Agreement for the other party's uncured material breach or insolvency. Subject to applicable terms of the ARV-471 Collaboration Agreement, including certain payments to Pfizer upon termination for our uncured material breach, effective upon termination of the ARV-471 Collaboration Agreement, we are entitled to retain specified licenses to be able to continue to exploit the Licensed Products.

Subject to specified exceptions, we and Pfizer have each agreed not to directly or indirectly research, develop, or commercialize any competing products outside of the ARV-471 Collaboration Agreement anywhere in the world during the term of the ARV-471 Collaboration Agreement.

Operating Expenses

Our operating expenses since inception have consisted solely of research and development costs and general and administrative costs.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of our product candidates, and include:

- salaries, benefits and other related costs, including stock-based compensation expense, for personnel engaged in research and development functions;
- expenses incurred under agreements with third parties, including CROs and other third parties that conduct research and preclinical activities on our behalf as well as third parties that manufacture our product candidates for use in our preclinical studies and clinical trials;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses;

- the costs of laboratory supplies and developing preclinical studies and clinical trial materials;
- facility-related expenses, which include direct depreciation costs of equipment and allocated expenses for rent and maintenance of facilities and other operating costs; and
- third-party licensing fees.

We expense research and development costs as incurred.

We typically use our employee and infrastructure resources across our development programs, and as such, do not track all of our internal research and development expenses on a program-by-program basis. The following table summarizes our research and development expenses for our AR program, which includes bavdegalutamide and ARV-766, ER program, which includes ARV-471, and all other platform and exploratory research and development costs:

	Years Ended December 31,		
(dollars in millions)	**2022**	**2021**	**2020**
AR program development costs	$ 57.5	$ 41.8	$ 24.4
ER program development costs	72.1	30.9	17.5
Other research and development costs	185.4	107.7	66.5
Total research and development costs	$ 315.0	$ 180.4	$ 108.4

Research and development activities are central to our business model. We expect that our research and development expenses will continue to increase substantially for the foreseeable future as we continue to conduct our ongoing clinical trials for ARV-471, bavdegalutamide and ARV-766, including our Phase 3 clinical trial for ARV-471, and continue to discover and develop additional product candidates. Research and development expenses related to ARV-471 are shared equally with Pfizer from July 22, 2021, the effective date of the ARV-471 Collaboration Agreement. The ER program development costs in the table above reflect the cost sharing with Pfizer.

We cannot determine with certainty the duration and costs of future clinical trials of ARV-471, bavdegalutamide and ARV-766 or any other product candidate we may develop or if, when, or to what extent we will generate revenue from the commercialization and sale of any product candidate for which we obtain marketing approval. We may never succeed in obtaining marketing approval for any product candidate. The successful development and commercialization of our product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- successful completion of preclinical studies and clinical trials;
- receipt and related terms of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our product candidates;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- obtaining and maintaining third-party coverage and adequate reimbursement;
- maintaining a continued acceptable safety profile of the products following approval; and
- effectively competing with other therapies.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct

clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in our clinical trials due to patient enrollment or other reasons, we would be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation for personnel in our executive, finance, business development and administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters; professional fees for accounting, auditing, tax and consulting services; insurance costs; travel expenses; and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expect that our general and administrative expenses will increase in the future as we increase our personnel headcount to support increased research and development activities relating to our product candidates. We also expect to incur increased expenses associated with being a public company, including costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with Nasdaq and Securities and Exchange Commission requirements; director and officer insurance costs; and investor and public relations costs.

Interest Income (Expense)

Interest income consists of interest earned on our cash, cash equivalents, restricted cash and marketable securities. Interest income increased in 2022 as compared to 2021 primarily due to a full year of an increased marketable securities balance resulting from funds received in July 2021 under the ARV-471 Collaboration Agreement and in September 2021 under the Pfizer Stock Purchase Agreement. Interest expense consists primarily of interest paid or accrued on our outstanding debt with the State of Connecticut.

Income Taxes

Since our inception in 2013, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in any year or for our federal or state earned research and development tax credits, due to our uncertainty of realizing a benefit from those items. During the year ended December 31, 2022, we fully utilized our previously held federal net operating loss and federal credit carryforwards due to taxable income resulting from revenue recognition for tax purposes from our ARV-471 Collaboration Agreement and the mandatory capitalization of qualified research and development expenses incurred on or after January 1, 2022 under the Tax Cuts and Jobs Act. We continue to carry state net operating losses and credit carryforwards. The revenue recognition and capitalization of research expenses are timing differences for tax purposes and deferred tax assets were established. We have provided a valuation allowance against the full amount of the deferred tax assets since, in the opinion of management, based upon our earnings history, it is more likely than not that the benefits will not be realized.

As of December 31, 2022, Arvinas, Inc. had four wholly owned subsidiaries organized as C-corporations: Arvinas Operations, Inc., Arvinas Androgen Receptor, Inc., Arvinas Estrogen Receptor, Inc., and Arvinas Winchester, Inc. Prior to December 31, 2018, these subsidiaries were separate filers for federal tax purposes. Net operating loss carryforwards are generated from the C-corporation subsidiaries' filings. We have provided a valuation allowance against the full amount of the deferred tax assets since, in the opinion of management, based upon our earnings history, it is more likely than not that the benefits will not be realized.

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, costs and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events and various other factors

that we believe are 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. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue Recognition

We recognize revenue under Accounting Standards Codification, or ASC, 606, *Revenue from Contracts with Customers.* Our revenue is generated through research collaboration and license agreements with pharmaceutical partners. The terms of these agreements contain multiple goods and services which may include (i) licenses, (ii) research and development activities and (iii) participation in joint research and development steering committees. The terms of these agreements may include non-refundable, upfront license or option fees, payments for research and development activities, payments upon the achievement of certain milestones and royalty payments based on product sales derived from the collaboration. Under ASC 606, we evaluate whether the license agreement, research and development services and participation in research and development steering committees represent separate or combined performance obligations. We have determined that these services within our existing contracts represent combined single performance obligations.

The research collaboration and license agreements typically include contingent milestone payments related to specified preclinical and clinical development milestones and regulatory milestones. These milestone payments represent variable consideration that are not initially recognized within the transaction price as they are fully constrained under the guidance in ASC 606. We continually assess the probability of significant reversals for any amounts that become likely to be realized prior to recognizing the variable consideration associated with these payments within the transaction price.

Revenue is recognized ratably over our expected performance period under each respective arrangement. We make our best estimate of the period over which we expect to fulfill our performance obligations, which includes access to technology through the license agreement and research activities. Given the uncertainties of these collaboration arrangements, significant judgement is required to determine the duration of the performance period.

For the years ended December 31, 2022, 2021 and 2020, the transaction price allocated to the combined performance obligations identified under the individual research collaboration and license agreements was recognized as revenue on either a straight-line basis over the estimated performance period under the arrangement or over the estimated performance period based on our best estimate of costs to be incurred. Straight-line basis was considered the best measure of progress for certain agreements in which control of the combined obligation transfers to the customers, due to the contract containing license rights to technology, research and development services, and joint committee participation, which in totality are expected to occur ratably over the performance period.

Our contracts may also call for certain sales-based milestone and royalty payments upon successful commercialization of a target. In accordance with ASC 606-10-55-65, we recognize revenues from sales-based milestone and royalty payments at the later of (i) the occurrence of the subsequent sale, or (ii) the performance obligation to which some or all of the sales-based milestone or royalty payments has been allocated has been satisfied (or partially satisfied). We anticipate recognizing these milestone and royalty payments if and when subsequent sales are generated by customers from the use of the technology. To date, no revenue from these sales-based milestone and royalty payments has been recognized for any periods.

Amounts received prior to satisfying the above revenue recognition criteria are recorded as contract liabilities in our accompanying consolidated balance sheets.

Research and Development Contract Costs and Accruals

As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of these estimates with the service providers and make adjustments, if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- vendors in connection with clinical development activities; and
- CROs and investigative sites in connection with pre-clinical, non-clinical, and human clinical trials

We base the expense recorded related to external research and development on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CMOs and CROs that supply, 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 streams. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

New Accounting Pronouncements

For information on new accounting standards, see Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Results of Operations

Comparison of Years Ended December 31, 2022 and 2021

	Years Ended December 31,		
(dollars in millions)	2022	2021	$ change
Revenue	$ 131.4	$ 53.6	$ 77.8
Research and development expenses	(315.0)	(180.4)	(134.6)
General and administrative expenses	(79.6)	(61.6)	(18.0)
Other income	12.2	4.3	7.9
Income tax expense	(20.9)	—	(20.9)
Loss from equity method investment	(10.6)	(6.9)	(3.7)
Net loss	$ (282.5)	$ (191.0)	$ (91.5)

Revenue

Revenues for the year ended December 31, 2022 totaled $131.4 million, compared with $53.6 million for the year ended December 31, 2021. The increase of $77.8 million was primarily due to $72.5 million of

revenue from the ARV-471 Collaboration Agreement entered into during the third quarter of 2021 and $3.7 million of previously constrained deferred revenue related to our Oerth Bio joint venture.

Research and Development Expenses

Research and development expenses for the year ended December 31, 2022 totaled $315.0 million, compared with $180.4 million for the year ended December 31, 2021. The increase of $134.6 million was primarily due to investments in our platform and exploratory programs of $77.7 million and increases in expenses related to our AR and ER programs of $15.7 million and $41.2 million, respectively. The increase in spending over all of our programs was primarily due to increased personnel and personnel costs utilized across all of our programs of $42.3 million, which includes $11.2 million related to stock compensation expense. Clinical trial costs and related drug manufacturing costs increased by $37.0 million as we continued to expand our AR and ER programs into additional clinical trials. ER program costs include a year over year cost sharing increase of $16.0 million in accordance with our ARV-471 Collaboration Agreement with Pfizer. Direct expenses related to our platform and exploratory targets increased by $28.7 million as we expanded the number of protein targets in the exploratory and lead optimization phases as well as more investments in our platform discovery efforts.

General and Administrative Expenses

General and administrative expenses totaled $79.6 million for the year ended December 31, 2022, compared with $61.6 million for the year ended December 31, 2021. The increase of $18.0 million was primarily due to an increase of personnel related costs of $15.0 million, which includes $7.2 million related to stock compensation expense, and professional fees of $5.6 million.

Other Income

Other income totaled $12.2 million for the year ended December 31, 2022, compared with $4.3 million for the year ended December 31, 2021. The increase of $7.9 million was primarily due to higher interest income of $10.2 million from marketable securities as compared to the prior year period on a higher average investment balance, partially offset by lower refundable research and development credits from the State of Connecticut of $1.0 million, as we are no longer eligible to receive a cash refund for research and development credits in the State of Connecticut, $0.3 million of higher year-over-year realized losses and forgiveness of debt of $1.0 million in 2021 equal to 50% of the then outstanding loan balance, related to the State of Connecticut loan upon our satisfaction of certain jobs criteria.

Income Tax Expense

Income tax expense totaled $20.9 million for the year ended December 31, 2022, compared with zero for the year ended December 31, 2021, primarily due to current income taxes resulting from revenue recognition for tax purposes from our ARV-471 Collaboration Agreement and the mandatory capitalization of research and development expenses incurred on or after January 1, 2022. Under the Tax Cuts and Jobs Act of 2017, qualified research expenses incurred after 2021 are no longer immediately deductible for tax purposes and instead must be capitalized and amortized for tax purposes. As a result of these items, we expect to fully utilize our federal net operating loss and credit carryforwards in the current year, resulting in current income tax expense for the period.

Loss from Equity Method Investment

Loss from equity method investment totaled $10.6 million for the year ended December 31, 2022, compared with $6.9 million for the year ended December 31, 2021. The increase of $3.7 million was due to increased operating losses incurred by Oerth Bio.

Results of Operations — Years Ended December 31, 2021 and 2020

Discussion and analysis of the results of operations for the year ended December 31, 2021 compared to the year ended December 31, 2020 is included under the heading "Comparison of Years Ended December 31, 2021 and 2020" in Part II, Item 7, Management's Discussion and Analysis of Financial Condition and Results of Operations, in our 2021 Annual Report on Form 10-K as filed with the SEC on February 28, 2022 and incorporated by reference into this Annual Report on Form 10-K.

Liquidity and Capital Resources

Sources of Liquidity

We do not currently have any approved products and have never generated any revenue from product sales. To date, we have financed our operations primarily through the sale of equity interests and through payments from collaboration partners, grant funding and loans from the State of Connecticut. Since inception through December 31, 2022, we had received an aggregate of $780.5 million in payments from collaboration partners, grant funding and forgivable and partially forgivable loans from the State of Connecticut and raised approximately $1.3 billion in gross proceeds from the sale of equity interests and the exercise of stock options, including:

- October 2018: completion of our IPO, in which we issued and sold 7,700,482 shares of common stock for aggregate gross proceeds of $123.2 million, before fees and expenses;
- July 2019: sale of 1,346,313 shares of common stock to Bayer AG for aggregate gross proceeds of $32.5 million;
- November 2019: completion of a follow-on offering in which we issued and sold 5,227,273 shares of common stock for aggregate gross proceeds of $115.0 million, before fees and expenses;
- September - December 2020: sale of 2,593,637 shares of common stock in an "at-the-market offering" for aggregate gross proceeds of $65.6 million, before fees and expenses;
- December 2020: completion of a follow-on offering in which we issued and sold 6,571,428 shares of common stock for aggregate gross proceeds of $460.0 million, before fees and expenses; and
- September 2021: issuance of 3,457,815 share of common stock to Pfizer for aggregate gross proceeds of $350.0 million.

