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 001-38419

Arcus Biosciences, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**47-3898435**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

3928 Point Eden Way
Hayward, CA 94545
(Address of principal executive offices)

Registrant's telephone number, including area code: (510) 694-6200

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

Titles of Each Class	Trading Symbol(s)	Name of Each Exchange on which Registered
Common Stock, Par Value $0.0001 Per Share	RCUS	The New York Stock Exchange

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

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

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

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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. ☒

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The New York Stock Exchange on June 30, 2022 was $1,298,340,892. This excludes 13,813,029 shares of the Registrant's Common Stock held by Gilead Sciences, Inc., and 7,035,629 shares held by executive officers, directors and stockholders affiliated with directors at that date. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

The number of shares of Registrant's Common Stock outstanding as of February 17, 2023 was 73,011,325.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement relating to the 2023 Annual Meeting of Shareholders are incorporated by reference into Part III of this Report. The Definitive Proxy Statement will be filed within 120 days of the Registrant's fiscal year ended December 31, 2022.

Auditor Firm ID: 42 Auditor Name: Ernst & Young, LLP Auditor Location: San Mateo, California, USA

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INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (Annual Report) includes "forward-looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

- our expectations regarding our relationship with Gilead;
- our expectations regarding the timing and achievement of our investigational product development activities and ongoing and planned clinical trials;
- our expectations for reporting data from clinical trials in certain timeframes;
- our ability to develop intra-portfolio combinations and highly-differentiated small-molecule investigational products, including our ability to create small-molecule investigational products with ideal pharmacological properties and desired clinical effects;
- our expectations regarding the efficiency and speed with which we can create and advance small-molecule investigational products and develop our investigational products and combination therapies;
- our reliance on third parties to conduct our ongoing and future clinical trials and third-party manufacturers to manufacture and supply our investigational products;
- our expectations regarding the nature of the immuno-oncology pathways we are targeting, the size of the potential patient population and the potential market size;
- our ability to obtain and maintain control of our combination investigational products and maximize the commercial potential of our investigational products;
- our ability to obtain and maintain regulatory approvals of our investigational products and the potential market opportunities for commercializing our investigational products;
- our ability to retain and recruit key personnel, estimates of our expenses, future revenue, capital requirements and our needs for additional financing;
- our ability to develop, acquire and advance investigational products into, and successfully complete, clinical trials;
- our initiation, timing, progress and results of future research and development programs, preclinical studies and clinical trials;
- our ability to obtain and maintain intellectual property rights covering our investigational products;
- our expectations regarding the developments and projections relating to our competitors;
- our expectations as to the effect that the COVID-19 pandemic will have on our company; and
- our expectations regarding our industry.

The words "believe," "may," "will," "estimate," "continue," "anticipate," "design," "intend," "expect," "could," "plan," "potential," "predict," "seek," "should," "would" or the negative version of these words and similar expressions are intended to identify forward-looking statements. We have based these forward-looking statements on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, strategy, short- and long-term business operations and objectives and financial needs.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in the Risk Factor Summary below and in Item 1A of this Annual Report, "Risk Factors." Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this Annual Report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, advancements, discoveries, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Moreover, except as required by law, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this Annual Report to conform these statements to actual results or to changes in our expectations.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report on Form 10-K, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

RISK FACTOR SUMMARY

The following is a summary of the key risks and uncertainties that make an investment in our securities speculative and risky. The below summary does not contain all of the information that may be important to you, and you should read this summary together with the more detailed description risks related to an investment in our securities set forth in this report under "Item 1A. Risk Factors".

Risks Related to our Limited Operating History, Financial Position and Capital Requirements

- We have a history of operating losses, have never generated any revenue from product sales and anticipate that we will continue to incur significant losses for the foreseeable future.
- We may need to obtain additional funding to finance our operations and complete the development and any commercialization of our investigational products. If we do not receive substantial capital when needed, we may be forced to restrict our operations or delay, reduce or eliminate our product development programs.

Risks Related to the Discovery and Development of our Investigational Products

- Clinical drug development is a lengthy, expensive and uncertain process, if we are unable to develop, obtain regulatory approval for and commercialize our investigational products, or experience significant delays in doing so, our business will be materially harmed.
- The results of preclinical studies and early clinical trials are not always predictive of future results.
- Enrollment and retention of subjects in clinical trials is expensive and time consuming, can be made more difficult or rendered impossible by competing treatments, clinical trials of competing investigational products, and public health epidemics, each of which could result in significant delays and additional costs in our product development activities, or in the failure of such activities.
- Preliminary and interim data from our clinical studies that we announce or publish from time to time could materially change due to audit and verifications procedures or as more patient data becomes available.
- Serious adverse events, undesirable side effects or other unexpected properties of our investigational products may be identified during development or after approval, which could lead to the discontinuation of our clinical development programs, refusal by regulatory authorities to approve our investigational products or limitations on the use of our investigational products or revocation of any marketing authorizations or subsequent limitations on the use of our investigational products.
- If we are not successful in discovering, developing and commercializing investigational products that take advantage of different mechanisms of action to achieve superior outcomes relative to the use of single agents or other combination therapies, our ability to achieve our strategic objectives would be impaired.
- Development of combination therapies may present more or different challenges than other therapies.
- Failure to successfully develop, validate and obtain regulatory clearance or approval for any required companion diagnostics could prevent us from realizing the commercial potential of our investigational products.

Risks Related to Reliance on Third Parties, Manufacturing and Commercialization

- If our collaboration with Gilead is not successful, our business could be adversely affected.
- We rely on third parties to conduct our clinical trials, to manufacture and supply us with sufficient quantities of our investigational products, and to perform some of our research and preclinical studies. If these third parties do not satisfactorily carry out their contractual duties or fail to meet expected deadlines, our development programs may be delayed or subject to increased costs, each of which may have an adverse effect on our business and prospects.
- Even if we receive marketing approval, we may not be successful in commercializing our investigational products or obtaining coverage and reimbursement approval for a product from a government or other third-party payor, which coverage may be delayed or may not be sufficient to cover our costs.

- Our investigational products may never be approved or commercialized outside the United States, which would limit our ability to realize their full market potential.
- Any investigational products for which we intend to seek approval as biologic products may face competition sooner than anticipated.

Risks Related to In-Licenses, Strategic Arrangements and Intellectual Property

- We are currently party to several in-license agreements under which we acquired rights to use, develop, manufacture and/or commercialize certain of our investigational products. If we breach our obligations under these agreements, we may be required to pay damages, lose our rights to these investigational products or both, which would adversely affect our business and prospects.
- If we are unable to obtain and maintain sufficient intellectual property protection for our investigational products, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our products may be adversely affected.
- We may need to obtain additional licenses of third-party technology which may cause us to operate our business in a more costly or otherwise adverse manner that was not anticipated.
- We may become involved in lawsuits alleging that we have infringed the intellectual property rights of third parties or to protect or enforce our patents or other intellectual property, which litigation could affect our ability to develop or commercialize our investigational products.
- Changes in patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our investigational products.
- If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

Risks Related to our Business Operations and Industry

- We expect to expand our business operations and, as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.
- We face substantial competition, which may result in others discovering, developing or commercializing products more quickly or marketing them more successfully than us. If their investigational products are shown to be safer or more effective than ours, then our commercial opportunity will be reduced or eliminated.
- Our internal information technology systems, and those of the third parties upon which we rely, are subject to failure, security breaches and other disruptions, which could result in a material disruption of our investigational products' development programs, jeopardize sensitive information, or prevent us from accessing critical information or result in a loss of our assets, and potentially expose us to notification obligations, loss, liability or reputational damage and otherwise adversely affect our business.
- Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.
- Changes in healthcare law and implementing regulations, as well as changes in healthcare policy, may impact our business in ways that we cannot currently predict, and may have a significant adverse effect on our business and results of operations.

PART I

Item 1. Business

Company Overview

We are a clinical-stage biopharmaceutical company focused on creating best-in-class therapies. Using our robust and highly efficient drug discovery capability, we have created a significant portfolio of investigational products which are in clinical development, with our most advanced molecule, an anti-TIGIT antibody, now in four Phase 3 registrational studies targeting lung and gastrointestinal cancers. Our deep portfolio of novel small molecules and enabling antibodies allows us to create highly differentiated therapies, which we are developing to treat multiple large indications. We expect our clinical-stage portfolio to continue to expand and to include molecules targeting immuno-oncology, cancer cell-intrinsic and immunological pathways. Our vision is to create, develop and commercialize highly differentiated therapies that have a meaningful impact on patients.

The following chart summarizes our clinical pipeline:

Doce: docetaxel; dom: domvanalimab; durva: durvalumab; etruma: etrumadenant; gem/nab-pac: gemcitabine/nab-paclitaxel; quemli: quemliclustat; rego: regorafenib; zim: zimberelimab

CRC=colorectal cancer; CRPC=castrate-resistant prostate cancer; GI=gastrointestinal; NSCLC=non-small cell lung cancer; PDAC=pancreatic ductal adenocarcinoma; RCC=renal cell carcinoma

*+/- biologic

Our anti-PD-1 antibody, zimberelimab, is a cornerstone of many of the combination therapies we are pursuing. We are evaluating zimberelimab in combination with several of our other five investigational products, such as domvanalimab, quemliclustat and etrumadenant. In addition, we have an expanding preclinical pipeline which currently includes AB598, a CD39 antibody, and AB801, a potentially best-in-class Axl inhibitor discovered internally by us. We also expect to advance our first small molecule against an inflammation target into preclinical development in 2023.

Our Clinical Product Portfolio

We currently have five clinical programs focused on unique targets including TIGIT, PD-1, adenosine A2a and A2b receptors, CD73 and HIF-2α. Within these programs, we are currently evaluating three antibodies and three small molecules across 13 different clinical studies, including four Phase 3 studies. In 2020, we entered into an Option, License and Collaboration Agreement (as amended, the Gilead Collaboration Agreement) with Gilead Sciences, Inc. (Gilead) to strategically advance our portfolio through a collaborative relationship. The Gilead Collaboration Agreement provides Gilead with an exclusive license to our anti-PD-1 program (including zimberelimab) and time-limited exclusive option rights to our clinical programs, which they have exercised for our anti-TIGIT program (including domvanalimab and AB308), adenosine receptor antagonist program (including etrumadenant) and CD73 program (including quemliclustat). For all such optioned programs, we are co-developing investigational products with Gilead. The Collaboration Agreement and our strategic partnership with Gilead is discussed in more detail below under “License and Collaborations—Gilead Collaboration”.

Anti-TIGIT Program

Domvanalimab, our Fc-silent Anti-TIGIT Antibody

TIGIT is believed to play an important role in suppressing the immune response to cancer. The primary ligand for TIGIT (T-cell immunoreceptor with Ig and ITIM domains) is CD155, a protein that plays both inhibitory and stimulatory roles in regulating the activity of effector immune cells such as T and NK cells. TIGIT is an inhibitory receptor highly expressed on T cells displaying an exhausted phenotype, tumor-infiltrating T_{reg}, and NK cells. During the past couple of years, expression of TIGIT, along with PD-1, on precursor exhausted T cells (Tpex), a key population that mediates some of the therapeutic effects of anti-PD-1 agents, has become well documented. The ligands for TIGIT, including CD155, are broadly expressed on multiple cell types in the tumor microenvironment, including cancer cells. CD155 binding to TIGIT results in inhibition of immune cells.

As T cells are important in the immune response, domvanalimab was engineered to lack Fc-receptor binding in order to minimize the risk of depleting such cells, which we believe may provide domvanalimab with an advantage over Fc-enabled anti-TIGIT antibodies.

We are pursuing a broad Phase 2 and Phase 3 development program for domvanalimab in combination with our anti-PD-1 antibody, zimberelimab, in multiple lung and gastrointestinal cancer settings, each of which we believe represents a multi-billion dollar revenue opportunity. Our clinical program for domvanalimab currently includes four ongoing Phase 3 studies each evaluating domvanalimab plus zimberelimab versus the relevant global standard of care. We estimate that the total addressable market for the ongoing Phase 3 trials of domvanalimab is over $10 billion annually, based on the size of the drug treatable U.S. patient populations.

We have the following ongoing Phase 3 studies for domvanalimab:

- **ARC-10** is a Phase 3 study evaluating domvanalimab in combination with zimberelimab versus pembrolizumab, the global standard of care in first-line metastatic, PD-L1≥50% NSCLC. The U.S. patient population for this setting is approximately 33,000 individuals. We are operationalizing this study and sharing costs with Gilead.
- **STAR-121** is a Phase 3 study evaluating domvanalimab in combination with zimberelimab and chemotherapy versus pembrolizumab and chemotherapy in first-line non-small cell lung cancer (NSCLC). The U.S. patient population for this setting is approximately 119,000 individuals. Gilead is operationalizing this study and sharing costs with us.
- **STAR-221** is a Phase 3 evaluating domvanalimab in combination with zimberelimab and chemotherapy versus nivolumab and chemotherapy in first-line unresectable or metastatic gastrointestinal cancers. The U.S. patient population for this setting is approximately 25,000 individuals. We are operationalizing this study and sharing costs with Gilead.
- **PACIFIC-8** is a Phase 3 study evaluating domvanalimab in combination with durvalumab following chemoradiation in Stage 3 NSCLC, a setting in which durvalumab is already approved. The U.S. patient population for this setting is approximately 21,000 individuals. AstraZeneca plc (AstraZeneca) is operationalizing this study and sharing costs with us and Gilead.

In addition, we are evaluating domvanalimab in the following Phase 2 studies:

- **ARC-7** is a randomized Phase 2 study evaluating the combination of domvanalimab plus zimberelimab (to which we refer as the "doublet") vs. domvanalimab plus zimberelimab plus etrumadenant (to which we refer as the "triplet") vs. zimberelimab monotherapy in first-line metastatic, PD-L1≥50% NSCLC. We are operationalizing this study and sharing costs with Gilead.
- **EDGE-Gastric** (formerly known as ARC-21) is a Phase 2 study evaluating the combination of domvanalimab and zimberelimab, with and without FOLFOX in gastrointestinal cancers. We are operationalizing this study and sharing costs with Gilead.
- **EDGE-Lung** is a Phase 2 study evaluating the combination of domvanalimab and zimberelimab with and without quemliclustat and chemotherapy in first- and second-line NSCLC. We are operationalizing this study and sharing costs with Gilead.
- **Velocity-Lung** is a Phase 2 study evaluating domvanalimab with and without zimberelimab, etrumadenant and sacituzumab govitecan-hziy (Trodelvy®) in first- and second-line NSCLC. Gilead is operationalizing this study and sharing costs with us.

In December 2022, we presented data from our ARC-7 study which demonstrated clinically meaningful improvements in median progression-free survival (PFS) and six-month landmark PFS rates compared to zimberelimab monotherapy, with a 45% reduction in risk of disease progression or death for the doublet and 35% for the triplet. With a median follow-up time of 12 months, the doublet and triplet combinations demonstrated median PFS of 12.0 and 10.9 months, respectively, relative to 5.4 months for zimberelimab monotherapy. Each of the domvanalimab-containing study arms also demonstrated clinically meaningful improvements in objective response rate (ORR) compared to zimberelimab monotherapy. Confirmed ORR was 27%, 41% and 40% for the zimberelimab monotherapy arm and the domvanalimab-doublet and -triplet arms, respectively. While the triplet arm did not show an improvement over the doublet arm, it reinforces the results observed in the doublet arm, and the study will continue to monitor PFS, as well as overall survival, for the triplet arm as these data mature.

AB308, our Fc-enabled Anti-TIGIT Antibody

An Fc-enabled anti-TIGIT antibody is able to engage with Fc receptors on immune cells, inducing antibody dependent cellular toxicity, or death, of TIGIT-expressing cells. In 2021, we initiated ARC-12, our Phase 1/1b study evaluating AB308 together with zimberelimab. We are operationalizing this study and sharing costs with Gilead. Given the clinical data generated to date with our Fc-silent anti-TIGIT antibody domvanalimab in the ARC-7 trial, we have decided to de-prioritize the clinical development of AB308.

Anti-PD-1 Program

In 2017, we in-licensed zimberelimab, a fully human IgG4 antibody, from WuXi Biologics. We are currently using zimberelimab as the cornerstone of our combination strategy and evaluating it with various intra-portfolio combination partners in nearly all our ongoing clinical studies. Zimberelimab has been approved in China for classical Hodgkin's Lymphoma, based on data generated independently by Guangzhou Gloria Biosciences, Co. (Gloria Biosciences), which owns the commercial rights to zimberelimab in China. In addition, in December 2022, Gloria Biosciences presented Phase 2 data for zimberelimab in recurrent or metastatic cervical cancer. To date, zimberelimab has been evaluated by us and Gloria Biosciences, either alone or in combination with other agents, in nearly 1,000 patients.

Adenosine Pathway Programs

Under conditions of cellular damage or cell death, such as in response to certain chemotherapies, large amounts of adenosine triphosphate (ATP) are released into the extracellular environment, where it is converted into adenosine monophosphate by the enzyme CD39 and then into adenosine by the enzyme CD73. The generation of large amounts of extracellular adenosine results in an immunosuppressive response that counteracts some of the potentially beneficial effects of chemotherapy. Two receptors important in mediating the effect of adenosine are A2a, which is expressed on T and natural killer (NK) cells, and A2b, which is co-expressed with A2a on myeloid cells. We currently have two programs targeting the adenosine pathway.

Adenosine Receptor Antagonist Program

Etrumadenant is an orally bioavailable small molecule. Unlike most other clinical-stage adenosine receptor antagonists, which only target one of the two receptors, etrumadenant is a highly potent and reversible antagonist of the adenosine A2a and A2b receptors. We believe that activation of the adenosine A2a receptors on T cells and NK cells mediates a significant portion of the immunosuppressive effects of adenosine but that binding of adenosine to A2b receptors on myeloid cells also contributes significantly to intra-tumoral immune suppression; consequently, etrumadenant could prove to have more robust anti-tumor effects and activity in a broader range of tumor types than other adenosine A2a or A2b antagonists in clinical development.

In addition to the ARC-7 study described above, we have two ongoing studies evaluating etrumadenant:

- **ARC-6** is a Phase 2 study evaluating etrumadenant plus zimberelimab and docetaxel vs. docetaxel in 2L+ mCRPC**.** At ASCO 2021, we presented early data demonstrating that the etrumadenant combination showed a 35% PSA response (defined as a >50% reduction in PSA level) in the Stage 1 portion of this study in 17 evaluable patients. The safety profile was consistent with the known profiles of each individual agent, and no significant additive toxicity was observed with the addition of etrumadenant. We are operationalizing this study and sharing costs with Gilead.

- **ARC-9** is a Phase 2 study evaluating etrumadenant plus zimberelimab and FOLFOX with and without bevacizumab vs. FOLFOX with and without bevacizumab or regorafenib in second- and third-line metastatic colorectal cancer. We are operationalizing this study and sharing costs with Gilead.

All these studies are designed to support the potential of etrumadenant in multiple indications that represent substantial market opportunities with significant unmet need.

CD73 Program

Quemliclustat targets the ATP-adenosine pathway, specifically the CD73 enzyme, which plays a critical role in the last step of the process of extracellular ATP conversion into adenosine. CD73 inhibition should therefore be a highly effective approach to inhibiting adenosine-mediated immune suppression, as it could significantly suppress adenosine generation.

We believe quemliclustat was the first small-molecule CD73 inhibitor to enter clinical development. While there are several anti-CD73 antibodies in development, we believe that a small-molecule approach to CD73 inhibition could offer several advantages, including more complete inhibition of CD73 enzymatic activity, deeper tumor penetration, and potential for both intravenous and oral delivery.

In addition to the EDGE-Lung study described above, we are evaluating quemliclustat in ARC-8. ARC-8 is a Phase 1/1b clinical study in metastatic pancreatic cancer evaluating quemliclustat + zimberelimab + gemcitabine and nab-paclitaxel (the standard-of-care chemotherapies used for advanced pancreatic cancer). In the first half of 2023, we expect PFS and overall survival data from all 90 patients in the randomized portion of the study that is evaluating quemliclustat plus chemotherapy with or without zimberelimab in first-line pancreatic cancer. We are operationalizing this study and sharing costs with Gilead.

HIF-2α Program

HIF-2α is a master transcriptional regulator of multiple genes involved in tumor progression. In 2021, the first HIF-2α inhibitor, belzutifan (WELIREG™), was approved by the FDA for the treatment of patients with VHL disease who require therapy for associated RCC.

AB521 is our oral, small-molecule inhibitor of HIF-2α and is our first investigational product against a cancer cell-intrinsic target to enter clinical development. In October 2022, we presented data at the EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium from the fourth cohort of ARC-14, a healthy volunteer study of AB521. The pharmacokinetic and pharmacodynamic data in healthy volunteers support a potentially improved clinical profile compared to that of the approved HIF-2α inhibitor. We believe that AB521 could have activity in multiple tumor types, particularly when combined with our investigational products targeting the adenosine pathway.

We are currently evaluating AB521 in ARC-20, a Phase 1 clinical study in second-line renal cell carcinoma. We are operationalizing this study.

Our Early-Stage Drug Discovery Programs

We have active early-stage discovery efforts focused on the creation of additional development candidates aimed at regulating various aspects of the anti-tumor immune response as well as other cancer-intrinsic pathways which we believe play an important role in many human cancers. These include AB598, our recently selected antibody development candidate that targets CD39, which represents another key node along the ATP-adenosine pathway and rounds out our portfolio of ATP-adenosine targeting molecules, and AB801, our potentially best-in-class small molecule Axl inhibitor. We are also pursuing several small molecules aimed at modulating key biological pathways in various types of cancer that are responsible for the abnormal growth and resistance to current therapies.

We have also initiated our first research program for a non-oncology target; this program is supported with funding from BVF Partners L.P. (BVF) and is focused on the discovery and development of a potentially first-in-class small molecule that may be useful in a wide range of inflammatory conditions.

Commercialization Plans

Subject to timely exercise of Taiho and Gilead's respective option rights, the Taiho Agreement provides us with a potential commercialization partner for Japan and certain other Asian countries, and the Gilead Collaboration

Agreement provides us with a potential commercialization partner for the rest of the world. Under our Gilead Collaboration Agreement, we retain co-promotion rights for the U.S. Therefore, we intend to build the necessary infrastructure and sales, marketing and commercial product distribution capabilities to co-promote our products, if approved, for the United States. Clinical data, the size of the addressable patient population, and the size of the commercial infrastructure and manufacturing needs may all influence or alter our commercialization plans.