In May 2021, we entered into a lease, which was amended in August 2022, for approximately 160,000 square feet of laboratory and office space to be occupied in 2024. In connection with the signing of the lease, as amended, and at our election to increase the landlord's contribution to the tenant's improvement allowance, we issued a letter of credit for $5.5 million, collateralized by a certificate of deposit in the same amount. Once occupied, the base rent will range from $7.7 million to $8.8 million annually over a ten-year lease term.

In July 2021, we entered into the ARV-471 Collaboration Agreement with Pfizer, pursuant to which we granted Pfizer worldwide co-exclusive rights to develop and commercialize products containing our proprietary compound ARV-471. Under the ARV-471 Collaboration Agreement, Pfizer made an upfront, nonrefundable payment of $650.0 million.

In August 2021, we entered into an Equity Distribution Agreement with Piper Sandler & Company and Cantor Fitzgerald & Co., as agents, pursuant to which we may offer and sell from time to time, through the agents, up to $300.0 million of the common stock registered under the universal shelf registration statement pursuant to one or more "at-the-market" offerings. During the years ended December 31, 2022 and 2021, no shares were issued under this agreement.

Cash Flows

Our cash, cash equivalents, restricted cash and marketable securities totaled $1.2 billion and $1.5 billion as of December 31, 2022 and 2021, respectively. We had an outstanding loan balance of $1.0 million as of December 31, 2022 and 2021.

The following table summarizes our sources and uses of cash for the period presented:

	Years Ended December 31,		
(dollars in millions)	2022	2021	2020
Net cash (used in) provided by operating activities	$ (273.5)	$ 559.4	$ (89.7)
Net cash provided by (used in) investing activities	242.8	(1,313.6)	164.3
Net cash provided by financing activities	4.7	278.6	504.6
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (26.0)	$ (475.6)	$ 579.2

Operating Activities

Net cash used in operating activities for the year ended December 31, 2022 totaled $273.5 million, primarily due to our net loss of $282.5 million and a decrease in deferred revenue of $116.8 million, driven largely by the ARV-471 Collaboration Agreement with Pfizer, partially offset by non-cash charges of $91.6 million and a decrease in accounts receivable of $14.0 million, related to payments pursuant to the ARV-471 Collaboration Agreement. Non-cash charges were primarily stock compensation expense of $75.5 million, depreciation and amortization of $6.3 million and net accretion of bond discounts/premiums of $5.7 million.

Net cash provided by operating activities for the year ended December 31, 2021 totaled $559.4 million, primarily due to an increase in deferred revenue of $695.5 million driven largely by the ARV-471 Collaboration Agreement with Pfizer, a net increase in accrued expenses and accounts payable of $27.9 million, and non-cash charges of $72.1 million, partially offset by our net loss of $191.0 million, an increase in accounts receivable of $14.0 million related primarily to the ARV-471 Collaboration Agreement, prepaid expenses related in part to clinical trials and drug manufacturing contracts of $13.6 million, and the payment to obtain a contract of $12.9 million related to the ARV-471 Collaboration Agreement. Non-cash charges were primarily stock compensation expense of $57.1 million, net accretion of bond discounts/premiums of $9.4 million and depreciation and amortization of $4.8 million.

Net cash used in operating activities for the year ended December 31, 2020 totaled $89.7 million, resulting from our net loss of $119.3 million and a decrease in deferred revenue of $13.3 million, partially offset by non-cash expenses of $35.6 million and an increase in accounts payable and accrued expenses of $12.8 million. Non-cash expenses included $30.2 million of stock compensation expense. The decrease in deferred revenue is primarily due to $21.8 million of revenue recognized, partially offset by $8.5 million in payments received and an accounts receivable from collaboration partners.

Investing Activities

Net cash provided by investing activities for the year ended December 31, 2022 totaled $242.8 million, attributable to maturities and sales of marketable securities in excess of purchases of $249.6 million, partially offset by purchases of property and equipment of $6.8 million.

Net cash used in investing activities for the year ended December 31, 2021 totaled $1.3 billion, attributable to purchases of marketable securities in excess of the maturities of marketable securities of $1.3 billion due in part to funds received as part of the ARV-471 Collaboration Agreement and purchases of property and equipment of $4.7 million, partially offset by sales of marketable securities of $7.2 million.

Net cash provided by investing activities for the year ended December 31, 2020 totaled $164.3 million, attributable to the net maturities and sales of marketable securities in excess of purchases of $170.7 million, offset by the purchases of property and equipment of $6.4 million.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2022 totaled $4.7 million, attributable to proceeds from the exercise of stock options.

Net cash provided by financing activities for the year ended December 31, 2021 totaled $278.6 million, attributable to the proceeds from the issuance of shares of our common stock to Pfizer of $260.0 million (after allocation of a portion of the proceeds to deferred revenue), net of expenses, and proceeds from the exercise of stock options of $18.6 million.

Net cash provided by financing activities for the year ended December 31, 2020 totaled $504.6 million, primarily attributable to the proceeds from sales of our common stock from our public offering and at-the-market offering of $496.3 million, net of combined underwriter discounts from the public offering and offering costs of $29.3 million and the proceeds from the exercise of stock options of $8.3 million.

Funding Requirements

Since our inception, we have incurred significant operating losses. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future as we advance the preclinical and clinical development of our product candidates.

Specifically, we anticipate that our expenses will increase substantially if, and as we:

- continue a Phase 1/2 clinical trial of our product candidate ARV-471, a Phase 1b clinical trial of ARV-471 in combination with palbociclib, Phase 1b cohort expansion in combination with a standard of care agent, and a Phase 3 trial with ARV-471 as a second-line treatment, and initiate a Phase 3 trial of ARV-471 in combination with palbociclib, each in patients with locally advanced or metastatic ER+ / HER2- breast cancer;
- continue a Phase 1/2 clinical trial of our product candidate bavdegalutamide (ARV-110) and a Phase 1b clinical trial of bavdegalutamide in combination with abiraterone for the treatment of men with metastatic castration-resistant prostate cancer, or mCRPC, and initiate one or more additional Phase 1b cohort expansions of bavdegalutamide in combination with standard of care agents and a Phase 3 clinical trial, in men with mCRPC;
- continue a Phase 1/2 clinical trial of our product candidate ARV-766 in men with mCRPC;
- apply our PROTAC Discovery Engine to advance additional product candidates into preclinical and clinical development;
- expand the capabilities of our PROTAC Discovery Engine;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any products for which we may obtain marketing approval;
- expand, maintain and protect our intellectual property portfolio;
- hire additional development, including clinical and regulatory, and scientific personnel; and
- add operational, financial and management information systems and personnel to support our research, product development and future commercialization efforts and support our operations as a public company.

We had cash, cash equivalents, restricted cash and marketable securities of approximately $1.2 billion as of December 31, 2022. We believe that our cash, cash equivalents, restricted cash and marketable securities as of December 31, 2022 will enable us to fund our planned operating expenses and capital expenditure requirements into 2026. We have based this estimate on assumptions that may prove to be wrong and we could use our capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the progress, costs and results of our ongoing clinical trials for ARV-471, bavdegalutamide (ARV-110), and ARV-766 and any future clinical development of ARV-471, bavdegalutamide, (ARV-110) and ARV-766;
- the scope, progress, costs and results of preclinical and clinical development for our other product candidates and development programs;
- the number of, and development requirements for, other product candidates that we pursue, including our other oncology and neurodegenerative research programs;
- the success of our collaborations with Pfizer, Inc., or Pfizer; Genentech, Inc. and F. Hoffman LaRoche Ltd., collectively referred to as Genentech; and Bayer AG, or Bayer;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- our ability to establish additional collaboration arrangements with other biotechnology or pharmaceutical companies on favorable terms, if at all, for the development or commercialization of our product candidates.

As a result of these anticipated expenditures, we will need to obtain substantial additional financing in connection with our continuing operations. Until such time, if ever, as we can generate substantial revenue from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. Although we may receive potential future payments under our collaborations with Pfizer, Genentech and Bayer, we do not currently have any committed external source of funds. Adequate additional funds may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we may be required to delay, limit, reduce or terminate our research, product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making acquisitions or capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us.

Borrowings

In January 2014, we entered into an Assistance Agreement with the State of Connecticut, or the 2014 Assistance Agreement, under which we borrowed $2.5 million. Borrowings under the 2014 Assistance Agreement were forgivable if we maintained a minimum number of full-time jobs in the State of Connecticut for

a minimum period at a minimum annual salary. Effective in March 2016, the full principal amount under the 2014 Assistance Agreement had been forgiven. While borrowings under the 2014 Assistance Agreement have been forgiven, we remain subject to an ongoing covenant to be located in the State of Connecticut through January 2024. Upon violation of this covenant, we would be required to repay the full original funding amount of $2.5 million plus liquidated damages of 7.50%.

In June 2018, we entered into an additional Assistance Agreement with the State of Connecticut, or the 2018 Assistance Agreement, to provide funding for the expansion and renovation of laboratory and office space. We borrowed $2.0 million under the 2018 Assistance Agreement in September 2018, of which $1.0 million was forgiven upon meeting certain employment conditions. Borrowings under the agreement bear an interest rate of 3.25% per annum, with interest only payments required for the first 60 months, and mature in September 2028. The 2018 Assistance Agreement requires that we be located in the State of Connecticut through September 2028 with a default penalty of repayment of the full original funding amount of $2.0 million plus liquidated damages of 7.5% of the total amount of funding received. As of December 31, 2022, $1.0 million remains outstanding under the 2018 Assistance Agreement.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. Our interest-earning assets consist of cash, cash equivalents, restricted cash and marketable securities. Interest income earned on these assets totaled $12.0 million in 2022. Our interest income is sensitive to changes in the general level of interest rates, primarily U.S. interest rates. As of December 31, 2022, our cash equivalents consisted of bank deposits and money market funds and our marketable securities included interest-earning securities. Such interest-earning instruments carry a degree of interest rate risk. Our outstanding debt totaled $1.0 million as of December 31, 2022 and carries a fixed interest rate of 3.25% per annum.

Item 8. Financial Statements and Supplementary Data.

Our financial statements, together with the report of our independent registered public accounting firm, appear on pages F-1 through F-28 of this Annual Report on Form 10-K.

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

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2022. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by the company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2022, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for the company. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the company's board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of consolidated 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
- 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. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. 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.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2022. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control - Integrated Framework (2013). Based on that assessment, our management concluded that, as of December 31, 2022, our internal control over financial reporting was effective.

Deloitte & Touche LLP, the independent registered public accounting firm that audited the consolidated financial statements included in this Annual Report on Form 10-K, has issued an attestation report on the effectiveness of internal control over financial reporting as of December 31, 2022, included below.

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the quarter ended December 31, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. We have not experienced any material impact to our internal control over financial reporting due to the COVID-19 pandemic. We are continually monitoring and assessing the COVID-19 pandemic on our internal controls to minimize the impact on their design and operating effectiveness.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Arvinas, Inc.

Opinion on Internal Control over Financial Reporting

We have audited the internal control over financial reporting of Arvinas, Inc. and subsidiaries (the "Company") as of December 31, 2022, based on criteria established in Internal Control — Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control — Integrated Framework (2013) issued by COSO.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated financial statements as of and for the year ended December 31, 2022, of the Company and our report dated February 23, 2023, expressed an unqualified opinion on those financial statements.

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 Annual 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/ Deloitte & Touche LLP

Stamford, Connecticut
February 23, 2023

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions That Prevent Inspection

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2023 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.

We have adopted a Code of Business Conduct and Ethics that applies to our officers, including our principal executive, financial and accounting officers and our directors and employees. We have posted the text of our Code of Business Conduct and Ethics under the “Investors and Media – Corporate Governance” section of our website, www.arvinas.com. We intend to disclose on our website any amendments to, or waivers from, the Code of Business Conduct and Ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K.

Item 11. Executive Compensation.

The information required by this Item (other than the information required by Item 402(v) of Regulation S-K) is incorporated by reference from the information that will be contained in our Proxy Statement for our 2023 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2023 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2023 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.

Item 14. Principal Accounting Fees and Services.

The information required by this Item is incorporated by reference from the information that will be contained in our Proxy Statement for our 2023 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates pursuant to General Instruction G(3) of Form 10-K.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) **Financial Statements** - The following consolidated financial statements are filed as part of this Annual Report on Form 10-K:

(2) Financial Statement Schedules

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the consolidated financial statements or the notes thereto.