License and Collaborations

Gilead Collaboration

Clinical Programs

In May 2020, we entered into the Gilead Collaboration Agreement pursuant to which Gilead obtained an exclusive license to our anti-PD-1 program (including zimberelimab) and time-limited exclusive options to (i) all clinical programs existing at the time of entering into the Gilead Collaboration Agreement and (ii) any programs that enter clinical development during the 10-year collaboration term. Gilead's continued option rights are contingent upon Gilead making $100 million continuation payments on each of the fourth, sixth, and eighth anniversaries of the agreement. Gilead's options expire, on a program-by-program basis, after a prescribed period, following the achievement of a clinical development milestone in such program and our delivery to Gilead of the requisite data package. To date, Gilead has exercised its option to our anti-TIGIT program (including domvanalimab and AB308), adenosine receptor antagonist program (including etrumadenant) and CD73 program (including quemliclustat). Gilead may exercise its option to additional programs at any time prior to the expiration of the option and upon payment of an option fee of $150 million per program.

For each program that Gilead has exercised its option, the two companies will co-develop and equally share global development costs for such optioned program, subject to opt-out rights applicable to certain programs, expense caps on our spending and true-up adjustments. For each optioned program, provided we have not exercised our opt-out rights (if applicable), we have an option to co-promote in the United States with equal sharing of related profits and losses. Gilead has the right to exclusively commercialize any optioned programs outside of the U.S., subject to the rights of our existing partners to any territories, and Gilead will pay to us tiered royalties as a percentage of revenues ranging from the high teens to the low twenties. Further, with respect to domvanalimab, we remain eligible to receive up to $500 million in milestone payments.

Preclinical Programs

We have also agreed with Gilead to collaborate on two research programs for which we will lead discovery and early development activities. With respect to these two research programs, Gilead has the right to exercise its option, on a program-by-program basis, upon our completion of certain IND-enabling activities for an option payment of $60 million. If the option is exercised by Gilead at this stage, the collaboration terms for optioned programs will be applicable to each research program except, with respect to commercialization outside of the U.S., Gilead would pay us tiered royalties as a percentage of revenues ranging from high single digits to low double digits. If Gilead declines to exercise its option at this stage, Gilead maintains an option, on a program-by-program basis, which must be exercised prior to the expiration of a prescribed period following the achievement of a clinical development milestone in such program and our delivery to Gilead of the requisite data package. If the option is exercised by Gilead at this later clinical stage for an option payment of $150 million, the collaboration terms for optioned programs will be applicable to the joint development program including that, with respect to commercialization outside of the U.S., Gilead would pay us tiered royalties as a percentage of revenues ranging from the high-teens to the low twenties.

Common Stock Purchase Agreement and Investor Rights Agreement

In connection with our entry into the Gilead Collaboration Agreement, we and Gilead entered into a Common Stock Purchase Agreement (as amended, the Stock Purchase Agreement) and Investor Rights Agreement (as amended, the Investor Rights Agreement). We refer to the Gilead Collaboration Agreement, Stock Purchase Agreement and Investor Rights Agreement as the Gilead Agreements. Under the Stock Purchase Agreement, Gilead has the right, at its option, to purchase additional shares from us, up to a maximum ownership of 35% of our then-outstanding voting common stock, from time to time until July 2025, at a purchase price per share equal to the greater of a 20% premium to market (based on a trailing five-day average closing price) at the time Gilead exercises such option, and the $33.54 initial purchase price per share. The Investor Rights Agreement includes a three-year standstill and lockup restrictions,

and provides Gilead with registration rights, pro rata participation rights in certain future financings and the right to designate two individuals to be appointed to our Board of Directors.

Taiho License

In 2017, we entered into the Taiho Agreement pursuant to which Taiho obtained an exclusive option to in-license development and commercialization rights to programs during a five-year term for which IND-enabling studies had begun. These rights are geographically limited to Japan and certain other territories in Asia (excluding China) (the Taiho Territory). To date, Taiho has exercised its option to (i) etrumadenant (the adenosine receptor antagonist program); (ii) zimberelimab (the anti PD-1 program); and (iii) domvanalimab and AB308 (collectively, the anti-TIGIT program). While the five-year term expired in September 2022, Taiho retains option rights to our CD73 program, HIF-2α program and CD39 program. Taiho's options to these programs expire, on a program-by-program basis, after a prescribed period following the achievement of a clinical development milestone in such program and our delivery to Taiho of the requisite data package.

For each Taiho optioned program, Taiho is obligated to pay to us (i) an option exercise payment for each program that is between $3 million to $15 million, (ii) clinical, regulatory and commercialization milestones of up to $275 million and (iii) royalties on net sales in Taiho's territories ranging from high single digits to mid-teens. Royalties will be payable on a licensed product-by-licensed product and country-by-country basis during the period of time commencing on the first commercial sale of a licensed product in a country and ending upon the later of: (a) ten (10) years from the date of first commercial sale of such licensed product in such country; and (b) expiration of the last-to-expire valid claim of our patents covering the manufacture, use or sale or exploitation of such licensed product in such country. Taiho is also responsible for the development and commercialization of licensed products in the Taiho Territory. During the fourth quarter 2022, Taiho opted to participate in two Phase 3 trials of domvanalimab combinations, STAR-121 and STAR-221, and would be obligated to make certain milestone payments contingent upon successfully satisfying the related clinical milestones.

WuXi Biologics License - anti-PD-1

Our PD-1 license agreement (the WuXi PD-1 Agreement) with WuXi Biologics Ireland Limited (successor-in-interest to WuXi Biologics (Cayman) Inc., WuXi Biologics), which we entered into in 2017 as subsequently amended, provides us with an exclusive license to (i) develop, use and manufacture products that include an anti-PD-1 antibody, including zimberelimab, throughout the world and (ii) commercialize any such products, throughout the world except in Greater China. Pursuant to the terms of the WuXi PD-1 Agreement, we may incur future clinical and regulatory milestone payments, commercialization milestone payments up to $375 million, and royalty payments that range from high single-digits to low teens of net sales beginning on the first commercial sale and ending on the later of (i) ten (10) years following such first commercial sale and (ii) the expiry of all patents that may subsequently be issued or granted that cover the product in such country, hereafter referred to as the royalty term.

Under the WuXi PD-1 Agreement, we are obligated to appoint WuXi Biologics as our exclusive manufacturer of the drug substance for such licensed products for a specified period of time subject to certain exceptions. Our sublicensees, however, may manufacture, at any time, certain portions of their requirements for such product subject to certain conditions. We made certain covenants not to commercialize any anti-PD-1 antibody licensed or obtained by us after the date of the license agreement with WuXi Biologics other than anti-PD-1 antibodies licensed from WuXi Biologics, subject to certain exceptions as set forth in the WuXi Agreement. This agreement terminates, on a licensed product-by-licensed product and country-by-country basis, on expiration of the royalty term for such licensed product for the applicable country.

Abmuno License

In 2016, we entered into a license agreement (the Abmuno Agreement) with Abmuno Therapeutics LLC (Abmuno) for a worldwide exclusive license to develop, use, manufacture, and commercialize products that include an anti-TIGIT antibody, including domvanalimab. Under the agreement, we may be required to make additional clinical, regulatory and commercialization milestone payments of up to $88 million.

The Abmuno Agreement terminates on the latest of (i) the expiry of the last-to-expire Abmuno licensed patent that covers a product that contains an anti-TIGIT antibody, (ii) the date on which there is no longer an Abmuno licensed patent application that is still pending and has been pending for a certain period of time that covers a product that contains an anti-TIGIT antibody and (iii) 10 years from the date of first commercial sale.

Our Strategy

Our overarching vision is to create a broad portfolio of best-in-class therapies and develop combinations that bring transformative clinical benefits over current treatment options. Our clinical development approach aims to generate meaningful data in the most efficient manner possible in order to rapidly advance our investigational products through clinical trials. Some of the key elements of our strategy include:

- **Building a differentiated portfolio by focusing on intra-portfolio combinations.** We are building a diverse portfolio of small-molecule investigational products that target different immune mechanisms, as well as cell-intrinsic pathways important for cancer growth and metastasis. In addition to small molecules, we are also developing antibody investigational products that target what we believe are some of the most important immune checkpoint receptors, including PD-1 and TIGIT, as well as our anti-CD39 antibody which is advancing into IND-enabling studies, and that we expect to be critical components of our intra-portfolio combinations. By combining these antibody candidates with our internally discovered small-molecule investigational products, we believe we can create highly differentiated combination products.
- **Designing our clinical trials to advance our compounds as quickly and efficiently as possible**. Our goal is to identify the best combinations and settings and to rapidly generate randomized proof-of-concept data for our investigational products early in their development. We leverage platform trial designs, such as our ARC-6, ARC-9 and EDGE-Lung studies, which allow us to evaluate multiple combinations and settings for a single tumor type in one clinical trial and compare those combinations against standard-of-care control arms.
- **Pursuing combinations and indications based on strong biological rationales**. In selecting indications to pursue, we are focusing on those that are most dependent on the pathways targeted by our agents. We are also focusing on patient populations and settings in which we believe there is still considerable unmet need. As an example, several oncology indications, such as pancreatic cancer and colorectal cancer, have a high percentage of cases that are driven by certain oncogenic mutations (e.g., KRAS mutations) which are associated with poor responses to current available therapies and poor overall survival, and are associated with high expression levels of CD73.
- **Maximizing the value of our portfolio through strategic collaborations and research and development arrangements.** We seek to establish collaborative relationships that will provide us with access to capital, opportunities and/or expertise. In 2020, we entered into the Gilead Collaboration Agreement with Gilead which, to date, has provided us with nearly $1.4 billion in funding, through both non-dilutive payments and equity investments. For each program that Gilead exercises its option to, we have received, or will receive, a substantial option payment and Gilead will share 50% of the global costs for that program, while preserving for us the option to co-promote our investigational products in the U.S., should they be approved. In 2017, we entered into an Option and License Agreement (Taiho Agreement) with Taiho Pharmaceutical Co., Ltd. (Taiho) to secure a development and, if approved, commercialization partner for Japan and certain other Asian countries. We intend to continue to establish strategic collaborations, such as our clinical collaboration with AstraZeneca to evaluate domvanalimab in combination with durvalumab in a registrational phase 3 clinical trial in patients with unresectable Stage 3 NSCLC, so that we can bring our investigational products to the broadest patient population possible.

Manufacturing and Supply

We do not own or operate, and currently have no plans to establish, any manufacturing or storage facilities. We rely, and expect to continue to rely, on third parties for the manufacture of our investigational products for preclinical and clinical testing, as well as for commercial manufacture if any of our investigational products obtain marketing approval. We also rely, and expect to continue to rely, on third parties to package, label, store and distribute our investigational products, as well as for our commercial products if marketing approval is obtained. We believe that this strategy allows us to maintain a more efficient infrastructure by eliminating the need for us to invest in our own manufacturing facilities, equipment and personnel while also enabling us to focus our expertise and resources on the development of our investigational products. Our third-party contract manufacturers are operating at or near normal levels despite the continuing COVID-19 pandemic; however, some of our supply chain logistics providers have been more challenged by prolonged government-imposed lockdowns and capacity constraints. We are actively monitoring

our manufacturing and supply chain needs in order to prevent or minimize the impact of any disruptions to our clinical programs.