(3) Index to Exhibits

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Number	Description
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38672) filed with the SEC on October 1, 2018).
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-38672) filed with the SEC on October 1, 2018).
4.1	Specimen Stock Certificate evidencing the shares of common stock (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-227112) filed with the SEC on August 30, 2018).
4.2	Registration Rights Agreement among the Registrant and the other parties thereto, dated September 26, 2018 (incorporated by reference to Exhibit 4.2 to the Registrant's Annual Report on Form 10-K (File No. 001-38672) filed with the SEC on March 26, 2019).
4.3	Second Amended and Restated Put Agreement among the Registrant, Connecticut Innovations, Incorporated and the other parties thereto, dated March 29, 2018 (incorporated by reference to Exhibit 4.3 to the Registrant's Registration Statement on Form S-1 (File No. 333-2271121) filed with the SEC on August 30. 2018).

4.4	Description of the Registrant's Securities Registered Under Section 12 of the Exchange Act (incorporated by reference to Exhibit 4.4 to the Registrant's Annual Report on Form 10-K (File No. 001-38672) filed with the SEC on March 16, 2020).
10.1+	Incentive Share Plan, as amended by First Amendment, dated October 16, 2015, Second Amendment, dated December 22, 2016, Third Amendment, dated September 8, 2017, and Fourth Amendment, dated March 29, 2018 (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-227112) filed with the SEC on August 30, 2018).
10.2+	Form of Incentive Share Award Agreement under Incentive Share Plan (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-227112) filed with the SEC on August 30, 2018).
10.3+	Form of Restricted Stock Agreement under Incentive Share Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1/A (File No. 333-227112) filed with the SEC on September 14, 2018).
10.4+	2018 Stock Incentive Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1/A (File No. 333-227112) filed with the SEC on September 14, 2018).
10.5+	Form of Stock Option Agreement under 2018 Stock Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1/A (File No. 333-227112) filed with the SEC on September 14, 2018).
10.6+	Form of Restricted Stock Unit Agreement under 2018 Stock Incentive Plan (incorporated by reference to Exhibit 10.6 to the Registrant's Annual Report on Form 10-K (File No. 001-38672) filed with the SEC on March 26, 2019).
10.7+	2018 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1/A (File No. 333-227112) filed with the SEC on September 14, 2018).
10.8	Form of Restricted Stock Unit Agreement under 2018 Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36874) filed with the SEC on May 5, 2022).
10.9+	Form of Director and Officer Indemnification Agreement (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1/A (File No. 333-227112) filed with the SEC on September 14, 2018).
10.10+	Employment Agreement between the Registrant and John Houston, Ph.D., dated September 13, 2018 (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1/A (File No. 333-227112) filed with the SEC on September 14, 2018).
10.11+	Employment Agreement between the Registrant and Sean Cassidy, dated August 28, 2018 (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1/A (File No. 333-227112) filed with the SEC on September 14, 2018).
10.12+	Employment Agreement between the Registrant and Ian Taylor, Ph.D., dated August 28, 2018 (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1/A (File No. 333-227112) filed with the SEC on September 14, 2018).
10.13+	Employment Agreement between the Registrant and Ronald Peck, M.D., dated July 18, 2019 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38672) filed with the SEC on April 28, 2020).
10.14	Lease Agreement between the Arvinas Operations, Inc. (formerly Arvinas, Inc.) and Science Park Development Corporation, dated December 31, 2017, as amended by First Amendment to Lease, dated May 23, 2018, and Second Amendment to Lease, dated September 4, 2018 (incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1/A (File No. 333-227112) filed with the SEC on September 14, 2018).
10.15	Third Amendment to Lease between Arvinas Operations, Inc. (formerly Arvinas, Inc.) and Science Park Development Corporation, dated March 12, 2019 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-38672) filed with the SEC on March 15, 2019).

10.16	Fourth Amendment to Lease between Arvinas Operations, Inc. (formerly Arvinas, Inc.) and Science Park Development Corporation, dated January 31, 2020 (incorporated by reference to Exhibit 10.14 to the Registrant's Annual Report on Form 10-K (File No. 001-38672) filed with the SEC on March 16, 2020).
10.17	Fifth Amendment to Lease between Arvinas Operations, Inc. (formerly Arvinas, Inc.) and Science Park Development Corporation, dated January 4, 2021 (incorporated by reference to Exhibit 10.34 to the Registrant's Annual Report on Form 10-K (File No. 001-38672) filed with the SEC on March 1, 2021).
10.18	Lease Agreement between Arvinas Operations, Inc. and Science Park Development Corporation, dated November 15, 2019 (incorporated by reference to Exhibit 10.15 to the Registrant's Annual Report on Form 10-K (File No. 001-38672) filed with the SEC on March 16, 2020).
10.19	First Amendment to Lease between Arvinas Operations, Inc. and Science Park Development Corporation, dated February 27, 2020 (incorporated by reference to Exhibit 10.16 to the Registrant's Annual Report on Form 10-K (File No. 001-38672) filed with the SEC on March 16, 2020).
10.2	Second Amendment to Lease between Arvinas Operations, Inc. (formerly Arvinas, Inc.) and Science Park Development Corporation, dated January 4, 2021 (incorporated by reference to Exhibit 10.35 to the Registrant's Annual Report on Form 10-K (File No. 001-38672) filed with the SEC on March 1, 2021).
10.21	Lease between 101 College Street, LLC and Arvinas Operations, Inc., dated May 4, 2021 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36874) filed with the SEC on August 5, 2021).
10.22	First Amendment to Lease between 101 College Street, LLC and Arvinas Operations, Inc., dated August 5, 2022 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36874) filed with the SEC on November 9, 2022).
10.23†	License Agreement between Yale University and Arvinas Operations, Inc. (formerly Arvinas, Inc.), dated July 5, 2013, as amended by Amendment No. 1, dated May 8, 2014, Amendment No. 2, dated October 23, 2014, and Letter Amendment Number 3, dated April 1, 2015 (incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1/A (File No. 333-227112) filed with the SEC on September 14, 2018).
10.24†	Amendment No. 4 to License Agreement between Yale University and Arvinas Operations, Inc. (formerly Arvinas, Inc.), dated January 9, 2019 (incorporated by reference to Exhibit 10.16 to the Registrant's Annual Report on Form 10-K (File No. 001-38672) filed with the SEC on March 26, 2019).
10.25†	Amendment No. 5 to License Agreement between Yale University and Arvinas Operations, Inc. (formerly Arvinas, Inc.), dated June 3, 2019 (incorporated by reference to Exhibit 10.7 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38672) filed with the SEC on August 5, 2019).
10.26	Amended and Restated Consulting Agreement between Craig Crews and Arvinas Operations, Inc. (formerly Arvinas, Inc.), dated October 16, 2015, as amended by Amendment No. 1, dated August 27, 2018 (incorporated by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1 (File No. 333-227112) filed with the SEC on August 30, 2018).
10.27†	Corporate Sponsored Research Agreement between Yale University and Arvinas Operations, Inc. (formerly Arvinas, Inc.), dated July 1, 2016, as amended by Amendment No. 1, dated April 1, 2018 (incorporated by reference to Exhibit 10.15 to the Registrant's Registration Statement on Form S-1 (File No. 333-227112) filed with the SEC on August 30, 2018).
10.28†	Amended and Restated License and Option Agreement among Genentech, Inc., F. Hoffmann-La Roche Ltd and Arvinas Operations, Inc. (formerly Arvinas, Inc.), dated November 8, 2017 (incorporated by reference to Exhibit 10.16 to the Registrant's Registration Statement on Form S-1/A (File No. 333-227112) filed with the SEC on September 14, 2018).
10.29†	Research Collaboration and License Agreement between Pfizer Inc. and Arvinas Operations, Inc. (formerly Arvinas, Inc.), dated December 22, 2017 (incorporated by reference to Exhibit 10.17 to the Registrant's Registration Statement on Form S-1/A (File No. 333-227112) filed with the SEC on September 14, 2018).

10.30†	Amendment No. 1 to Research Collaboration and License Agreement between Pfizer Inc. and Arvinas Operations, Inc. (formerly Arvinas, Inc.), dated December 9, 2019 (incorporated by reference to Exhibit 10.24 to the Registrant's Annual Report on Form 10-K (File No. 001-38672) filed with the SEC on March 16, 2020).
10.31†	Amendment No. 2 to Research Collaboration and License Agreement between Pfizer Inc. and Arvinas Operations, Inc. (formerly Arvinas, Inc.), dated January 14, 2022 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38672) filed with the SEC on May 5, 2022).
10.32†*	Amendment No. 3 to Research Collaboration and License Agreement between Pfizer Inc. and Arvinas Operations, Inc (formerly Arvinas, Inc.), dated December 21, 2022
10.33†	Collaboration and License Agreement between Arvinas Operations, Inc. and Bayer AG, dated June 3, 2019 (incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38672) filed with the SEC on August 5, 2019).
10.34†*	Amended and Restated IP Contribution Agreement between Arvinas Operations, Inc. and Oerth Bio LLC f/k/a Protag LLC, effective December 20, 2022.
10.35†	Collaboration Agreement by and between Arvinas, Inc., Arvinas Operations, Inc., Arvinas Estrogen Receptor, Inc. and Pfizer, Inc., dated July 21, 2021 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-38672) filed with the SEC on July 22, 2021)
10.36†	Master In Vitro Diagnostics Agreement between Foundation Medicine, Inc. and Arvinas Operations, Inc., dated June 4, 2022 Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38672) filed with the SEC on August 4, 2022).
10.37†	Stock Purchase Agreement between the Registrant and Bayer AG, dated June 3, 2019 (incorporated by reference to Exhibit 10.5 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38672) filed with the SEC on August 5, 2019).
10.38†	Investor Agreement between the Registrant and Bayer AG, dated July 16, 2019 (incorporated by reference to Exhibit 10.6 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38672) filed with the SEC on August 5, 2019).
10.39	Equity Distribution Agreement by and between the Registrant and Piper Jaffray & Co., dated October 1, 2019, (incorporated by reference to Exhibit 1.2 to the Registrant's Registration Statement on Form S-3 (File No. 333-234035) filed with the SEC on October 1, 2019).
10.40†	Stock Purchase Agreement, dated July 21, 2021, by and between Arvinas, Inc. and Pfizer, Inc. (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-38672) filed with the SEC on July 22, 2021).
10.41†	Investor Agreement, dated July 21, 2021, by and between Arvinas, Inc. and Pfizer, Inc. (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K (File No. 001-38672) filed with the SEC on July 22, 2021).
10.42	Equity Distribution Agreement, dated August 6, 2021, by and among Arvinas, Inc., Piper Sandler & Co. and Cantor Fitzgerald & Co. (incorporated by reference to Exhibit 1.1 to the Registrant's Current Report on Form 8-K (File No. 001-38672) filed with the SEC on August 6, 2021).
21.1*	Subsidiaries of the Registrant.
23.1*	Consent of Deloitte & Touche LLP, independent registered public accounting firm.
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1**	Certification of Principal 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 Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

99.1	Audited Financial Statements of Oerth Bio, LLC, as of December 31, 2020.
101.INS*	Inline XBRL Instance Document
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Date File (formatted as Inline XBRL and contained in Exhibit 101)

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* Filed herewith.

** Furnished herewith.

† Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

+ Management contract or compensatory plan or arrangement.

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, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ARVINAS, INC.

Date: February 23, 2023

By: /s/ David K. Loomis
David K. Loomis
Vice President and Chief Accounting Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ John Houston, Ph.D. John Houston, Ph.D.	President, Chief Executive Officer and Director (principal executive officer)	February 23, 2023
/s/ Sean Cassidy Sean Cassidy	Chief Financial Officer (principal financial officer)	February 23, 2023
/s/ David K. Loomis David K. Loomis	Vice President and Chief Accounting Officer (principal accounting officer)	February 23, 2023
/s/ Timothy Shannon, M.D. Timothy Shannon, M.D.	Chairman of the Board of Directors	February 23, 2023
/s/ Linda Bain Linda Bain	Director	February 23, 2023
/s/ Everett Cunningham Everett Cunningham	Director	February 23, 2023
/s/ Wendy Dixon, Ph.D. Wendy Dixon, Ph.D.	Director	February 23, 2023
/s/ Edward Kennedy, Jr. Edward Kennedy, Jr.	Director	February 23, 2023
/s/ Briggs Morrison, M.D. Briggs Morrison, M.D.	Director	February 23, 2023
/s/ Leslie Norwalk, Esq. Leslie Norwalk, Esq.	Director	February 23, 2023
/s/ Laurie Smaldone Alsup, M.D. Laurie Smaldone Alsup, M.D.	Director	February 23, 2023
/s/ John Young John Young	Director	February 23, 2023

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Arvinas, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Arvinas, Inc. and subsidiaries (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity, 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 "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of 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 accounting principles generally accepted in the United States of America.