To date, we have obtained active pharmaceutical ingredients (API) and drug product for our investigational products from single-source third party contract manufacturers. We are in the process of developing our supply chain for each of our investigational products and intend to put in place framework agreements under which third-party contract manufacturers will generally provide us with necessary quantities of API and drug product on a project-by-project basis based on our development needs. With respect to zimberelimab, we agreed, as part of the WuXi PD-1 Agreement, that WuXi Biologics would be our exclusive manufacturer of zimberelimab drug substance with respect to clinical and commercial supplies until a certain number of years after marketing approval for zimberelimab, subject to certain exceptions.

As we advance our investigational products through development, we will consider our lack of redundant supply for the API and drug product for each of our investigational products to protect against any potential supply disruptions. We generally expect to rely on third parties for the manufacture of any companion diagnostics we may develop.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including large pharmaceutical and biotechnology companies, academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for the research, development, manufacturing and commercialization of cancer immunotherapies. Any investigational products that we successfully develop and commercialize will compete with new immunotherapies that may become available in the future.

We will compete in the segments of the pharmaceutical, biotechnology and other related markets that develop immuno-oncology treatments. There are many other companies that have commercialized and/or are developing immuno-oncology treatments for cancer including large pharmaceutical and biotechnology companies, such as AstraZeneca, Beigene, Bristol-Myers Squibb, Merck, Novartis, Pfizer, Regeneron in partnership with Sanofi Genzyme, and Roche/Genentech.

For our anti-TIGIT antibodies, domvanalimab and AB308, we are aware of several pharmaceutical companies developing antibodies against this target, including Beigene, Roche/Genentech, and Merck. To our knowledge, there are no approved anti-TIGIT antibodies and the most advanced agents are in Phase 3 development.

For our dual adenosine receptor antagonist, etrumadenant, we are aware that Incyte and Merck KGaA have initiated clinical development of dual adenosine receptor antagonists. We are aware of clinical-stage selective adenosine A2a receptor antagonists being developed by other companies, including AstraZeneca, Incyte, iTeos, and Novartis. Clinical-stage selective adenosine A2b receptor antagonists are also being developed by companies such as Palobiofarma and Tarus. To our knowledge, there are no adenosine receptor antagonists approved for the treatment of cancer and the most advanced is in Phase 2 development.

For our small molecule CD73 inhibitor, quemliclustat, we are aware of several pharmaceutical companies developing antibodies against this target, including AstraZeneca, Bristol-Myers Squibb, Corvus, Novartis and Tracon/I-Mab, all of which have advanced their CD73 antibodies into clinical development. Other pharmaceutical companies have small-molecule programs against this target, of which only Antengene and ORIC are believed to be in clinical development. To our knowledge, there are no approved CD73 molecules and the most advanced is in Phase 3 development.

For our anti-PD-1 antibody, zimberelimab, multiple large pharmaceutical companies have already received regulatory approvals for their anti-PD-1/PD-L1 antibodies, including AstraZeneca, Beigene/Novartis, Bristol-Myers Squibb, Merck, Pfizer in partnership with Merck KGaA, Regeneron in partnership with Sanofi Genzyme and Roche/Genentech, and there are also many other anti-PD-1 and anti-PD-L1 antibodies in clinical development.

For our HIF-2α inhibitor, AB521, Merck received approval for belzutifan in Von Hippel-Lindau disease in 2021 and has a number of clinical studies assessing its activity in cancer settings. Other pharmaceutical companies,

including Novartis and NiKang Therapeutics have small-molecule HIF-2α inhibitors in development. Arrowhead Pharmaceuticals has an RNA-based anti-HIF-2α agent in Phase 2 development.

Many of the companies against which we may compete have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic 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 potential competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and enrolling subjects for our clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We could see a reduction or elimination of our commercial opportunity 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 or our collaborators may develop. Our competitors also may obtain FDA or foreign 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 or our collaborators are able to enter the market. The key competitive factors affecting the success of all of our investigational products, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics (if required), the level of biosimilar or generic competition and the availability of reimbursement from government and other third-party payors.

Intellectual Property

Our commercial success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries for our investigational products, to operate without infringing valid and enforceable patents and proprietary rights of others, and to prevent others from infringing on our proprietary or intellectual property rights. We seek to protect our proprietary position by filing, in the United States and other foreign jurisdictions, patent applications intended to cover the composition of matter of our investigational products, their methods of use, and related discoveries, technologies, inventions and improvements that may be commercially important to our business. We may also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We also intend to take advantage of regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions where available.

As of February 1, 2023, we have 7 issued U.S. patents directed to compositions of matter, pharmaceutical compositions and methods of use for our investigational programs. As of February 1, 2023, our company-owned and licensed patent portfolio consists of 38 pending or issued U.S. patent applications, three pending Patent Cooperation Treaty (PCT) patent applications, and approximately 426 pending or issued foreign patent applications directed to compositions of matter, methods of synthesis and methods of use. The term of any patents that issue will vary in accordance with the laws of each jurisdiction, but is typically 20 years from the earliest effective filing date. Our issued patents and any patents that may issue in the future from our company-owned or licensed pending applications are projected to expire between 2035 and 2042, absent any patent term adjustments or extensions.

The patent positions for biotechnology and pharmaceutical companies like us are generally uncertain and can involve complex legal, scientific and factual issues. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our investigational products and enforce the patent rights that we own or license, and could affect the value of such intellectual property. With respect to both company-owned and licensed intellectual property, we cannot guarantee that the patent applications we are currently pursuing or may file in the future will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Our competitors may independently develop similar investigational products or technologies that are outside the scope of the rights granted under any issued patents that we own or exclusively in-license. We cannot be sure that any patents granted to us will be commercially useful in protecting our products or their methods of use or manufacture. Moreover, even issued patents do not guarantee us the right to commercialize our products. For example, third parties may have blocking patents that could be used to prevent us from commercializing or manufacturing our investigational products.

Because of the extensive time required for development, testing and regulatory review of an investigational product, it is possible that, before a product can be commercialized, any patent protection for such product may expire or remain in force for only a short period following commercialization, thereby reducing the commercial advantage the patent provides. In the United States, the term of a patent covering an FDA-approved product may, in certain cases, 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, 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 and only those claims covering the approved product, a method for using it or a method for manufacturing it 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 product. While we intend to seek patent term extensions in any jurisdictions where they are available, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

Government Regulation

Government Regulation and Product Approval

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

FDA Approval Process

In the United States, the Food and Drug Administration (FDA) regulates drugs and biological products under the Federal Food, Drug, and Cosmetic Act (FDCA), the Public Health Service Act (PHSA), and implementing regulations. These laws and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of therapeutic products. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as clinical hold, FDA refusal to approve pending regulatory applications, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

The process required by the FDA before a drug or biological product may be marketed in the United States generally includes the following:

- Completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices (GLP) or other applicable regulations;
- Submission to the FDA of an investigational new drug application (IND), which must become effective before human clinical trials may begin in the United States;
- Performance of adequate and well-controlled human clinical trials according to Good Clinical Practices (GCP), to establish the safety and efficacy of the investigational product for its intended use;
- Submissions to the FDA of a New Drug Application (NDA) or Biologic License Application (BLA) for a new product.
- Satisfactory completion of an FDA inspection of the facility or facilities where the investigational product is manufactured to assess compliance with the FDA's current good manufacturing practices (cGMP), to

assure that the facilities, methods and controls are adequate to preserve the investigational product's identity, strength, quality, purity, and potency;

- Potential FDA audit of the preclinical and clinical trial sites that generated the data in support of the NDA/BLA; and
- FDA review and approval of the NDA/BLA.

Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity, and novelty of the investigational product or disease. A clinical hold may occur at any time during the life of an IND and may affect one or more specific trials or all trials conducted under the IND.

Preclinical tests include laboratory evaluation of an investigational product's chemistry, formulation, and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the investigational product. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLP. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about an investigational product's chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted. A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. Clinical trials involve the administration of the investigational product to healthy volunteers or subjects under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with GCP, an international standard meant to protect the rights and health of subjects and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. subjects and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time, or impose other sanctions if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial subjects. The trial protocol and informed consent information for subjects in clinical trials must also be submitted to an institutional review board (IRB) for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions. The study sponsor may also suspend a clinical trial at any time on various grounds, including a determination that the subjects are being exposed to an unacceptable health risk.

Clinical trials to support NDAs/BLAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the investigational product usually into healthy human subjects, the investigational product is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the investigational product for a particular indication, dosage tolerance, and optimal dosage, and to identify common adverse effects and safety risks. If an investigational product demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain additional information about clinical efficacy and safety in a larger number of subjects, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit risk relationship of the investigational product and to provide adequate information for the labeling of the investigational product. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the investigational product. A single Phase 3 trial may be sufficient in certain circumstances.

Concurrent with clinical trials, sponsors usually complete additional animal safety studies and also develop additional information about the chemistry and physical characteristics of the investigational product and finalize a process for manufacturing commercial quantities of the investigational product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the investigational product and the manufacturer must develop methods for testing the quality, purity and potency of the investigational product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the investigational product does not undergo unacceptable deterioration over its proposed shelf-life. After completion of the required clinical testing, an NDA, for a drug investigational product, or a BLA, for a biological investigational product, is prepared and submitted to the FDA. FDA approval of the NDA or

BLA is required before marketing of the product may begin in the United States. The NDA or BLA must include the results of all preclinical, clinical, and other testing and a compilation of data relating to the investigational product's pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting an NDA or BLA is substantial. The submission of most NDAs and BLAs is additionally subject to a substantial application user fee, and the applicant under an approved NDA or BLA is also subject to program user fees. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA or BLA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. The FDA may refuse to file any NDA or BLA that it deems incomplete or not properly reviewable at the time of submission, and may request additional information. In this event, the NDA or BLA must be resubmitted with the additional information and the resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs and BLAs. Most such applications for standard review investigational products are reviewed within ten months of the date the FDA files the NDA or BLA; most applications for priority review investigational products are reviewed within six months of the date the FDA files the NDA or BLA. Priority review can be applied to an investigational product that the FDA determines has the potential to treat a serious or life-threatening condition and, if approved, would be a significant improvement in safety or effectiveness compared to available therapies. The review process for both standard and priority review may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

Among other things, the FDA reviews an NDA to determine whether the product is safe and effective for its intended use, a BLA to determine whether the product is safe, pure, and potent, and in each case, whether the investigational product is being manufactured in accordance with cGMP. The FDA may also refer applications for novel investigational products, or investigational products that present difficult questions of safety or efficacy, to an advisory committee—typically a panel that includes clinicians and other experts—for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the investigational product is manufactured. The FDA will not approve the investigational product 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. To assure GCP and cGMP compliance, an applicant must incur significant expenditures of time, money and effort in the areas of training, record keeping, production and quality control.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive. The FDA may disagree with our trial design or interpret data from preclinical studies and clinical trials differently than we interpret the same data. If the agency decides not to approve the NDA or BLA in its present form, the FDA will issue a complete response letter that describes all of the specific deficiencies in the application identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. If a complete response letter is issued, the applicant may either resubmit the NDA or BLA, addressing the deficiencies identified in the letter, or withdraw the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA or BLA, the FDA will issue an approval letter. An approval letter authorizes commercial marketing of the drug or biological product in the United States with specific prescribing information for specific indications.