We have also 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 (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 23, 2023, expressed an unqualified opinion on the Company's internal control over financial reporting.

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 Matter

The critical audit matter communicated below is a matter arising from the current-period audit of the financial statements that was communicated or required to be communicated to the audit committee and that (1) relates 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 financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Prepaid and Accrued Research and Development - Refer to Note 2 in the Consolidated Financial Statements

Critical Audit Matter Description

The Company has entered into various contracts with third parties to perform research and development, including clinical research and contract manufacturing. When billing terms under these contracts do not coincide with the timing of when the work is performed, the Company makes estimates of the costs incurred by third parties during the period and the outstanding obligations to those third parties as of period-end. Estimates of costs incurred during the period that are included in period-end prepaid or accrued expense balances are based on a number of factors, including the Company's knowledge of the research and development programs and clinical manufacturing activities associated with project status and milestones, invoicing to date, and the provisions in the contract. Significant judgments and estimates are made by the Company in determining the costs incurred during the period that are included in prepaid or accrued expense balances at the end of each reporting period.

We identified the measurement of the accruals and prepaid expense related to these types of research and development costs as a critical audit matter because of the judgments and estimates necessary for management to determine the status and progress of each contract. The expense recorded related to external research and development is based off of estimates as to the services received and efforts expended pursuant

to quotes and contracts with the Company's contract manufacturing vendors and contract research organizations that supply, conduct and manage clinical trials on the Company's behalf. Assessing such estimates required an increased extent of audit effort and a high degree of auditor judgment when performing procedures to audit the prepaid and accrued expenses related to these costs.

How the Critical Audit Matter Was Addressed in the Audit:

Our audit procedures related to the management's estimation of costs incurred included the following, among others:

- Testing the effectiveness of controls over the accounting for prepaid and accrued research and development expenses, including the Company's assessment and estimation of the costs incurred for significant research and development activities performed by third parties
- On a sample basis, we tested the accrued and prepaid expense balances by:
    - inspecting related contracts and agreeing key provisions of the contracts to the Company's analysis of estimated expenses incurred to date;
    - inspecting correspondence from the third-party vendors to the Company, including status reports, and comparing such information to the amounts used in the Company's estimates;
    - meeting with clinical and manufacturing operational personnel within the Company to understand the status of significant research and development activities for a sample of project activities, and comparing such information to the amounts used in the Company's estimates;
    - comparing the estimated accrual balance as of December 31, 2022, to the invoices received after year-end to evaluate the Company's ability to estimate the accrual.

/s/ Deloitte & Touche LLP

Stamford, Connecticut
February 23, 2023

We have served as the Company's auditor since 2016.

ARVINAS, INC. AND SUBSIDIARIES

Consolidated Balance Sheets

(dollars and shares in millions)	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 81.3	$ 108.3
Restricted cash	5.5	4.5
Marketable securities	1,124.0	1,394.3
Accounts receivable	1.0	15.0
Other receivables	7.0	10.7
Prepaid expenses and other current assets	21.4	19.7
Total current assets	1,240.2	1,552.5
Property, equipment and leasehold improvements, net	13.4	12.7
Operating lease right of use assets	4.4	3.9
Collaboration contract asset and other assets	10.8	12.5
Total assets	$ 1,268.8	$ 1,581.6
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable and accrued liabilities	$ 74.7	$ 54.4
Deferred revenue	218.6	206.2
Current portion of operating lease liability	1.8	1.1
Total current liabilities	295.1	261.7
Deferred revenue	405.1	534.3
Long term debt	1.0	1.0
Operating lease liability	2.7	2.9
Total liabilities	703.9	799.9
Commitments and contingencies		
Stockholders' equity:		
Common stock, $0.001 par value, 53.2 and 53.0 shares issued and outstanding as of December 31, 2022 and 2021, respectively	0.1	—
Accumulated deficit	(965.4)	(682.9)
Additional paid-in capital	1,549.4	1,469.2
Accumulated other comprehensive loss	(19.2)	(4.6)
Total stockholders' equity	564.9	781.7
Total liabilities and stockholders' equity	$ 1,268.8	$ 1,581.6

See accompanying notes to the consolidated financial statements

ARVINAS, INC. AND SUBSIDIARIES

Consolidated Statements of Operations and Comprehensive Loss

(dollars and shares in millions, except per share amounts)	Year Ended December 31,		
Consolidated Statements of Operations	**2022**	**2021**	**2020**
Revenue	$ 131.4	$ 53.6	$ 25.9
Operating expenses:			
Research and development	315.0	180.4	108.4
General and administrative	79.6	61.6	38.3
Total operating expenses	394.6	242.0	146.7
Loss from operations	(263.2)	(188.4)	(120.8)
Other income (expense)			
Other income, net	0.2	2.5	2.1
Interest income, net	12.0	1.8	3.5
Total other income	12.2	4.3	5.6
Net loss before income taxes and loss from equity method investment	(251.0)	(184.1)	(115.2)
Income tax expense	(20.9)	—	—
Loss from equity method investment	(10.6)	(6.9)	(4.1)
Net loss	$ (282.5)	$ (191.0)	$ (119.3)
Net loss per common share - basic and diluted	$ (5.31)	$ (3.82)	$ (3.02)
Weighted average common shares outstanding - basic and diluted	53.2	50.0	39.5

(dollars in millions)	Year Ended December 31,		
Consolidated Statements of Comprehensive Loss	**2022**	**2021**	**2020**
Net loss	$ (282.5)	$ (191.0)	$ (119.3)
Other comprehensive loss:			
Unrealized (loss) gain on available-for-sale securities	(14.5)	(5.2)	0.5
Comprehensive loss	$ (297.0)	$ (196.2)	$ (118.8)

See accompanying notes to the consolidated financial statements

ARVINAS, INC AND SUBSIDIARIES

Consolidated Statements of Changes in Stockholders' Equity

(dollars and shares in millions)	Common Shares	Common Amount	Accumulated Deficit	Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Total Stockholders' Equity
Balance as of December 31, 2019	38.5	—	(372.6)	599.1	0.1	226.6
Issuances of common stock, net of underwriters' discounts and issuance costs of $28.1 million	6.6	—	—	431.9	—	431.9
Stock-based compensation	—	—	—	30.2	—	30.2
Net loss	—	—	(119.3)	—	—	(119.3)
Restricted stock vesting	0.4	—	—	—	—	—
Proceeds from exercise of stock options	0.5	—	—	8.2	—	8.2
Common stock issued in at-the- market offering, net of offering costs of $1.6 million	2.5	—	—	64.1	—	64.1
Unrealized gain on available-for-sale securities	—	—	—	—	0.5	0.5
Balance as of December 31, 2020	48.5	—	(491.9)	1,133.5	0.6	642.2
Stock-based compensation	—	—	—	57.1	—	57.1
Net loss	—	—	(191.0)	—	—	(191.0)
Restricted stock vesting	0.2	—	—	—	—	—
Proceeds from exercise of stock options	0.8	—	—	18.7	—	18.7
Common stock issued, net of issuance costs of $4.6 million	3.5	—	—	259.9	—	259.9
Unrealized loss on available-for-sale securities	—	—	—	—	(5.2)	(5.2)
Balance as of December 31, 2021	53.0	—	(682.9)	1,469.2	(4.6)	781.7
Stock-based compensation	—	—	—	75.5	—	75.5
Net loss	—	—	(282.5)	—	—	(282.5)
Proceeds from exercise of stock options	0.2	0.1	—	4.7	—	4.8
Unrealized loss on available-for-sale securities	—	—	—	—	(14.6)	(14.6)
Balance as of December 31, 2022	53.2	$ 0.1	$ (965.4)	$ 1,549.4	$ (19.2)	$ 564.9

See accompanying notes to the consolidated financial statements

ARVINAS, INC. AND SUBSIDIARIES

Consolidated Statements of Cash Flows

(dollars in millions)	Years Ended December 31, 2022	2021	2020
Cash flows from operating activities:			
Net loss	$ (282.5)	$ (191.0)	$ (119.3)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:			
Depreciation and amortization	6.3	4.8	3.2
Net accretion of bond discounts/premiums	5.7	9.4	1.7
Forgiveness of debt income	—	(1.0)	—
Loss (gain) on sale of marketable securities	0.4	0.2	(0.4)
Amortization of right-of-use assets	1.9	1.2	0.9
Amortization of collaboration contract asset	1.8	0.4	—
Stock-based compensation	75.5	57.1	30.2
Changes in operating assets and liabilities:			
Accounts receivable	14.0	(14.0)	(1.0)
Other receivables	3.7	(3.3)	(1.2)
Prepaid expenses and other current assets	(1.8)	(13.6)	(2.4)
Collaboration contract asset	—	(12.9)	—
Accounts payable and accrued liabilities	20.2	27.9	12.8
Operating lease liabilities	(1.9)	(1.3)	(0.9)
Deferred revenue	(116.8)	695.5	(13.3)
Net cash (used in) provided by operating activities	(273.5)	559.4	(89.7)
Cash flows from investing activities:			
Purchase of marketable securities	(886.4)	(1,744.6)	(41.2)
Maturities of marketable securities	1,076.9	428.5	174.1
Sale of marketable securities	59.1	7.2	37.8
Purchase of property, equipment and leasehold improvements	(6.8)	(4.7)	(6.4)
Net cash provided by (used in) investing activities	242.8	(1,313.6)	164.3
Cash flows from financing activities:			
Proceeds from issuance of common stock	—	264.6	460.0
Payment of common stock offering costs	—	(4.6)	(27.7)
Proceeds from sale of common stock in at-the-market offering	—	—	65.6
Payment of common stock offering costs for at-the-market offering	—	—	(1.6)
Proceeds from exercise of stock options	4.7	18.6	8.3
Net cash provided by financing activities	4.7	278.6	504.6
Net (decrease) increase in cash, cash equivalents and restricted cash	(26.0)	(475.6)	579.2
Cash, cash equivalents and restricted cash, beginning of the period	112.8	588.4	9.2
Cash, cash equivalents and restricted cash, end of the period	$ 86.8	$ 112.8	$ 588.4
Supplemental disclosure of cash flow information:			
Purchases of property, equipment and leasehold improvements unpaid at period end	$ 0.1	$ 0.5	$ 0.5
Cash paid for interest	$ —	$ 0.1	$ 0.1
Cash paid for taxes	$ 11.1	$ —	$ —

See accompanying notes to the consolidated financial statements

1. Nature of Business and Basis of Presentation

Nature of Business

Arvinas, Inc. is a clinical-stage biotechnology company dedicated to improving the lives of patients suffering from debilitating and life-threatening diseases throughout the discovery, development and commercialization of therapies that degrade disease-causing proteins. Arvinas, Inc. has four wholly owned subsidiaries; Arvinas Operations, Inc. formed in 2013, Arvinas Androgen Receptor, Inc. formed in 2015, Arvinas Estrogen Receptor, Inc. formed in 2016, and Arvinas Winchester, Inc. formed in 2018 (collectively, "Arvinas" or the "Company").

Basis of Presentation

The Company's consolidated financial statements are prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") and include the accounts of Arvinas, Inc. and its wholly owned subsidiaries. All intercompany transactions have been eliminated upon consolidation. The accounting policies used to prepare the Company's consolidated financial statements are the same as those used to prepare the consolidated financial statements in prior years.

Certain reclassifications have been made to prior period financial information in order to conform with current period presentation. Accounts payable and Accrued expenses have been condensed into Accounts payable and accrued liabilities, Interest income and Interest expense have been condensed into Interest income, net and in Note 11, *Income Taxes*, within the reconciliation of U.S. federal statutory income tax rate table, a portion of the stock compensation rate effect was reclassified to return to provision.

The Company identified and recorded an adjustment to prior periods related to the accounting for its investment in Oerth Bio. See Note 10, *Equity Method Investments*, for further details.

The preparation of the Company’s consolidated financial statements in conformity with U.S. GAAP requires management to make certain estimates and assumptions that affect the reported amounts and disclosures in the consolidated financial statements and notes. While management believes that estimates and assumptions used in the preparation of the consolidated financial statements and notes are appropriate, actual results could differ from those estimates. The most significant estimates are those used in the determination of the Company’s revenue recognition, uncertain tax positions and research and development expenses.

Risks and Uncertainties

The Company is subject to a number of risks similar to other biotechnology companies in the early stage, including, but not limited to, the need to obtain adequate additional funding, possible failure of preclinical testing or clinical trials, the need to obtain marketing approval for its product candidates, competitors developing new technological innovations, the need to successfully commercialize and gain market acceptance of the Company’s products and protection of proprietary technology. If the Company does not successfully obtain regulatory approval, it will be unable to generate revenue from product sales or achieve profitability.

To date, the Company has not generated any revenue from product sales and expects to incur additional operating losses and negative operating cash flows for the foreseeable future. The Company has financed its operations primarily through sales of equity interests, proceeds from collaborations, grant funding and debt financing. The Company had cash, cash equivalents, restricted cash and marketable securities of approximately $1.2 billion as of December 31, 2022.

2. Summary of Significant Accounting Policies

Cash and Cash Equivalents

The Company classifies as cash and cash equivalents amounts on deposit in banks and cash invested temporarily in various instruments, primarily money market accounts, with original maturities of three months or less at time of purchase. The carrying amounts reported in the consolidated balance sheets represent the fair values of cash and cash equivalents and are considered Level 1 financial instruments.

Restricted Cash

Restricted cash represents a letter of credit collateralized by a certificate of deposit in the same amount as required under the terms of the Company's laboratory and office space lease entered into in May 2021 and amended in August 2022.

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported withing the consolidated balance sheets to the total amounts shown in the consolidated statements of cash flows for the years ended December 31, 2022, 2021 and 2020:

	Year Ended December 31,		
(dollars in millions)	**2022**	**2021**	**2020**
Cash and cash equivalents	$ 81.3	$ 108.3	$ 588.4
Restricted cash	5.5	4.5	
Cash, cash equivalents and restricted cash	$ 86.8	$ 112.8	$ 588.4

Concentration of Credit Risk

The Company maintains its cash in financial institution accounts that may at times exceed federally insured limits. The cash balances in the financial institutions are insured by the Federal Deposit Insurance Corporation ("FDIC") up to $250,000. Cash may also be maintained at commercial institutions that are not insured by the FDIC.

For the years ended December 31, 2022 and 2021, one collaborator represented 88% and 68% of the Company's revenue, respectively, and for the year ended December 31, 2020, three collaborators represented 37%, 32% and 31% of the Company's revenue. For each of the years ended December 31, 2022 and 2021, one collaborator accounted for the entire accounts receivable balance.

Marketable Securities

The Company's marketable securities are classified as available-for-sale securities and are carried at their fair value based on the quoted market prices of the securities, with unrealized gains and losses reported as accumulated other comprehensive income (loss), a separate component of stockholders' equity. Realized gains and losses on available-for-sale securities are included in other income in the period earned or incurred.

Property, Equipment, and Leasehold Improvements

Property and equipment are recorded at cost. Depreciation is calculated using the straight-line method over the estimated useful lives, which range from three years for office equipment to five years for laboratory equipment. Maintenance and repairs which do not extend the lives of the assets are charged directly to expense as incurred. Upon retirement or disposal, cost and related accumulated depreciation is removed from the related accounts, and any resulting gain or loss is recognized as a component of income or loss for the period. Leasehold improvements are recorded at cost and amortized using the straight-line method over the shorter of the lease term or the useful life of the asset.

Impairment of Long-Lived Assets

The Company evaluates the carrying value of long-lived assets when indications of potential impairments are present. The Company adjusts the carrying value of the long-lived assets if the sum of undiscounted expected future cash flows is less than the carrying value. No such impairments were recorded during 2022, 2021 or 2020.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker in assessing performance and allocating resources. The Company, through its Chief Executive Officer in his role as chief operating decision maker, views Company operations and manages the business as one operating segment. All of the Company's tangible assets are held in the United States and all of the Company's revenue has been generated in the United States.

Revenue Recognition and Deferred Revenue

Revenues from Contracts

The Company recognizes revenue under Accounting Standards Codification ("ASC") 606, *Revenue from Contracts with Customers.* The Company's revenue is generated through research collaboration and license agreements with pharmaceutical partners. The terms of these agreements contain multiple goods and services which may include (i) licenses, (ii) research and development activities, and (iii) participation in joint research and development steering committees. The terms of these agreements may include non-refundable, upfront license or option fees, payments for research and development activities, payments upon the achievement of certain milestones and royalty payments based on product sales derived from the collaboration. Under ASC 606, the Company evaluates whether the license agreement, research and development services and participation in research and development steering committees represent separate or combined performance obligations. The Company has determined that these services within its existing contracts represent combined single performance obligations.

The research collaboration and license agreements typically include contingent milestone payments related to specified preclinical and clinical development milestones and regulatory milestones. These milestone payments represent variable consideration to be included within the transaction price using the most likely amount method. The Company determined that the most likely amount to be recognized was zero, against which no constraint was applied. The Company continually assesses the probability of significant reversals for any amounts that become likely to be realized prior to recognizing the variable consideration associated with these payments within the transaction price.

Revenue is recognized ratably over the Company's expected performance period under each respective arrangement. The Company makes its best estimate of the period over which the Company expects to fulfill the Company's performance obligations, which includes access to technology through the license agreement and research activities. Given the uncertainties of these collaboration arrangements, significant judgment is required to determine the duration of the performance period.

For the years ended December 31, 2022, 2021 and 2020, the transaction price allocated to the combined performance obligation identified under the individual research collaboration and license agreements was recognized as revenue on either a straight-line basis over the estimated performance period under the arrangement or over the estimated performance period based on the Company's best estimate of costs to be incurred. Straight-line basis was considered the best measure of progress for certain agreements in which control of the combined obligation transfers to the customers, due to the contract containing license rights to technology, research and development services, and joint committee participation, which in totality are expected to occur ratably over the performance period.

The Company's contracts may also call for certain sales-based milestone and royalty payments upon successful commercialization of a target. The Company recognizes revenues from sales-based milestone and royalty payments at the later of a) the occurrence of the subsequent sale, or b) the performance obligation to which some or all of the sales-based milestone or royalty payments has been allocated has been satisfied (or

partially satisfied). The Company anticipates recognizing these milestones and royalty payments if and when subsequent sales are generated by customers from the use of the technology. To date, no revenue from these sales-based milestone and royalty payments has been recognized for any periods.

Amounts received prior to satisfying the above revenue recognition criteria are recorded as contract liabilities in the Company's accompanying consolidated balance sheets.

The Company expenses direct and incremental costs to obtaining and fulfilling a contract as and when incurred if the expected amortization period of the asset that would be recognized is one year or less, or if the amount of the asset is immaterial. Otherwise, such costs are capitalized as collaboration contract assets and amortized as general and administrative expenses over the total estimated period of performance of each underlying contract.

Equity Method Investments

The Company accounts for investments for which it does not have a controlling interest in accordance with ASC 323, *Investments – Equity Method and Joint Ventures*. The Company recognizes its pro-rata share of income and losses in the investment in "Loss from equity method investment" on the consolidated statement of operations and comprehensive loss, with a corresponding change to the investment in equity method investment in the consolidated balance sheet until such investment is reduced to zero.

Income Taxes

Arvinas, Inc. and its wholly owned subsidiaries use the asset and liability method of accounting for income taxes, as set forth in ASC 740, *Accounting for Income Taxes*. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequence of temporary differences between the carrying amounts and the tax basis of assets and liabilities and net operating loss carry forwards, all calculated using presently enacted tax rates. A valuation allowance is established to reduce deferred tax assets to their estimated realizable value. The Company provides a valuation allowance to the extent that it is more likely than not that all or a portion of the deferred tax assets will not be realized.

The Company follows the authoritative guidance for recognizing and measuring uncertainty in income tax positions taken or expected to be taken in a tax return. The Company recognizes interest accrued related to unrecognized tax benefits and penalties in tax expense. Management has evaluated the effect of ASC 740 guidance related to uncertain income tax positions and concluded that the Company has no significant uncertain income tax positions as of December 31, 2022 and 2021.

Equity-based Compensation

The Company measures employee, board of director and consultant equity-based compensation for stock option and restricted stock grants based on the grant date fair value of the equity awards. Equity-based compensation expense is recognized over the requisite service period of the awards, net of estimated forfeitures. Estimated forfeitures are updated on a periodic basis based on actual experience. For equity awards that have a performance condition, the Company recognizes compensation expense based on its assessment of the probability that the performance condition will be achieved.

The Company classifies equity-based compensation expense in its consolidated statement of operations in the same manner in which the award recipient's salary and related costs are classified or in which the award recipient's service payments are classified.

401(k) Savings plan

The Company has a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pretax basis. Under the 401(k) Plan, the Company made discretionary matching contributions on behalf of eligible employees totaling $2.2 million, $1.3 million and $0.9 million for the years ended December 31, 2022, 2021 and 2020, respectively.

Research and Development Expenses

Research and development expenses include (i) employee-related expenses, including salaries, benefits, travel and stock-based compensation expense; (ii) external research and development expenses incurred under arrangements with third parties, such as contract research organization agreements, investigational sites and consultants; (iii) the cost of acquiring, developing and manufacturing clinical study materials; (iv) costs associated with preclinical and clinical activities and regulatory operations; and (v) costs incurred in development of intellectual property. Costs incurred in connection with research and development activities are expensed as incurred.

The Company enters into consulting, research and other agreements with commercial entities, researchers, universities and others for the provision of goods and services. Such arrangements are generally cancellable upon reasonable notice and payment of costs incurred. Costs are considered incurred based on an evaluation of the progress to completion of specific tasks under each contract using information and data provided by the respective vendors, including the Company's clinical sites. These costs consist of direct and indirect costs associated with specific projects, as well as fees paid to various entities that perform certain research on behalf of the Company. Depending upon the timing of payments to the service providers, the Company recognizes prepaid expenses or accrued expenses related to these costs. These accrued or prepaid expenses are based on management's estimates of the work performed under service agreements, milestones achieved and experience with similar contracts. The Company monitors each of these factors and adjusts estimates accordingly.

Fair Value Measurements

ASC Topic 820, *Fair Value Measurements and Disclosures*, requires disclosure of the fair value of financial instruments held by the Company. ASC 825, *Financial Instruments*, defines fair value and establishes a three-level valuation hierarchy for disclosures of fair value measurement that enhances disclosure requirements for fair value measures. The three levels of valuation hierarchy are defined as follows:

Level 1— Inputs are based upon observable or quoted prices (unadjusted) for identical instruments traded in active markets. The Company's Level 1 financial instruments consist of cash equivalents.

Level 2— Inputs are based upon quoted prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets that are not active and model-based valuation techniques for which all significant assumptions are observable in the market or can be corroborated by observable market data for substantially the full term of the assets or liabilities. The Company's Level 2 investments consist primarily of corporate notes and bonds and U.S. government and agency securities.

Level 3— Inputs are generally unobservable and typically reflect management's estimates of assumptions that market participants would use in pricing the asset or liability. The fair values are therefore determined using model-based techniques that include option pricing models, discounted cash flow models and similar techniques.

In determining fair value, the Company utilizes valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible as well as considers counterparty credit risk in its assessment of fair value.

Net Loss per Common Share

Basic net loss per common share is computed by dividing net loss by the weighted-average number of common shares outstanding during the period. Diluted net loss per share is computed using the weighted-average number of common shares outstanding during the period and, if dilutive, the weighted average number of potential shares of common shares.

New Accounting Pronouncements

Recently Adopted Accounting Pronouncements

The Company reviews new accounting standards as issued. As of December 31, 2022, the Company has not identified any new standards that it believes will have a material impact on its consolidated financial statements.

3. Research Collaboration and License Agreements

ARV-471 Collaboration Agreement

In July 2021, the Company entered into a collaboration agreement with Pfizer (the "ARV-471 Collaboration Agreement") pursuant to which the Company granted Pfizer worldwide co-exclusive rights to develop and commercialize products containing the Company's proprietary compound ARV-471 (the "Licensed Products"). Under the ARV-471 Collaboration Agreement, the Company received an upfront, non-refundable payment of $650.0 million. In addition, the Company will be eligible to receive up to an additional $1.4 billion in contingent payments based on specific regulatory and sales-based milestones for the Licensed Products. Of the total contingent payments, $400.0 million in regulatory milestones are related to marketing approvals and $1.0 billion are related to sales-based milestones.

The Company and Pfizer share equally all development costs, including costs of conducting clinical trials, for the Licensed Products, subject to certain exceptions. Except for certain regions described below, the parties will also share equally all profits and losses in commercialization and medical affairs activities for the Licensed Products in all other countries, subject to certain exceptions.

The Company will be the marketing authorization holder in the United States and, subject to marketing approval, book sales in the United States, while Pfizer will hold marketing authorizations outside the United States. The parties will determine which, if any, regions within the world will be solely commercialized by one party, and in such region the parties will adjust their share of profits and losses for the Licensed Products based on the role each party will be performing.

In addition, in connection with the execution of the ARV-471 Collaboration Agreement, the Company and Pfizer entered into a Stock Purchase Agreement (the" Pfizer Stock Purchase Agreement") for the sale and issuance of 3,457,815 shares of the Company's common stock (the "Shares") to Pfizer at a price of $101.22 per share, for an aggregate purchase price of $350.0 million (the "Pfizer Equity Transaction"), less financial advisor fees of $4.6 million, which was consummated in September 2021. Pursuant to terms of the Pfizer Stock Purchase Agreement, Pfizer has agreed not to sell or transfer the Shares without prior written approval of the Company for a specified time period, subject to specified exceptions.