Even if an investigational product receives regulatory approval, the approval may be significantly limited to specific indications and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a risk evaluation and mitigation strategy (REMS), or otherwise limit the scope of any approval. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use (ETASU). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the product. In

addition, the FDA may require post marketing clinical trials, sometimes referred to as "Phase 4" clinical trials, designed to further assess a product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Foreign Clinical Trials to Support an IND, NDA, or BLA

The FDA will accept as support for an IND, NDA, or BLA a well-designed, well-conducted, non-IND foreign clinical trial if it was conducted in accordance with GCP and the FDA is able to validate the data from the trial through an on-site inspection, if necessary. A sponsor or applicant who wishes to rely on a non-IND foreign clinical trial to support an IND must submit the following supporting information to the FDA to demonstrate that the trial conformed to GCP:

- the investigator's qualifications;
- a description of the research facilities;
- a detailed summary of the protocol and trial results and, if requested, case records or additional background data;
- a description of the drug substance and drug product, including the components, formulation, specifications, and, if available, the bioavailability of the investigational product;
- information showing that the trial is adequate and well controlled;
- the name and address of the independent ethics committee that reviewed the trial and a statement that the independent ethics committee meets the required definition;
- a summary of the independent ethics committee's decision to approve or modify and approve the trial, or to provide a favorable opinion;
- a description of how informed consent was obtained;
- a description of what incentives, if any, were provided to subjects to participate;
- a description of how the sponsor monitored the trial and ensured that the trial was consistent with the protocol;
- a description of how investigators were trained to comply with GCP and to conduct the trial in accordance with the trial protocol; and
- a statement on whether written commitments by investigators to comply with GCP and the protocol were obtained.

Regulatory applications based solely on foreign clinical data meeting these criteria may be approved if the foreign data are applicable to the U.S. population and U.S. medical practice, the trials have been performed by clinical investigators of recognized competence, and the data may be considered valid without the need for an on-site inspection by FDA or, if FDA considers such an inspection to be necessary, FDA is able to validate the data through an on-site inspection or other appropriate means. Failure of an application to meet any of these criteria may result in the application not being approvable based on the foreign data alone.

Expedited Development and Review Programs

The FDA has various programs, including Fast Track, priority review, accelerated approval and breakthrough therapy, which are intended to expedite or simplify the process for reviewing investigational products, or provide for the approval of an investigational product on the basis of a surrogate endpoint. Even if an investigational product qualifies for one or more of these programs, the FDA may later decide that the investigational product no longer meets the conditions for qualification or that the time period for FDA review or approval will be lengthened. Generally, investigational products that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development and expedite the review of investigational products to treat serious or life-threatening diseases or conditions and fill unmet medical needs. Priority review is designed to give an investigational product that treats a serious condition and, if approved, would provide a significant

improvement in safety or effectiveness, an initial review within eight months as compared to a standard review time of twelve months.

Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated investigational product and expedite review of the application for an investigational product designated for priority review. Accelerated approval provides for an earlier approval for a new investigational product that meets the following criteria: is intended to treat a serious or life-threatening disease or condition, generally provides a meaningful advantage over available therapies and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality (IMM) that is reasonably likely to predict an effect on IMM or other clinical benefit. A surrogate endpoint is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. As a condition of approval, the FDA may require that a sponsor of an investigational product receiving accelerated approval perform post-marketing clinical trials to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the product may be subject to accelerated withdrawal procedures.

In addition to the Fast Track, accelerated approval and priority review programs discussed above, the FDA also provides Breakthrough Therapy designation. A sponsor may seek FDA designation of an investigational product as a "breakthrough therapy" if the investigational product is intended, alone or in combination with one or more other therapeutics, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the investigational 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.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biological product intended to treat a rare disease or condition—generally a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a product available in the United States for such disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested before submitting a marketing application for the therapeutic for that particular disease or condition. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding toward clinical trial costs, tax advantages and user-fee waivers. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The FDA may revoke orphan drug designation, and if it does, it will publicize the drug is no longer designated as an orphan drug.

If an investigational product with orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the investigational product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same investigational product for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, could also block the approval of one of our investigational products for seven years if a competitor obtains approval of the same investigational product as defined by the FDA or if our investigational product is determined to be contained within the competitor's investigational product for the same indication or disease.

Patent Term Restoration and Marketing Exclusivity

After approval, owners of relevant drug or biological product patents may apply for up to a five-year patent extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The allowable patent term extension is calculated as half of the product's testing phase—the time between IND and NDA or BLA submission—and all of the review phase—the time between NDA or BLA submission and approval, up to a maximum of five years. The time can be shortened if the FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years.

For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the U.S. Patent and Trademark Office must determine that approval of the investigational product covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for an investigational product for which an NDA or BLA has not been submitted.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to gain approval of an NDA for a new chemical entity. An investigational product is a new chemical entity if the FDA has not previously approved any other new investigational product containing the same active moiety, which is the molecule or ion responsible for the action of the investigational product substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application (ANDA) or a 505(b)(2) NDA submitted by another company for another version of such investigational product where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an approved NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing investigational product. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for investigational products containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Biosimilars

The Biologics Price Competition and Innovation Act of 2009 (BPCIA) created an abbreviated approval pathway for biological investigational products shown to be highly similar to or interchangeable with an FDA licensed reference biological product. Biosimilarity sufficient to reference a prior FDA-approved product requires that there be no differences in conditions of use, route of administration, dosage form, and strength, and no clinically meaningful differences between the biological investigational product and the reference product in terms of safety, purity, and potency. Biosimilarity must be shown through analytical trials, animal trials, and a clinical trial or trials, unless the Secretary of Health and Human Services waives a required element. A biosimilar investigational product may be deemed interchangeable with a prior approved product if it meets the higher hurdle of demonstrating that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

A reference biologic is granted 12 years of exclusivity from the time of first licensure of the reference product, and no application for a biosimilar can be submitted for four years from the date of licensure of the reference product. The first biologic investigational product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against a finding of interchangeability for other biologics for the same condition of use for the lesser of (i) one year after first commercial marketing of the first interchangeable biosimilar, (ii) 18 months after the first interchangeable biosimilar is approved if there is no patent challenge, (iii) 18 months after resolution of a lawsuit over the patents of the reference biologic in favor of the first interchangeable biosimilar applicant, or (iv) 42 months after the first interchangeable biosimilar's application has been approved if a patent lawsuit is ongoing within the 42-month period.

Post-approval 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 may result in restrictions on the product or even complete withdrawal of the product from the market. 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 FDA review and approval. In addition, the FDA may under some circumstances require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA under some circumstances has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs. Any product manufactured or distributed by us or our collaborators pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things:

- record-keeping requirements;
- reporting of adverse experiences associated with the product;
- providing the FDA with updated safety and efficacy information;
- therapeutic sampling and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes;
- registration and listing requirements; and
- complying with FDA promotion and advertising requirements, which include, among other things, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved labeling, limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet.

The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label may be subject to significant liability. However, physicians may, in their independent medical judgment, prescribe legally available products for off-label uses. The FDA does not regulate the behavior of physicians in their choice of treatments but the FDA does restrict manufacturer's communications on the subject of off-label use of their products.

Manufacturers, their subcontractors, and other entities involved in the manufacture and distribution of approved drug and biological products are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMP, including data integrity requirements, and other laws. The FDA periodically inspects manufacturing facilities to assess compliance with ongoing regulatory requirements, including cGMP, which impose extensive procedural, substantive and record-keeping requirements upon us and third-party manufacturers engaged by us if our products are approved. In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require FDA approval before being implemented. FDA regulations would also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and our third-party manufacturers. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory actions, such as warning letters, suspension of manufacturing, seizures of products, injunctive actions or other civil penalties. We cannot be certain we or our present or future third-party manufacturers or suppliers will be able to comply with the cGMP regulations and other ongoing FDA regulatory requirements. If we or our present or future third-party manufacturers or suppliers are not able to comply with these requirements, the FDA may halt our clinical trials or require us to recall a product from distribution.

In addition, therapeutic manufacturers in the United States must comply with applicable provisions of the Drug Supply Chain Security Act and provide and receive product tracing information, maintain appropriate licenses, ensure

they only work with other properly licensed entities, and have procedures in place to identify and properly handle suspect and illegitimate product.

Disclosure of Clinical Trial Information

Sponsors of clinical drug trials (other than Phase 1 trials) are required to register and disclose certain clinical trial information. Information related to the investigational product, comparator(s), patient population, phase of investigation, trial sites and investigators and other aspects of the clinical trial is made public as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of certain trials may be delayed until the new product or new indication being studied has been approved. However, there are evolving rules and increasing requirements for publication of trial-related information, and it is possible that data and other information from trials involving drugs that never garner approval could in the future be required to be disclosed. In addition, publication policies of major medical journals mandate certain registration and disclosures as a pre-condition for potential publication, even when this is not presently mandated as a matter of law. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Additional Controls for Biological Products

To help reduce the increased risk of the introduction of adventitious agents, the PHSA emphasizes the importance of manufacturing controls for products whose attributes cannot be precisely defined. The PHSA also provides authority to the FDA to immediately suspend licenses in situations where there exists a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction or spread of communicable diseases in the United States and between states.

After a BLA is approved, the biological product may also be subject to official lot release as a condition of approval. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA may also perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer.

In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products. As with drugs, after approval of biological products, manufacturers must address any safety issues that arise, are subject to recalls or a halt in manufacturing, and are subject to periodic inspection after approval.

FDA Regulation of Companion Diagnostics

If use of an *in vitro* diagnostic is essential to safe and effective use of a drug or biologic product, then the FDA generally will require approval or clearance of the diagnostic, known as a companion diagnostic and regulated by FDA as a medical device, at the same time that the FDA approves the investigational product. The review of an *in vitro* companion diagnostic in conjunction with the review of an investigational product involves coordination of review between internal organizations within FDA. Most companion diagnostics require approval of a premarket approval application (PMA). The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMAs are subject to a substantial application fee. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, the applicant must demonstrate that the diagnostic produces reproducible results when the same sample is tested multiple times by multiple users at multiple laboratories. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation (QSR) which imposes elaborate testing, control, documentation and other quality assurance requirements.

PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that

may be expensive and time-consuming to generate and that can substantially delay approval. If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution.

After a device is placed on the market following appropriate approval or clearance from the FDA, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

Other U.S. Healthcare Laws and Compliance Requirements

In the United States, our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare & Medicaid Services (CMS) other divisions of the U.S. Department of Health and Human Services (HHS), such as the Office of Inspector General and the Health Resources and Service Administration, the U.S. Department of Justice (DOJ) and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, sales, marketing and scientific/educational grant programs may have to comply with the anti-fraud and abuse provisions of the Social Security Act, the false claims laws, the privacy and security provisions of the Health Insurance Portability and Accountability Act (HIPAA) and similar state laws, each as amended, as applicable.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between therapeutic product manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (ACA), to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act (FCA) (discussed below).

The federal false claims, including the FCA, which imposes significant penalties and can be enforced by private citizens through civil qui tam actions, and civil monetary penalty laws prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal healthcare programs, including Medicare and Medicaid, or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. For instance, historically, pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free

product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, off-label, and thus generally non-reimbursable, uses.

HIPAA created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the Anti-Kickback Statute, the ACA amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Also, many states have similar, and typically more prohibitive, fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Additionally, to the extent that our product is sold in a foreign country, we may be subject to similar foreign laws.

We may be subject to data privacy and security regulations by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH) and its implementing regulations, imposes requirements on "covered entities," including certain healthcare providers, health plans, and healthcare clearinghouses, and their respective "business associates" that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity as well as their covered subcontractors relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, many state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways, are often not pre-empted by HIPAA, and may have a more prohibitive effect than HIPAA, thus complicating compliance efforts.