The Company determined that the ARV-471 Collaboration Agreement and the Pfizer Equity Transaction entered into with Pfizer concurrently should be evaluated as a combined contract in accordance with Accounting Standards Codification ("ASC") 606, *Revenue from Contracts with Customers*. The Company determined the fair value of the shares sold under the Pfizer Equity Transaction to be $85.4 million less than the contractual purchase price stipulated in the agreement. In accordance with the applicable accounting guidance in ASC 815-40, *Contracts in Entity's Own Equity*, the Company determined that the sale of stock should be recorded at fair value and therefore allocated the excess consideration received under the Pfizer Equity Transaction to the ARV-471 Collaboration Agreement, which, along with the non-refundable payment of $650.0 million, is being recognized as revenue over the total estimated period of performance based on the Company's best estimate of costs to be incurred.

As a direct result of the Company's entry into the ARV-471 Collaboration Agreement, the Company incurred direct and incremental costs to obtain the contract, paid to a financial advisor, totaling $12.9 million. In accordance with ASC 340, *Other Assets and Deferred Costs*, the Company recognized an asset of $12.9 million in collaboration contract asset and other assets in the consolidated balance sheet, which is being amortized as general and administrative expense over the total estimated period of performance under the ARV-471 Collaboration Agreement.

Bayer Collaboration Agreement

In June 2019, the Company and Bayer AG entered into a Collaboration and License Agreement (the "Bayer Collaboration Agreement") setting forth the Company's collaboration with Bayer AG to identify or optimize proteolysis targeting chimeras, or PROTAC targeted protein degraders, that mediate for degradation of target proteins ("Targets"), using the Company's proprietary platform technology, which Targets will be selected by Bayer AG, subject to certain exclusions and limitations. Under the terms of the Bayer Collaboration Agreement, the Company received an upfront, non-refundable payment of $17.5 million in exchange for the use of the Company's technology license. In addition, Bayer AG is committed to fund an additional $12.0 million through 2023, of which $10.5 million was received from inception through December 31, 2022, including $3.0 million received in each of the years ended December 31, 2022, 2021 and 2020. These payments are being recognized over the total estimated period of performance.

The Company is also eligible to receive up to $197.5 million in development milestone payments and up to $490.0 million in sales-based milestone payments for all designated Targets. In addition, the Company is eligible to receive, on net sales of PROTAC targeted protein degrader-related products, mid-single digit to low-double digit tiered royalties, which may be subject to reductions. There were no development or sales-based milestone payments or royalties received through December 31, 2022.

The Company determined that the Bayer Collaboration Agreement and a Stock Purchase Agreement entered into with Bayer AG at the same time should be evaluated as a combined contract in accordance with ASC 606, *Revenue from Contracts with Customers*. The Company determined the fair value of the shares sold under the Stock Purchase Agreement to be $2.9 million less than the contractual purchase price stipulated in the agreement. In accordance with the applicable accounting guidance in ASC 815-40, *Contracts in Entity's Own Equity*, the Company determined that the sale of stock should be recorded at fair value. Therefore, the Company allocated the additional $2.9 million of consideration received under the Stock Purchase Agreement to the Bayer Collaboration Agreement and added such amount to the total transaction price.

Pfizer Research Collaboration Agreement

In December 2017, the Company entered into a Research Collaboration and License Agreement with Pfizer (the "Pfizer Research Collaboration Agreement"). Under the terms of the Pfizer Research Collaboration Agreement, the Company received an upfront, non-refundable payment and certain additional payments totaling $28.0 million in 2018 in exchange for use of the Company's technology license and to fund Pfizer-related research as defined within the Pfizer Research Collaboration Agreement. These payments are being recognized over the total estimated period of performance. The Company is eligible to receive up to an additional $37.5 million in non-refundable option payments if Pfizer exercises its options for all targets under the Pfizer Research Collaboration Agreement. The Company is also entitled to receive up to $225.0 million in development milestone payments and up to $550.0 million in sales-based milestone payments for all designated targets under the Pfizer Research Collaboration Agreement, as well as tiered royalties based on sales. In 2021 and 2020, the Company received payments totaling $1.2 million and $4.4 million, respectively, which are being recognized as revenue over the total period of performance. Pfizer selected additional targets and initiated additional services totaling $1.0 million and $3.5 million in December 2022 and 2021, respectively, which were included in accounts receivable as of December 31, 2022 and 2021. There were no sales-based milestone payments or royalties received through December 31, 2022.

Genentech Modification

In November 2017, the Company entered into an Amended and Restated Option, License, and Collaboration Agreement (the "Genentech Modification") with Genentech, Inc. and F. Hoffman-La Roche Ltd (together "Genentech"), amending a previous Genentech agreement entered into in September 2015. Under the Genentech Modification, the Company received upfront, non-refundable payments of $34.5 million (in addition to $11.0 million received under the previous agreement in 2015) to fund Genentech-related research and Genentech has the right to designate up to ten targets. The Company is eligible to receive up to $27.5 million in additional expansion target payments if Genentech exercises its options on all remaining targets. Upfront non-refundable payments are recognized as revenue over the total estimated period of performance.

The Company is eligible to receive up to $44.0 million per target in development milestone payments, $52.5 million in regulatory milestone payments and $60.0 million in commercial milestone payments based on sales as well as tiered royalties based on sales. There were no development, regulatory or commercial milestone payments or royalties received through December 31, 2022.

Changes in the Company's contract balances were as follows:

	December 31,	
(dollars in millions)	**2022**	**2021**
Accounts receivable		
Beginning balance	$ 15.0	$ 1.0
Additions	6.4	19.9
Payments received	(20.4)	(5.9)
Ending balance	$ 1.0	$ 15.0
Accounts payable related to collaborations		
Beginning balance	$ —	$ —
Additions	5.0	—
Payments made	—	—
Ending balance	$ 5.0	$ —
Contract assets: Collaboration contract asset		
Beginning balance	$ 12.5	$ —
Additions	—	12.9
Amortization	(1.8)	(0.4)
Ending balance	$ 10.7	$ 12.5
Contract liabilities: Deferred revenue		
Beginning balance	$ 740.5	$ 45.1
Additions to collaboration agreements	4.0	742.1
Revenue recognized from balances held at the beginning of the period	(120.0)	(18.6)
Revenue recognized from balances not held at the beginning of the period	(0.8)	(28.1)
Ending balance	$ 623.7	$ 740.5

During the years ended December 31, 2022, 2021 and 2020, the Company recorded cumulative catch-up adjustments from contract modifications totaling $0.7 million, $(0.8) million and $(0.4) million, respectively, relating to performance obligations which were satisfied in prior periods.

The aggregate amount of the transaction price allocated to performance obligations that were unsatisfied as of December 31, 2022 totaled $623.7 million, which is expected to be recognized in the following periods:

(dollars in millions)	
2023	$ 218.6
2024	193.9
2025	90.2
2026	55.3
2027	34.7
Thereafter	31.0
Total	$ 623.7

4. Marketable Securities and Fair Value Measurements

The following is a summary of the Company's assets measured at fair value on a recurring basis.

	December 31, 2022					
(dollars in millions)	Valuation Hierarchy	Effective Maturity	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Corporate bonds	Level 2	2023	$ 802.7	$ —	$ (9.3)	$ 793.4
Corporate bonds	Level 2	2024 - 2025	205.3	—	(9.2)	196.1
Government securities	Level 2	2023	61.9	—	(0.4)	61.5
Government securities	Level 2	2024	73.3	—	(0.3)	73.0
Total			$ 1,143.2	$ —	$ (19.2)	$ 1,124.0

	December 31, 2021					
(dollars in millions)	Valuation Hierarchy	Effective Maturity	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Corporate bonds	Level 2	2022	$ 784.0	$ —	$ (0.7)	$ 783.3
Corporate bonds	Level 2	2023 - 2024	582.5	—	(3.8)	578.7
Government securities	Level 2	2022	32.4	—	(0.1)	32.3
Total			$ 1,398.9	$ 0.0	$ (4.6)	$ 1,394.3

The Company generally does not intend to sell any investments prior to recovery of their amortized cost basis for any investment in an unrealized loss position. As such, the Company has classified these losses as temporary in nature.

The carrying value of accounts receivable and accounts payable and accrued liabilities approximate their fair values due to the short-term nature of these assets and liabilities.

Non-recurring fair value measures

In September 2021, in connection with the Pfizer Stock Purchase Agreement, the Company valued the common stock issued to Pfizer at fair value. The Pfizer Stock Purchase Agreement contains provisions restricting the sale or transfer for a period of time (the "lock-up period"). The resulting fair value of $264.6 million was determined by applying the discount due to lack of marketability during the contractual lock-up period to the public trading price of the common stock, which is a Level 1 input, on the date of sale. The Company accounted for the lack of marketability during the contractual lock-up period, by utilizing put option models, which are considered Level 3 inputs. Such option models included the Company's historical volatility and the risk-free rate based on U.S. Treasury bond rates, as key inputs.

5. Property, Equipment and Leasehold Improvements

Property, equipment and leasehold improvements consist of the following:

(dollars in millions)	December 31, 2022	December 31, 2021
Laboratory equipment	$ 17.1	$ 13.6
Office equipment	2.0	1.4
Leasehold improvements	10.9	8.4
Total property, equipment and leasehold improvements	30.0	23.4
Less: accumulated depreciation and amortization	(16.6)	(10.7)
Property, equipment and leasehold improvements, net	$ 13.4	$ 12.7

Depreciation expense totaled $6.3 million, $4.8 million, and $3.2 million for the years ended December 31, 2022, 2021 and 2020, respectively.

6. Right-of-Use Assets and Liabilities

The Company determines if an arrangement is a lease at inception. Operating leases are included in operating lease right-of-use (ROU) assets and operating lease liabilities in the accompanying consolidated balance sheets.

ROU assets represent the right to use an underlying asset for the lease term and lease liabilities represent the obligation to make lease payments arising from the lease. Operating lease ROU assets and liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term. As the Company's leases do not provide an implicit interest rate, the Company uses its incremental borrowing rate based on the information available at the lease commencement date in determining the present value of lease payments, which ranges from 3.0% – 4.1%. Lease expense is recognized on a straight-line basis over the lease term. The Company considers options to extend or terminate the lease in recognizing ROU assets and lease liabilities when it is reasonably certain that such options will be exercised.

In May 2021, the Company entered into a lease arrangement, which was amended in August 2022, for approximately 160,000 square feet of laboratory and office space to be occupied in 2024. In connection with the signing of the lease and the related amendment, and at the Company's election to increase the landlord's contribution to the tenant improvement allowance, the Company initially issued a letter of credit totaling $4.5 million, which was subsequently increased to $5.5 million, collateralized by a certificate of deposit in the same amount, which is presented as restricted cash in the accompanying consolidated balance sheets. Once occupied, the base rent will range from $7.7 million to $8.8 million annually over a ten-year lease term.

The Company has operating leases for its corporate office, laboratories and certain equipment, which expire no later than January 2026. The leases have a weighted average remaining term of 2.3 years.

The components of lease expense were as follows:

(dollars in millions)	Year Ended December 31, 2022	Year Ended December 31, 2021	Year Ended December 31, 2020
Operating lease cost	$ 2.1	$ 1.4	$ 1.0

Supplemental cash flow information related to leases was as follows:

(dollars in millions)	December 31, 2022	2021	2020
Cash paid for amounts included in the measurement of lease liabilities:			
Operating cash flows from operating leases	$ 1.9	$ 1.2	$ 0.9
Supplemental non-cash information:			
Right-of-use assets obtained in exchange for new lease obligations	$ 2.4	$ 3.2	$ 0.6

Maturities of operating lease liabilities as of December 31, 2022 were as follows:

(dollars in millions)	
2023	$ 2.0
2024	2.2
2025	0.5
2026	—
Total lease payments	4.7
Less: imputed interest	(0.2)
Total	$ 4.5

7. Accounts Payable and Accrued Liabilities

Accounts payable and accrued liabilities consisted of the following:

(dollars in millions)	December 31, 2022	2021
Accounts payable	$ 5.7	$ 31.3
Accrued liabilities		
Research and development expenses	35.9	9.5
Employee expenses	18.7	12.4
Income taxes	10.3	—
Professional fees and other	4.1	1.2
	$ 74.7	$ 54.4

8. Long-Term Debt

In June 2018, the Company entered into an Assistance Agreement with the State of Connecticut (the "2018 Assistance Agreement") to provide funding for the expansion and renovation of laboratory and office space (the "Project"). Under the terms of the 2018 Assistance Agreement, the Company was entitled to borrow from the State of Connecticut a maximum of $2.0 million, provided that the funding did not exceed more than 50% of the total Project costs. In September 2018, the Company borrowed $2.0 million under the 2018 Assistance Agreement, bearing interest at 3.25% per annum with interest payments required for the first 60 months from the funding date. Thereafter, the loan will begin to fully amortize through month 120, maturing in September 2028. In April 2021, borrowings totaling $1.0 million were forgiven by the State of Connecticut as the Company met certain employment conditions, as defined in the agreement. The 2018 Assistance Agreement requires that the Company be located in the State of Connecticut through September 2028 with a default penalty of repayment of the full original funding amount of $2.0 million plus liquidated damages of 7.5% of the total amount of funding received.