Certain of our products, once approved, may be administered by a physician. Under currently applicable U.S. law, certain products not usually self-administered (including injectable drugs) may be eligible for coverage under Medicare through Medicare Part B. Medicare Part B is part of original Medicare, the federal health care program that provides health care benefits to the aged and disabled, and covers outpatient services and supplies, including certain pharmaceutical products, that are medically necessary to treat a beneficiary's health condition. As a condition of receiving Medicare Part B reimbursement for a manufacturer's eligible drugs or biologicals, the manufacturer is required to participate in other government healthcare programs, including the Medicaid Drug Rebate Program and the 340B Drug Pricing Program. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of HHS as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing Program, the manufacturer must extend discounts to entities that participate in the program.

In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price (ASP) and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these 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. It is difficult to predict how Medicare coverage and reimbursement policies will be applied to our products in the future and coverage and reimbursement under different federal healthcare programs are not always consistent. Medicare reimbursement rates may also reflect budgetary constraints placed on the Medicare program.

Additionally, the federal Physician Payments Sunshine Act (Sunshine Act) within the ACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to CMS information related to certain payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other

healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members. Failure to report accurately could result in penalties. In addition, many states also govern the reporting of payments or other transfers of value, many of which differ from each other in significant ways, are often not pre-empted, and may have a more prohibitive effect than the Sunshine Act, thus further complicating compliance efforts.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

Ensuring business arrangements with third parties comply with applicable healthcare laws and regulations is a costly endeavor. If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other current or future governmental regulations that apply to us, we may be subject to significant penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, 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 other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any investigational products for which we may obtain regulatory approval. In the United States and in foreign markets, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage and establish adequate reimbursement levels for such products. In the United States, third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid in the United States, and commercial payors are critical to new product acceptance.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which therapeutics they will pay for and establish reimbursement levels. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a therapeutic is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

We cannot be sure that reimbursement will be available for any product that we commercialize and, if coverage and reimbursement are available, what the level of reimbursement will be. Coverage may also be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities. Reimbursement may impact the demand for, or the price of, any product for which we obtain regulatory approval. Additionally, our collaborators will be required to obtain coverage and reimbursement for any companion diagnostic tests they develop separate and apart from the coverage and reimbursement we seek for our investigational products, once approved.

Third-party payors are increasingly challenging the price, examining the medical necessity, and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with branded drugs and drugs administered under the supervision of a physician. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA approvals. Our investigational products may not be considered medically necessary or cost-effective. Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our product on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. 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 for the product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any investigational product that we successfully develop.

Different pricing and reimbursement schemes exist in other countries. In the European Union, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular investigational product to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any investigational products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care, the increasing influence of health maintenance organizations, and additional legislative changes in the United States has increased, and we expect will continue to increase, the pressure on healthcare pricing. The downward pressure on the rise in healthcare costs in general, particularly prescription medicines, medical devices and surgical procedures and other treatments, has become very intense. 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 we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of investigational products, restrict or regulate post-approval activities, and affect the ability to profitably sell investigational products for which marketing approval is obtained. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

For example, the ACA has substantially changed healthcare financing and delivery by both governmental and private insurers. Among the ACA provisions of importance to the pharmaceutical and biotechnology industries, in addition to those otherwise described above, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price (AMP);
- a Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the 340B Drug Discount Program;
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- expansion of healthcare fraud and abuse laws, including the FCA and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected;
- requirements to report certain financial arrangements with physicians and teaching hospitals;
- a requirement to annually report certain information regarding drug samples that manufacturers and distributors provide to physicians;
- establishment of a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending; and
- a licensure framework for follow on biologic products.

There have been legal and political challenges to certain aspects of the ACA. For example, in December 2017, Congress repealed the tax penalty for an individual's failure to maintain ACA-mandated health insurance that is commonly referred to as the "individual mandate" as part of a tax reform bill. For example, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Further, there have been a number of health reform measures by the Biden administration that have impacted the ACA. For example, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 (IRA), into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and by creating a new manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how such challenges and the healthcare reform measures of the Biden administration will impact the ACA and our business.

Further legislation or regulation could be passed that could harm our business, financial condition and results of operations. Other legislative changes have been proposed and adopted since the ACA was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction of at least $1.2 trillion for

fiscal years 2012 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect beginning on April 1, 2013 and, due to subsequent legislation, including the Infrastructure Investment and Jobs Act, will stay in effect until 2031 unless additional Congressional action is taken. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the IRA, among other things, (i) directs the Secretary of HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare Part B and Medicare Part D, and subjects drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law, and (ii) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. Individual states in the United States have also become 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.

We anticipate that current and future healthcare reform measures could result in additional downward pressure on coverage and the price that we receive for any approved product, and could seriously harm our business. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability from product sales, or commercialize our products. Such reforms could have an adverse effect on anticipated revenue from investigational products that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop investigational products.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act (FCPA), prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws

and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

Other Regulations

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

Rest of World Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Whether or not we obtain FDA approval to conduct clinical trials or market a product, we must obtain the requisite approvals from regulatory authorities in foreign jurisdictions prior to the commencement of clinical trials or marketing of the product in those countries. The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials must be conducted in accordance with GCP and the applicable regulatory requirements. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Europe

Similar to the United States and Australia, the conduct of clinical trials in the EU are subject to regulatory controls. Under the current EU Clinical Trials Directive 2001/20/EC (Directive), before a clinical trial can be initiated in the EU, it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the national Competent Authority and one or more Ethics Committees. In 2014, the EU adopted a new Clinical Trials Regulation 536/2014 (Regulation) to replace the current Directive, with a three-year transition period. The Regulation aims to simplify and streamline the approval of clinical trials in the EU. For example, the sponsor shall submit a single application for approval of a clinical trial via the EU portal. As part of the application process, the sponsor shall propose a reporting Member State, who will coordinate the validation and evaluation of the application. The reporting Member State shall consult and coordinate with the other concerned Member States. If an application is rejected, it can be amended and resubmitted through the EU portal. If an approval is issued, the sponsor can start the clinical trial in all concerned Member States. However, a concerned Member State can in limited circumstances declare an "opt-out" from an approval. In such a case, the clinical trial cannot be conducted in that Member State. The Regulation also aims to streamline and simplify the rules on safety reporting, and introduces enhanced transparency requirements such as mandatory submission of a summary of the clinical trial results to the EU database. The Regulation will become directly applicable in all EU Member States once the centralized portal and database for clinical trials are fully functional.

The Directive will still apply for three years from the date of application of the Regulation for clinical trial applications submitted before the date of application of the Regulation and for clinical trial applications submitted under the Directive within one year after the date of application of the Regulation.

Commercialization of our investigational products may only occur in the EU following approval of a marketing application, which can be obtained through either a centralized or a decentralized procedure:

- Under the centralized procedure, a marketing application is submitted to the European Medicines Agency (EMA), where it will be evaluated by the Committee for Medicinal Products for Human Use. If this committee delivers a favorable opinion, this typically results in the grant by the European Commission of a single marketing authorization that is valid for all European Union member states. The centralized procedure is mandatory for certain types of drugs, such as biotechnology medicinal drugs, orphan medicinal drugs, and medicinal drugs containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, autoimmune and viral diseases. The centralized procedure is optional for drugs containing a new active substance not yet authorized in the EEA, or for drugs that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.
- Under the decentralized procedure, an identical dossier is submitted to the competent authorities of each of the Member States in which a marketing authorization is sought, one of which is selected by the

applicant as the Reference Member State (RMS). The competent authority of the RMS prepares a draft assessment report, a draft summary of the drug characteristics (SPC) and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging proposed by the RMS, the drug is subsequently granted a national marketing authorization in all the Member States (*i.e.*, in the RMS and the Member States Concerned).

We will be subject to additional regulations with respect to any activities we conduct in the EU. For example, the EU General Data Protection Regulation (GDPR) applies to health-related and other personal data of individuals in the European Union. The GPDR, which went into effect in May 2018, imposes more stringent operational requirements on processors and controllers of personal data, including, for example, expanded disclosures about how personal data is collected, used and shared, limitations on retention of personal data, more stringent requirements pertaining to genetic, biometric and health data, mandatory data breach notification requirements, and higher standards for controllers to demonstrate valid consent for certain data processing activities. The GDPR further provides that European Union Member States may implement their own additional laws and regulations in relation to the processing of genetic, biometric or health data, which could result in differences in the GDPR's implementation among Member States. The GDPR increases our responsibility and liability in relation to personal data that we process, and we must put in place additional mechanisms to ensure compliance with the new EU data protection rules.

Human Capital Resources

Our culture and values can be defined by one overarching concept: We do the right things for the right reasons. We take pride in hard work and approach our mission—to create, develop and commercialize highly differentiated combination therapies that have the potential to cure—with a great sense of urgency. We recognize that our employees are a critical component to our success and we strive to attract the best talent from a range of sources, including an internship program through which we have developed strong relationships with multiple universities to foster talent and attract skilled graduates.

As of December 31, 2022, we had just over 500 full-time employees, approximately 35% of whom hold Ph.D., M.D., R.N., or similar degrees and certifications. Of our employees, approximately 80% were engaged in research and development activities. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

We recognize that attracting skilled talent is only one part of the equation. We endeavor to retain and motivate our employees by empowering them to make the decisions they are most qualified and best positioned to decide and by providing opportunities for growth and development, such as through our education reimbursement program. We focus on wellness through our company-funded lunch program, a stipend to assist with wellness and commuter expenses, and our coverage of 95% of the costs for healthcare benefits. Further, we conduct periodic talent reviews to identify high performing and high potential talent within the organization. This data is used to inform specific development opportunities for current and future leaders, create custom leadership training, drive meaningful development conversations and enable succession planning for key roles. We conduct an employee survey to measure employee engagement and to inform future talent initiatives. We regularly update our safety protocols, taking into consideration national and local public health guidelines and input from our employees.

We are committed to increasing representation of under-represented populations at our company, particularly in leadership roles. As of December 31, 2022, among our employees, 55% were female. Among our leadership (which we define as employees at the vice president level and above), approximately 30% were female. As of December 31, 2022, 55% of our employees and 37% of our leadership identify as being from diverse racial and ethnic groups. On our Board of Directors, four of our twelve directors self-identify as female and three self-identify as being from a diverse racial or ethnic group. As of December 31, 2022, our company turnover rate is lower than the industry average. While the competition for talent remains strong as the number of biotechnology and pharmaceutical companies headquartered in the San Francisco Bay Area increases, we believe we can attract and retain the talent we need to be successful.

Corporate Information

We were incorporated under the laws of the State of Delaware in April 2015. Our principal executive offices are located at 3928 Point Eden Way, Hayward, CA 94545, and our telephone number is (510) 694-6200. Our website

address is www.arcusbio.com. The information on, or that can be accessed through, our website is not incorporated by reference into this Annual Report on Form 10-K.

We operate and manage our business as one reportable and operating segment. See Note 1, Organization, liquidity and capital resources, in Part II, Item 8 for additional information.

We file Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other information with the Securities and Exchange Commission (SEC). Our filings with the SEC are available free of charge on the SEC's website at *www.sec.gov* and on our website under the "Investors" tab as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

Item 1A. Risk Factors.

You should consider carefully the following risk factors, together with all the other information in this report, including our Consolidated Financial Statements and notes thereto, and in our other public filings with the SEC. The occurrence of any of the following risks could harm our business, financial condition, results of operations and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. You should consider all of the risk factors described when evaluating our business.

Risks Related to our Limited Operating History, Financial Position and Capital Requirements

We have a history of operating losses, have never generated any revenue from product sales and anticipate that we will continue to incur significant losses for the foreseeable future.

We are a pre-commercial immuno-oncology company with a limited operating history that may make it difficult to evaluate the success of our business to date and to assess our future viability. All of our investigational products are in development, and none have been approved for commercial sale nor have we ever generated any revenue from product sales. Our revenues to date have been primarily from upfront and milestone payments, research and development support and clinical materials reimbursement from our strategic partners. For the years ended December 31, 2022 and 2021 we had net losses of $267 million and net income of $53 million, respectively. As of December 31, 2022, we had an accumulated deficit of $542 million. We expect that it will be several years, if ever, before we have an investigational product ready for commercialization. While we may receive income from year to year under the Gilead Agreement and Taiho Agreement, we generally expect to incur substantial and increasing levels of operating losses over the next several years and for the foreseeable future as we advance our investigational products. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital.

To become and remain profitable on a sustained basis, we must develop and eventually commercialize a product with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our investigational products, obtaining marketing approval for these investigational products, manufacturing, marketing and selling those products for which we may obtain marketing approval and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we succeed in commercializing one or more of our investigational products, we may never generate revenues that are significant or large enough to achieve sustained profitability. In addition, as a young business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown challenges. If we do achieve profitability from product sales, we may not be able to sustain or increase profitability on a quarterly or annual basis and we will continue to incur substantial research and development and other expenditures to develop and market additional investigational products. Our failure to become and remain profitable on a sustained basis would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or 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 may need to obtain additional funding to finance our operations and complete the development and any commercialization of our investigational products. If we do not receive substantial opt-in, milestone or royalty

payments from our existing collaboration agreements, or are unable to raise additional capital when needed, we may be forced to restrict our operations or delay, reduce or eliminate our product development programs.

The development of biopharmaceutical investigational products is capital intensive. Since our inception, we have used substantial amounts of cash to fund our operations and expect our expenses to increase substantially during the next few years as our investigational products enter and advance into and through large late-stage or registrational clinical trials and we expand our clinical, regulatory, quality and manufacturing capabilities. In addition, if we obtain marketing approval for any of our investigational products, we expect to incur significant commercialization expenses related to marketing, sales, manufacturing and distribution.

As of December 31, 2022, we had $1.14 billion of cash, cash equivalents and marketable securities. While we believe that our cash position will be sufficient to fund our anticipated level of operations into 2026, our future capital requirements will depend on many factors, including:

- the number, scope, rate of progress and costs of clinical programs and investigational products as well as drug discovery, preclinical development activities, and laboratory testing;
- the scope and costs of manufacturing development and commercial manufacturing activities;
- the scope of any cost sharing arrangements with our strategic partners;
- the timing and amount of milestone payments and option fees we receive under the Gilead Collaboration Agreement and Taiho Agreement;
- the extent to which we acquire or in-license other investigational products and technologies;
- the cost, timing and outcome of regulatory review of our investigational products;
- the cost and timing of establishing sales and marketing capabilities, if any of our investigational products receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the costs associated with being a public company; and
- the cost associated with commercializing our investigational products, if they receive marketing approval.

We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our investigational products. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts. In addition, if we are able to raise additional capital, raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or investigational products.

Risks Related to the Discovery and Development of our Investigational Products

If we are unable to obtain regulatory approval for our investigational products, or experience significant delays in doing so, our business will be materially harmed.

We have no products approved for sale and our investigational products must be approved by the Food and Drug Administration (FDA) in the United States and similar regulatory authorities outside the United States, such as the EMA, prior to commercialization. The process of obtaining marketing approvals, both in the United States and abroad, is expensive and takes many years, if approval is obtained at all, and can vary substantially based upon a variety of factors. 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 investigational product'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, among other requirements. Our investigational products may not be effective, may be only moderately effective, may not have an acceptable durability of response, may not have an acceptable risk-benefit profile or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude us from obtaining marketing approval

or limit their commercial use. Our investigational products may not be approved even if they achieve their primary endpoints in any Phase 3 clinical trials or registrational trials we or our collaborators conduct.

The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and in determining when or whether marketing approval will be obtained for any of our investigational products. Regulatory authorities may refuse to accept any application or may decide that our data are 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 an investigational product. 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 also cause delays in or prevent the approval of an application. For example, since a key element of our strategy is the development of intra-portfolio combinations, regulatory authorities may disagree that we have sufficiently demonstrated the contribution of each investigational product or other agent in our combination trials and require further studies.

Even if we are able to obtain marketing approvals for any of our investigational products, those approvals may be for indications that are not as broad as desired or may contain other limitations that would adversely affect our ability to generate revenue from sales of those products. Moreover, if we are not able to differentiate our product against other approved products within the same class of drugs, or if any of the other circumstances described above occur, our business would be materially harmed and our ability to generate revenue from that class of drugs would be severely impaired.

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

Clinical drug development is a lengthy, expensive and uncertain process.

The research and development of drugs and biological products is an extremely risky industry. Only a small percentage of investigational products that enter the development process ever receive marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any investigational product, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our investigational products in humans. Clinical testing is expensive, can take many years to complete and its outcome is uncertain.

The results of preclinical studies and early clinical trials are not always predictive of future results.

The results of preclinical and early clinical trials of our investigational products and other products with the same mechanism of action may not be predictive of the results of later-stage clinical trials. Clinical trial failure may result from a multitude of factors including flaws in study design, dose selection, placebo effect, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits. As such, failure in clinical trials can occur at any stage of testing. A number of companies in the biopharmaceutical industry have suffered setbacks in the advancement of clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Based upon negative or inconclusive results, we may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. In addition, data obtained from clinical trials are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may further delay, limit or prevent marketing approval. In particular, results from uncontrolled trials, meaning trials in which there is no control group such as a placebo group, are inherently difficult to interpret. This difficulty is compounded in clinical trials such as ours, in which two or more investigational products that have not yet been approved are being evaluated. Accordingly, the preliminary data from clinical trials of certain of our investigational products may not be predictive of future clinical trial results for these or other investigational products when studied in a randomized environment or larger patient populations.

Most of our clinical trials are open-label studies and may be susceptible to bias.

Most of our clinical trials, including our Phase 3 trials, are open-label studies in which both the patient and investigator know whether the patient is receiving the investigational products or either an existing approved drug or placebo. Open-label clinical trials are susceptible to bias that may exaggerate any therapeutic effect or overestimate the risk associated with the investigational product. Patients may perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. Investigators may interpret the information of the

treated group more favorably given their awareness of the treatment regimen or may attribute safety risks to the investigational product.

Enrollment and retention of subjects in clinical trials is expensive and time consuming, can be made more difficult or rendered impossible by competing treatments, clinical trials of competing investigational products, and public health epidemics, each of which could result in significant delays and additional costs in our product development activities, or in the failure of such activities.

We may encounter delays in enrolling, or be unable to enroll and maintain, a sufficient number of subjects to complete any of our clinical trials. Patient enrollment and retention in clinical trials is a significant factor in the timing of clinical trials and depends on many factors, including the size of the patient population required for analysis of the trial's primary endpoints, the nature of the trial protocol, our ability to recruit clinical trial investigators with the appropriate competencies and experience, the existing body of safety and efficacy data with respect to the investigational product, the number and nature of competing products or investigational products and ongoing clinical trials of competing investigational products for the same indication, the proximity of subjects to clinical trial sites, the eligibility criteria for the clinical trial and our ability to obtain and maintain subject consents.

For example, enrollment of oncology subjects in our clinical trials evaluating zimberelimab may be hampered by nivolumab from Bristol-Myers Squibb and pembrolizumab from Merck, both of which are approved and on the market. Subjects may opt to be treated with an approved product rather than our anti-PD-1 antibody investigational product. In addition, Roche/Genentech, Merck and Beigene have initiated numerous Phase 3 trials with their respective anti-TIGIT antibodies, which could reduce the number of clinical sites and subjects available for our registrational program for domvanalimab (our anti-TIGIT antibody), including ARC-10 and STAR-121, each Phase 3 trials in lung cancer and STAR-221, our Phase 3 trial in upper gastrointestinal tract cancer.

Public health outbreaks, such as the COVID-19 pandemic, may also have an adverse impact our clinical trial operations. Regulatory authorities and ethics committees may divert resources, prolonging the time for review of new studies and any protocol or other amendments for ongoing studies. For example, our investigational sites may intermittently divert resources in order to respond to an ongoing health crisis, which could cause delays and limit their ability to initiate new studies. The limited resources at investigational sites would further hinder their ability to screen and enroll subjects, conduct and report all patient assessments and collect all patients samples, thereby impacting our ability to assess the activity of our investigational products in a timely manner. Furthermore, supply chain challenges have made it more difficult to procure standard-of-care chemotherapy drugs utilized in our trials and timely ship materials to investigational sites, which has and may continue to delay or limit their screening and enrollment of patients.

In addition, recruiting and retaining subjects in our clinical trials may be adversely impacted by negative results that we report in our other clinical trials using the same investigational products or by negative results reported by others using investigational products with the same mechanism of action as our investigational products. Delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our investigational products. Failures in planned subject enrollment or retention may result in increased costs or program delays and could render further development impossible.

If we do not achieve our product development goals in the time frames we announce and expect, the commercialization of our investigational products may be delayed, our share price may decline and our commercial prospects may be adversely affected.

Drug development is inherently risky and uncertain. The actual timing of our development milestones can vary significantly compared to our estimates, in some cases for reasons beyond our control, for any number of reasons, including:

- delays in completing IND-enabling preclinical studies or developing manufacturing processes and associated analytical methods that meet good manufacturing practice (cGMP) requirements;
- the FDA placing a clinical trial on hold;
- the FDA requesting additional information, which could necessitate generating additional information at significant cost in terms of both time and expenses;

- our prioritization of other of our investigational products for advancement or the emergence of competing investigational products developed by others;
- challenges and delays in trial execution associated with our testing of multiple investigational products in the same indication in different clinical trials;
- subjects failing to enroll or remain in our trial at the rate we expect;
- subjects choosing an alternative treatment or other investigational products, or participating in competing clinical trials;
- lack of adequate funding to continue our clinical trials;
- subjects experiencing severe or unexpected drug-related adverse effects;
- any interruptions or delays in the supply of our investigational products for our clinical trials;
- a facility manufacturing any of our investigational products or any of their components being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of cGMP regulations or other applicable requirements, or infections or cross-contaminations of investigational products in the manufacturing process;
- any changes to our manufacturing process or product specifications that may be necessary or desired;
- any failure or delay in reaching an agreement with contract research organizations (CROs) and clinical trial sites;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, good clinical practices (GCP) or regulatory requirements or other third parties not performing data collection or analysis in a timely or accurate manner;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other comparable foreign regulatory authorities for violations of applicable regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications;
- one or more Institutional Review Boards (IRBs) refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing its approval of the trial;
- changes in regulatory requirements and policies which may require us to amend clinical trial protocols to comply with these changes and resubmit our clinical trial protocols to IRBs for reexamination;
- delays due to new regulatory requirements which may take time for us and the third-parties we engage to incorporate into our operations to ensure compliance; or
- health crises, such as the COVID-19 pandemic, which may restrict the ability of trial sites to initiate new trials, screen patients for enrollment or treat enrolled patients, and divert clinical trial site resources away from the conduct of our clinical trials.