In connection with an Assistance Agreement with the State of Connecticut (the "Assistance Agreement") entered into in 2014, under which all the borrowings by the Company were forgiven in accordance with the Assistance Agreement, the Company is required to be located in the State of Connecticut through January 2024, with a default penalty of repayment of the full original funding amount of $2.5 million plus liquidated damages of 7.5%.

Minimum future principal payments on long-term debt as of December 31, 2022 are as follows:

(dollars in millions)	
2023	$ —
2024	0.2
2025	0.2
2026	0.2
2027	0.2
Thereafter	0.2
Total	$ 1.0

During the years ended December 31, 2022 and 2021, interest expense was immaterial. During the year ended December 31, 2020, interest expense totaled $0.1 million.

9. Equity

Common Stock

As of December 31, 2022 and 2021, the Company had authorized 200,000,000 shares of common stock, at a $0.001 par value per share. The holders of shares of common stock are entitled to one vote for each share of common stock held at all meetings of stockholders and written actions in lieu of meetings. The holders of shares of common stock are entitled to receive dividends, if and when declared by the Board of Directors. No dividends have been declared or paid by the Company since its inception.

In September 2021, in connection with the Pfizer Stock Purchase Agreement, the Company issued 3,457,815 shares of common stock to Pfizer at a price of $101.22 per share, which resulted in aggregate gross proceeds of $350 million, less financial advisor fees of $4.6 million, as further described in Note 3 to our consolidated financial statements. Pursuant to terms of the Pfizer Stock Purchase Agreement, Pfizer has agreed not to sell or transfer the Shares without prior written approval of the Company for a specified period, subject to specified exceptions.

In December 2020, the Company completed a public offering in which the Company issued and sold 6,571,428 shares of common stock at a public offering price of $70.00 per share, which resulted in aggregate gross proceeds of $460.0 million before underwriter discounts, commissions, and offering costs of $28.1 million.

Equity Distribution Agreements

In August 2021, the Company entered into an Equity Distribution Agreement with Piper Sandler & Company (“Piper Sandler”) and Cantor Fitzgerald & Co. (“Cantor”), as agents, pursuant to which the Company may offer and sell from time to time, through the agents, up to $300.0 million of the common stock registered under the universal shelf registration statement pursuant to one or more “at-the-market" offerings. During the years ended December 31, 2022 and 2021, no shares were issued under this agreement.

In October 2019, the Company entered into an Equity Distribution Agreement (the "Distribution Agreement") with Piper Sandler, pursuant to which the Company could offer and sell from time-to-time in an “at-the-market offering,” at its option, up to an aggregate of $100.0 million of shares of the Company’s common stock through Piper Sandler, as sales agent. During year ended December 31, 2020, the Company sold 2,593,637 shares of its common stock resulting in proceeds to the Company of $64.1 million, net of offering costs of $1.6 million. The Company terminated the Distribution Agreement in August 2021.

Share-based Compensation

2018 Employee Stock Purchase Plan

In September 2018, the Company adopted the 2018 Employee Stock Purchase Plan (the "2018 ESPP"), with the first offering period under the 2018 ESPP commencing on January 1, 2020, by initially providing participating employees with the opportunity to purchase an aggregate of 311,850 shares of the Company's common stock. The number of shares of the Company's common stock reserved for issuance under the 2018 ESPP increased, pursuant to the terms of the 2018 ESPP, by additional shares equal to 1% of the Company's then-outstanding common stock, effective as of January 1 of each year. As of December 31, 2022, 1,986,565 shares remained available for purchase. During the years ended December 31, 2022, 2021 and 2020, the Company issued 24,898, 19,357 and 11,046 shares, respectively, of common stock under the 2018 ESPP.

Incentive Share Plan

In the Fourth Amendment to the Company's Incentive Share Plan (the "Incentive Plan") adopted in March 2018, the Company was authorized to issue up to an aggregate of 6,199,477 incentive units pursuant to the Incentive Plan. Generally, incentive units were granted at no less than fair value as determined by the board of managers and had vesting periods ranging from one to four years. The Incentive Plan was terminated in September 2018. In September 2018, each outstanding incentive unit was converted into a number of shares of common stock based upon the IPO price. Certain of the shares of common stock issued in respect of incentive units continued to be subject to vesting in accordance with the vesting schedule that was applicable to such incentive units through the year ended December 31, 2022.

2018 Stock Incentive Plan

In September 2018, the Company's board of directors adopted, and the Company's stockholders approved, the 2018 Stock Incentive Plan (the "2018 Plan"), which became effective upon the effectiveness of the registration statement on Form S-1 for the Company's IPO. The number of common shares initially available for issuance under the 2018 Plan equaled the sum of (1) 4,067,007 shares of common stock; plus (2) the number of shares of common stock (up to 1,277,181 shares) issued in respect of incentive units granted under the Incentive Plan that were subject to vesting immediately prior to the effectiveness of the registration statement that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right; plus (3) an annual increase on the first day of each year beginning with the year ended December 31, 2019 and continuing to, and including, the year ending December 31, 2028, equal to the lesser of 4,989,593 shares of the Company's common stock, 4% of the number of shares of the Company's common stock outstanding on the first day of the year or an amount determined by the Company's board of directors. As of December 31, 2022, 2,048,284 shares are available for issuance under the 2018 Plan. Common shares subject to outstanding equity awards that expire or are terminated, surrendered, or cancelled without having been fully exercised or are forfeited in whole or in part are available for future grants of awards.

Compensation Expense

For the years ended December 31, 2022, 2021 and 2020, the Company recognized compensation expense of $75.5 million, $57.1 million and $30.2 million, respectively, related to the issuance of incentive awards, including $0.7 million, $0.3 million and $0.3 million, respectively, related to the 2018 ESPP. As of December 31, 2022, there was $67.3 million of compensation expense that is expected to be recognized over a weighted average period of approximately 1.7 years.

Stock Options

The fair value of the stock options granted during each of the years ended December 31, 2022, 2021 and 2020 was determined using the Black-Scholes option pricing model at the grant date with the following range of assumptions:

	Year ended December 31,		
	2022	2021	2020
Expected volatility	73% - 76%	74% - 78%	70% - 75%
Expected term (years)	5.5 - 7.0	5.3 - 7.0	5.3 - 7.0
Risk free interest rate	1.5% - 4.2%	0.5% - 1.3%	0.3% - 1.6%
Expected dividend yield	0 %	0 %	0 %
Exercise price	$36.79 - $78.91	$66.82 - $100.40	$22.70 - $50.00

Given the Company's common stock has not been trading for a sufficient period of time, the Company calculates volatility of its common stock by utilizing a weighted average of a collection of peer company volatilities and its own common stock volatility. The expected term is calculated utilizing the simplified method.

A summary of the stock option activity under the 2018 Plan as of December 31, 2022 is presented below. These amounts include stock options granted to employees, directors and consultants.

(dollars in millions, except weighted average exercise price)	Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2021	5,343,254	$ 44.98		
Granted	1,889,501	$ 59.23		
Exercised	(184,160)	$ 19.49		
Forfeited	(233,961)	$ 61.29		
Outstanding as of December 31, 2022	6,814,634	$ 49.06	7.7	$ 34.5
Exercisable as of December 31, 2022	3,601,334	$ 37.22	6.8	$ 33.0

The weighted-average grant date fair value of options granted during the years ended December 31, 2022, 2021 and 2020 was $39.17, $52.85 and $27.45, respectively. The total intrinsic value of options exercised during the years ended December 31, 2022, 2021 and 2020 was $7.9 million, $46.9 million and $19.4 million, respectively.

As of December 31, 2022, $53.8 million of total unrecognized compensation cost related to non-vested stock options granted under the 2018 Plan is expected to be recognized over a weighted average period of approximately 1.6 years.

As of December 31, 2022, there were 6,540,844 stock options under the 2018 Plan that have vested or are expected to vest.

Restricted Stock Awards

A summary of the restricted stock award activity under the Incentive Plan as of December 31, 2022 is presented below. These amounts include restricted stock granted to employees, directors and consultants.

	Shares		Weighted Average Grant Date Fair Value Per Share
Unvested restricted stock as of December 31, 2021	30,625	$	16.00
Vested	(29,305)	$	16.00
Forfeited	(1,320)	$	16.00
Unvested restricted stock as of December 31, 2022	—	$	16.00

Restricted Stock Units

A summary of restricted stock unit activity under the 2018 Plan for the year ended December 31, 2022 is presented below. These amounts include restricted stock units granted to employees.

	Shares		Weighted Average Grant Date Fair Value Per Share
Unvested restricted stock units as of December 31, 2021	88,307	$	20.02
Granted	460,763	$	54.59
Exercised	(42,500)	$	20.04
Forfeited	(17,354)	$	53.91
Unvested restricted stock units as of December 31, 2022	489,216	$	51.37

As of December 31, 2022, $13.5 million of total unrecognized compensation cost related to non-vested restricted stock units granted under the 2018 Plan is expected to be recognized over a weighted average period of approximately 2.1 years.

As of December 31, 2022, there were 414,450 restricted stock units under the 2018 Plan that have vested or are expected to vest.

10. Equity Method Investments

In July 2019, the Company and Bayer CropScience LP ("Bayer LP") formed Oerth Bio, a joint venture to research, develop and commercialize PROTAC targeted protein degraders for applications in the field of agriculture. Pursuant to the terms of the joint venture agreement, the Company made an in-kind intellectual property contribution to Oerth Bio in the form of a license to certain of the Company’s proprietary technology and Bayer LP committed and subsequently made cash contributions to Oerth Bio totaling $56.0 million, as well as an in-kind intellectual property contribution. The Company and Bayer LP each held an initial ownership interest in Oerth Bio representing 50% of the ownership interests. A 15% ownership interest of Oerth Bio was reserved for the future grants of incentive units to employees and service providers and, as a result, the Company's ownership interest totaled 46.5%, 48.4% and 49.4% as of December 31, 2022, 2021 and 2020, respectively, as a result of vested incentive units.

Under the joint venture agreement, the Company has no obligation to provide additional funding and the Company’s ownership interest will not be diluted from future contributions from Bayer LP. The activities of Oerth Bio are controlled by a management board under the joint control of the Company and Bayer LP. As Oerth Bio is jointly controlled by the Company and Bayer LP, the Company accounts for its interest using the equity method of accounting. The Company determined that Oerth Bio is a variable interest entity and, accordingly, the Company has evaluated the significant activities of Oerth Bio under the variable interest entity model and concluded that the significant activities consist primarily of research and development activities and, as the Company does not have the sole power to direct such activities, the Company is not the primary beneficiary.

The Company determined that the fair value of the equity interest it received in Oerth Bio in exchange for the license contributed totaled $49.4 million. The fair value of Oerth Bio was determined utilizing discounted cash flows based on reasonable estimates and assumptions of cash flows expected from Oerth Bio. The Company recognized revenue of $24.7 million in 2019 attributable to the license contributed to Oerth Bio. In 2019, the Company also recognized $24.7 million of equity in net losses of Oerth Bio reducing the carrying value of the Company's investment to zero.

In connection with the preparation of the Company's consolidated financial statements for the year ended December 31, 2022, the Company identified a prior period error related to the accounting of its investment in Oerth Bio in 2019. Previously, the Company disclosed that revenue of $24.7 million was deferred and would be recognized if and when Oerth Bio recognized revenue associated with the license. The Company has now determined that the consideration received for the amounts associated with the deferred revenue should have been constrained, because at the time Bayer LP had contributed only a portion of its full cash commitment to Oerth Bio, and Bayer LP had the right to all the cash contributed, but not yet spent, upon liquidation of Oerth Bio. The constrained revenue should have been recognized upon both cash being contributed by Bayer LP and the related cash spent by Oerth Bio on research and development activities. As such, the recognition of revenue is accompanied by corresponding equity method losses of the same amount for all periods presented.

The Company evaluated the error and determined that the related impact did not materially misstate the previously issued condensed consolidated financial statements for the years ended December 31, 2021 and 2020. Although the Company concluded that the error was not material to its previously issued consolidated financial statements, the Company has determined it is appropriate to adjust its previously issued consolidated financial statements for the years ended December 31, 2021 and 2020 to correct the error and improve comparability.

The following illustrates the effect of the correction of the immaterial error for the period presented. There was no impact to the balance sheets, net loss per common share, statements of cash flows or changes in shareholders' equity.

	Year ended December 31, 2021			Year ended December 31,2020		
(dollars in millions)	as previously reported	adjustments	as adjusted	as previously reported	adjustments	as adjusted
Revenue	$ 46.7	$ 6.9	$ 53.6	$ 21.8	$ 4.1	$ 25.9
Loss from operations	$ (195.3)	$ 6.9	$ (188.4)	$ (124.9)	$ 4.1	$ (120.8)
Loss from equity method investment	$ —	$ (6.9)	$ (6.9)	$ —	$ (4.1)	$ (4.1)
Net loss	$ (191.0)	$ —	$ (191.0)	$ (119.3)	$ —	$ (119.3)
Net loss per common share - basic and diluted	$ (3.82)	$ —	$ (3.82)	$ (3.02)	$ —	$ (3.02)
Comprehensive loss	$ (196.2)	$ —	$ (196.2)	$ (118.8)	$ —	$ (118.8)

Operating expenses and net loss of Oerth Bio for the years ended December 31 2022, 2021 and 2020 totaled $22.9 million, $14.3 million and $8.3 million, respectively. The Company recognized equity method losses of $10.6 million, $6.9 million and $4.1 million for the years ended December 31, 2022, 2021 and 2020, respectively. As of December 31, 2022, and 2021, the Company's carrying value of the investment was zero.

The Company also provides Oerth Bio with compensated research and development and administrative services through a separate agreement. The services rendered by the Company during the years ended December 31, 2022, 2021 and 2020 were immaterial.

11. Income Taxes

For the year ended December 31, 2022, income tax expense totaled $20.9 million, and consisted of the following:

	Year Ended December 31,		
	2022	2021	2020
Current:			
U.S.:			
Federal	$ 8.2	$ —	$ —
State and local	12.7	—	—
Total current	20.9	—	—
Deferred:			
U.S.:			
Federal	—	—	—
State and local	—	—	—
Total deferred	—	—	—
Income tax expense	$ 20.9	$ —	$ —

The Company generated taxable income for the year ended December 31, 2022 primarily due to revenue recognition for tax purposes from the ARV-471 Collaboration Agreement and the mandatory capitalization of qualified research and development expenses incurred on or after January 1, 2022, which, upon recognition for tax purposes, would create additional deferred tax assets. Under the Tax Cuts and Jobs Act of 2017, qualified research expenses incurred after 2021 are no longer immediately deductible for tax purposes and instead must be capitalized and amortized for tax purposes.

For the years ended December 31, 2021 and 2020, the Company had no income tax expense due to incurred operating losses. The Company had also not recorded any income tax benefits for the net operating losses incurred in each of those periods due to its uncertainty of realizing a benefit from those items. All of the Company's losses before income taxes were generated in the United States.

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate for the years ended December 31, 2022, 2021 and 2020 were as follows:

	Year ended December 31,		
	2022	2021	2020
Federal statutory rate	21.0%	21.0%	21.0%
Return to provision	3.6 %	1.1 %	— %
Federal research tax credit	3.4%	2.7%	4.1%
Other	(0.1%)	—%	—%
Uncertain tax positions	(1.2%)	—%	—%
Stock compensation	(1.4)%	(2.7)%	(1.7)%
State taxes	(1.6)%	16.3 %	(0.1)%
Change in valuation allowance	(31.7)%	(38.4)%	(23.3)%
	(8.0%)	0.0%	0.0%

Deferred income taxes represent the tax effect of transactions that are reported in different periods for financial and tax reporting purposes. Temporary differences and carryforwards that give rise to a significant portion of the deferred income tax benefits and liabilities were as follows as of December 31, 2022 and 2021:

	December 31,	
(dollars in millions)	**2022**	**2021**
Deferred income tax assets:		
Deferred revenue	$ 143.0	$ 10.0
Capitalized research and development	56.3	—
Stock compensation	25.9	15.4
Tax credits	10.4	18.8
Loss carryforwards	3.8	97.0
Other	7.7	3.3
Total deferred income tax assets	247.1	144.5
Deferred income tax liabilities:		
Property, equipment and leasehold improvements	(2.6)	(3.6)
Other	(1.0)	(1.4)
Total deferred income tax liabilities	(3.6)	(5.0)
Less valuation allowance	(243.5)	(139.5)
Net deferred income tax liability	$ —	$ —

A valuation allowance is established when it is more likely than not that some portion or all of a deferred tax asset will not be realized. The realization of deferred tax assets depends on the generation of future taxable income during the period in which related temporary differences become deductible. The Company has provided a valuation allowance against the full amount of the deferred tax assets since it is more likely than not that the benefits will not be realized. This assessment is based on the Company's historical cumulative losses, which provide strong objective evidence that cannot be overcome with projections of income, as well as the fact the Company expects continuing losses in the future.

All, or a portion of, the remaining valuation allowance may be reduced in future years based on an assessment of earnings sufficient to utilize these potential tax benefits. The valuation allowance increased by $104.0 million and $74.6 million in 2022 and 2021, respectively, due to revenue recognition for tax purposes from the ARV-471 Collaboration Agreement and the mandatory capitalization of qualified research and development costs in 2022, and increases in net operating loss carryforwards, tax credit carryforwards, stock compensation expense, and research and development tax credits in 2021.

The Company had zero and $373.6 million of federal net operating loss carryforwards as of December 31, 2022 and 2021, respectively. Federal net operating loss carryforwards as of December 31, 2017 expire at various dates through 2037 and federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such carryforwards is limited to 80% of the Company’s taxable income in the year in which carryforwards are used. The Company had $63.4 million and $346.9 million of state and local net operating loss carryforwards as of December 31, 2022 and 2021, respectively, that expire at various dates through 2041. The Company had zero and $15.2 million of federal tax credit carryforwards as of December 31, 2022 and 2021, respectively. The Company had $13.1 million and $4.5 million of state tax credit carryforwards as of December 31, 2022 and 2021, respectively, which expire at various dates through 2037.

During 2021, the Company performed a Section 382 analysis to determine whether an ownership change occurred for tax purposes. Based on this analysis, the Company determined that ownership changes occurred on July 31, 2018 and December 31, 2020 due to various equity offerings, vesting of restricted stock awards and stock option exercises. These ownership changes resulted in Section 382 limitations on the Company’s net operating loss and tax credit carryforwards generated before these dates. However, because the amount of the Section 382 limitations (including carryover of the unused Section 382 limitations and realized

built-in gains) exceeds the amount of the Company's carryforwards generated before these dates, the limitations will not affect the Company's ability to fully utilize these carryforwards.

The Company complies with the provisions of ASC 740 in accounting for its uncertain tax positions. ASC 740 addresses the determination of whether tax benefits claimed or expected to be claimed on a tax return should be recorded in the financial statements. Under ASC 740, the Company may recognize the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by the taxing authorities, based on the technical merits of the position. As of December 31, 2022, the Company recorded net uncertain tax positions of $3.2 million relating primarily to state income tax filing positions in various jurisdictions. As of December 31, 2021, the Company had no unrecognized tax benefits.

Changes in the Company's gross unrecognized tax benefits were as follows:

	Year ended December 31,		
(dollars in millions)	**2022**	**2021**	**2020**
Beginning of period balance - gross	$ —	$ —	$ —
Increases for tax positions taken during the current period	4.1	—	—
Decreases for tax positions taken during a prior period	—	—	—
End of period balance - gross	$ 4.1	$ —	$ —

The Company recognizes interest accrued related to unrecognized tax benefits and penalties in tax expense. The Company's accrual for interest and penalties as of December 31, 2022 was immaterial.

The Company is required to file income tax returns in the U.S. Federal and various state jurisdictions. As a result of the Company's net operating loss carryforwards, the Company's federal and state statutes of limitations generally remain open for all tax years until its net operating loss and tax credit carryforwards are utilized or expire prior to utilization. The Company does not currently have any federal or state income tax examinations in progress.

For the years ended December 31, 2022, 2021, and 2020, the Company recorded a benefit from expected cash refunds to be provided by the State of Connecticut, equal to 65% of research and development credits, of zero, $1.6 million, and $1.8 million, respectively, which is included in Other income, net in the accompanying consolidated statements of operations and comprehensive loss, due to the Company being a state income and franchise taxpayer in 2022, and a state franchise taxpayer in 2021 and 2020. The benefit results from the exchange of the state research and development tax credit carryforwards for cash refunds. As of December 31, 2022 and 2021, the Company had receivables of $1.9 million and $3.4 million, respectively, relating to research and development credits due to the Company.

12. Commitments and Contingencies

From time to time, the Company may be subject to legal proceedings, claims and disputes that arise in the ordinary course of business. The Company accrues a liability for such matters when it is probable that future expenditures will be made and that such expenditures can be reasonably estimated. Significant judgment is required to determine both probability and the estimated amount, which could differ materially. Legal fees and other costs associated with such actions are expensed as incurred. As of December 31, 2022, the Company has accrued $7.0 million for such matters, primarily related to a contract dispute that is in early stages. Due to the early stage of the dispute, the means of resolution are unknown and could involve contract modification and, or payment of consideration. An estimate of the possible range of loss associated with the dispute cannot be made at this time and the Company has accrued its best estimate as of December 31, 2022.

Clinical and Preclinical Development and Licensing Arrangements

From time to time, the Company enters into contracts in the normal course of business with various third parties who support its clinical trials, preclinical research studies, and other services related to its development activities. The scope of the services under these agreements can generally be modified at any time, and the agreement can be terminated by either party after a period of notice and receipt of written notice.

In addition, under licensing and related arrangements to which we are a party, we may be obligated to make milestone payments to third parties. The payment obligations under these arrangements are contingent upon future events, such as achievement of specified milestones or generation of product sales, and the amount, timing and likelihood of such payments are not known.

Yale University License Agreement

In July 2013, the Company entered into an exclusive license agreement, including the right to grant sublicenses, with Yale University to develop protein degradation technologies. Under the license agreement, the Company is required to pay a minimum license maintenance royalty totaling $0.1 million per year until the first sale to a third party of any licensed product, followed by success-based milestones for the first two licensed products for the development of the protein degradation technologies totaling approximately $3.0 million for the first licensed product and approximately $1.5 million for the second licensed product, and low single-digit royalties on aggregate worldwide net sales of certain licensed products, which may be subject to reductions, and subject to minimum royalty payments that range from $0.2 million to $0.5 million. During the years ended December 31, 2022, 2021 and 2020, the Company paid $0.1 million, $0.1 million and $0.2 million, respectively, under the license agreement.

FMI Agreement

In June 2022, the Company entered into a Master In Vitro Diagnostics Agreement with Foundation Medicine, Inc. (the "FMI Agreement") for the development and commercialization of one or more of Foundation Medicine’s companion in vitro diagnostic assays for use with one or more of the Company's therapeutic products.

The FMI Agreement does not have a fixed duration, and the Company may terminate the FMI Agreement for convenience by providing adequate written notice to Foundation Medicine, Inc., subject to payment of applicable termination fees. Either party may terminate the FMI Agreement in its entirety for an uncured material breach by the other party, upon the bankruptcy or insolvency of the other party or by the mutual written agreement of both parties. Additionally, Foundation Medicine may terminate the FMI Agreement with respect to an applicable program, if (a) a reasonably necessary third party license is not secured by Foundation Medicine or if the Company does not consent to payments for such license (b) Foundation Medicine reasonably determines that further development of the applicable assay is not technically feasible or (c) following a certain number of years after the first commercial launch of the applicable assay for use with the applicable therapeutic product. Certain license and other rights and certain obligations of Foundation Medicine survive termination of the FMI Agreement. If the FMI Agreement is terminated in its entirety or with respect to any program, the Company has certain payment obligations remaining to Foundation Medicine and may also be required to pay a termination fee, if applicable.

Bavdegalutamide

In exchange for the development of FoundationOne® Liquid CDx as a companion diagnostic for use with bavdegalutamide for AR mCRPC in the United States and European Union, pursuant to the terms of the FMI Agreement, the Company is subject to success-based milestone payments of up to low to mid tens of millions of dollars, in addition to certain validation fees per sample and related pass-through costs.

ARV-766

In exchange for the development of FoundationOne® Liquid CDx as a companion diagnostic for use with ARV-766 for AR mCRPC in the United States and European Union, pursuant to the terms of the FMI Agreement, the Company is subject to success-based milestone payments of up to low tens of millions of dollars, in addition to certain validation fees per sample and related pass-through costs.

13. Net Loss Per Share

Basic and diluted loss per common share was calculated as follows:

	Year ended December 31,		
(dollars and shares in millions, except per common share amounts)	**2022**	**2021**	**2020**
Net loss	$ (282.5)	$ (191.0)	$ (119.3)
Weighted average common shares outstanding - basic and diluted	53.2	50.0	39.5
Net loss per common share - basic and diluted	$ (5.31)	$ (3.82)	$ (3.02)

The Company reported net losses for each of the years ended December 31 2022, 2021 and 2020, and therefore excluded all stock options, restricted stock awards and restricted stock units from the computation of diluted net loss per common share as their inclusion would have had an anti-dilutive effect, as summarized below:

	Year ended December 31,		
(shares in millions)	**2022**	**2021**	**2020**
Stock options	6.8	5.3	4.3
Restricted stock awards	—	—	0.2
Restricted stock units	0.5	0.1	0.1
	7.3	5.4	4.6

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