These and other factors may also lead to the suspension or termination of clinical trials, and ultimately the denial of regulatory approval of an investigational product. Any delays in achieving our development goals may allow our competitors to bring products to market before we do and adversely affect our commercial prospects and cause our stock price to decline.

Preliminary and interim data from our clinical studies that we announce or publish from time to time are subject to audit and verification procedures that could result in material changes in the final data and may change as more patient data become available.

From time to time, we publish preliminary or interim data from our clinical studies. Preliminary data remain subject to audit confirmation and verification procedures that may result in the final data being materially different from the preliminary data we previously published. Interim data are also 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. As a result, preliminary and interim data should be viewed with caution until the final data are available. Material adverse changes in the final data could significantly harm our business prospects.

Serious adverse events, undesirable side effects or other unexpected properties of our investigational products may be identified during development or after approval, which could lead to the discontinuation of our clinical development programs, refusal by regulatory authorities to approve our investigational products or limitations on the use of our investigational products or, if discovered following marketing approval, revocation of marketing authorizations or subsequent limitations on the use of our investigational products.

As we continue our development of these investigational products and initiate clinical trials of our additional investigational products, serious adverse events, undesirable side effects or unexpected characteristics may emerge causing us to abandon these investigational products or limit their development to more narrow uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Even if our investigational products initially show promise in these early clinical trials, the side effects of drugs are frequently only detectable after they are tested in large, Phase 3 clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. Sometimes, it can be difficult to determine if the serious adverse or unexpected side effects were caused by the investigational product or another factor, especially in oncology subjects who may suffer from other medical conditions and be taking other medications. If serious adverse or unexpected side effects are identified during development and are determined to be attributed to our investigational product, we may be required to develop a Risk Evaluation and Mitigation Strategy (REMS) to mitigate those serious safety risks, which could impose significant distribution and use restrictions on our products.

Drug-related side effects could also affect subject recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business prospects significantly.

In addition, if one or more of our investigational products receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- regulatory authorities may impose subsequent limitations on the use of the product;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular investigational product, if approved, and could significantly harm our business, results of operations and prospects.

Adverse findings from clinical trials conducted by third parties investigating the same investigational products as us in different territories could adversely affect our development program.

Lack of efficacy, adverse events, undesirable side effects or other adverse findings may emerge in clinical trials conducted by third parties investigating the same investigational products as us in different territories. For example, we and Gloria Biosciences, each licensed our rights to the same anti-PD-1 antibody (which we refer to as zimberelimab) from WuXi Biologics (Cayman) Inc. (WuXi Biologics). Gloria Biosciences refers to this antibody as GLS-010 and is conducting clinical trials with GLS-010 in China. We have no control over their clinical trials or development program, and adverse findings from the results or their conduct of clinical trials could adversely affect our development of zimberelimab or even the viability of zimberelimab as an investigational product. We may be required to report Gloria Biosciences' adverse events or unexpected side effects to the FDA or comparable foreign regulatory authorities, which could, among other things, order us to cease further development of zimberelimab. We

may face similar risks from any independent development conducted with our investigational products by Gilead and Taiho, following any exercise of their respective options to our programs.

A key element of our strategy is the development of intra-portfolio combinations. If we are not successful in discovering, developing and commercializing investigational products that take advantage of different mechanisms of action to achieve superior outcomes relative to the use of single agents or other combination therapies, our ability to achieve our strategic objectives would be impaired.

A key element of our strategy is to build a broad portfolio of investigational products that will allow for the development of intra-portfolio combinations. We believe that by developing or licensing these investigational products, we can control the combinations we pursue and, if and when approved, maximize the commercial potential of these combinations. However, these combinations have not been tested before and may fail to demonstrate synergistic activity against immunological targets, may fail to achieve superior outcomes relative to the use of single agents or other combination therapies, may exacerbate adverse events associated with one of the investigational products when used as monotherapy, or may fail to demonstrate sufficient safety or efficacy traits in clinical trials to enable us to complete those clinical trials or obtain marketing approval for the combination therapy. In addition, our early clinical trials may test more than one investigational product in uncontrolled studies, and it may be difficult to interpret the results of those uncontrolled trials or evaluate the contribution of each investigational agent in such combination.

Even if we are successful in developing combination therapies, competition from other investigational products in the same class which are either already approved or further along in development than ours may prevent us from realizing the commercial potential of our combination therapies and prevent us from achieving our strategic objectives.

Development of combination therapies may present more or different challenges than development of single agent therapies.

Many of our investigational products are being pursued in combination with one or more additional products or investigational products. The development of combination therapies may be more complex than the development of single agent therapies and generally requires that sponsors demonstrate the contribution of each investigational product to the claimed effect and the safety and efficacy of the combination as a whole. This requirement may make the design and conduct of clinical trials more complex, requiring more clinical trial subjects. We also may not be able to meet the FDA's current or future approval standards required for combination therapies or combination products, if we decided to administer or package a combination therapy as a single drug product. For example, under the "combination rule", the FDA may not file or approve a fixed-dose combination product unless each component of a proposed drug product is shown to make a contribution to the claimed effects and the dosage of each component (amount, frequency, duration) is safe and effective for the intended population. To satisfy these requirements, the FDA typically requires a clinical factorial study, designed to assess the effects attributable to each drug in the combination product. This is particularly true when the ingredients are directed at the same sign or symptom of the disease or condition. The FDA has accepted a variety of approaches to satisfy the combination rule but the FDA has stated that factorial studies may be unethical (e.g., omitting a drug known to improve survival) or impractical (there may be too many components to conduct a factorial study, meaning the trial cannot be conducted). The FDA has also stated that it may be possible to use other types of clinical and nonclinical data and mechanistic information available to demonstrate the contributions of the individual active ingredients to the effect of the combination. Moreover, the applicable requirements for approval of a combination therapy may differ from country to country.

In the event that one of our investigational products were to fail to demonstrate sufficient safety and efficacy or establish its contribution to the claimed effects of a combination therapies, we would need to identify alternatives. For example, we expect that our anti-PD-1 antibody, zimberelimab, will form the backbone of many of the combination therapies we are pursuing. If we are unable to demonstrate the contribution of zimberelimab to the claimed effects of a combination therapy, we would need to identify an anti-PD-1 antibody for use in such combination therapy. In the event we are unable to do so or are unable to do so on commercially reasonable terms, our business and prospects would be materially harmed.

Certain of our investigational products may require companion diagnostics in certain indications. Failure to successfully develop, validate and obtain regulatory clearance or approval for such tests could harm our product development strategy or prevent us from realizing the full commercial potential of our investigational products.

Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as a medical device and may require separate regulatory authorization prior to commercialization. Certain clinical trials that we are conducting, such as our Phase 2 ARC-7 trial and our Phase 3 ARC-10 trial, which are each being conducted in patients with PD-L1≥50% NSCLC, include the use of a diagnostic test to help identify eligible patients. Our future trials may also use a diagnostic test to help identify eligible patients. In addition, we have significant efforts directed to identifying changes in various cells and proteins to understand their relationship, if any, to the clinical activity observed in our clinical trials and to assess if such cells and/or proteins could be used as predictive biomarkers to select for patients more likely to respond to our investigational products. However, we cannot be certain that we will be able to identify any such biomarkers, that such biomarkers will result in us identifying the appropriate patients for our investigational products or that we or any third-party collaborators will be able to validate any diagnostic tests incorporating any predictive biomarkers we may identify.

We currently do not have any plans to develop diagnostic tests internally. We are therefore dependent on the sustained cooperation and effort of third-party collaborators in developing and, if our investigational products are approved for use only with an approved companion diagnostic test, obtaining approval and commercializing these tests. If these parties are unable to successfully develop companion diagnostics for these investigational products, or experience delays in doing so, the development of our investigational products may be adversely affected and we may not be able to obtain marketing authorization for these investigational products. Furthermore, our ability to market and sell, as well as the commercial success, of any of our investigational products that require a companion diagnostic will be tied to, and dependent upon, the receipt of required regulatory authorization and the continued ability of such third parties to make the companion diagnostic commercially available on reasonable terms in the relevant geographies. Any failure to develop, validate, obtain and maintain marketing authorization and supply for a companion diagnostic we need will harm our business prospects.

The design or our execution of our ongoing and future clinical trials may not support marketing approval.

The design or execution of a clinical trial can determine whether its results will support marketing approval, and flaws in the design or execution of a clinical trial may not become apparent until the clinical trial is well advanced. In some instances, there can be significant variability in safety or efficacy results between different trials with the same investigational product due to numerous factors, including differences in trial protocols, size and type of the patient populations, variable adherence to the dosing regimen or other protocol requirements and the rate of dropout among clinical trial participants. The FDA or comparable foreign regulatory authorities may disagree with our trial designs and our interpretation of data from preclinical studies or clinical trials. Even if we adhere to guidance or advice given by the FDA or comparable foreign regulatory authorities, such adherence does not guarantee that the FDA will agree with our trial designs or data interpretations or prevent the FDA from changing the requirements for the approval of any investigational product.

We have conducted, and continue to conduct, portions of our clinical trials outside the United States, and the FDA may not accept data from trials conducted in foreign locations.

We have conducted, and we expect to continue to conduct, portions of our clinical trials outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and 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 general, the patient population for any clinical trials conducted outside the United States must be representative of the population for which we intend to label the product in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. We cannot assure you that the FDA will accept data from trials conducted outside the United States. If the FDA does not accept the data from such clinical trials, we would likely need to conduct additional trials, which would be costly and time-consuming and delay or permanently halt our development of our investigational products.

Risks Related to Reliance on Third Parties, Manufacturing and Commercialization

We expect to depend on our collaboration with Gilead for the research, development, manufacture and commercialization of our investigational products. If this collaboration is not successful, our business could be adversely affected.

Our strategy for fully developing and commercializing our investigational products is dependent upon maintaining our current arrangements with Gilead and our other strategic partners. Our ability to leverage these arrangements to produce commercial success will depend, among other things, on our collaborators' cooperation and ability to successfully meet their responsibilities with regards to a clinical program. We cannot predict the success of any collaboration that we enter into. Our partnership with Gilead poses a number of risks including, but not limited to, the following:

- conflicts may arise between us and Gilead, such as conflicts regarding the combinations or indications to pursue or concerning the interpretation of clinical data, the commercial potential of any optioned investigational products, the interpretation of financial provisions or the ownership of intellectual property developed during the collaboration. Any such conflicts could slow or prevent the development or commercialization of our investigational products;
- if our joint development program does not result in the successful development and commercialization of products or if Gilead terminates the collaboration 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 our investigational products could be delayed and we may need additional resources to develop our investigational products;
- we will be heavily dependent on Gilead for its further development and commercialization of the investigational products from the programs that it opts into;
- we may not be successful in this collaboration due to various other factors, including our ability to demonstrate proof of concept in one or more clinical studies so that Gilead will exercise its option to these programs;
- we have appointed two individuals designated by Gilead to our board of directors pursuant to the terms of the investor rights agreement, and Gilead owns approximately 18.9% of our outstanding common stock and will have the right (but not the obligation) to acquire additional shares from us up to an amount resulting in Gilead owning a total of 35% of our outstanding common stock and, as a result, may be able to exert significant influence over our company;
- Gilead could independently develop, or develop with third parties, products that compete directly or indirectly with our investigational products if Gilead believes that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours; and
- because Gilead has an option to all of our programs, it will be difficult for us to enter into new collaborations.

We rely on third parties to conduct our clinical trials and perform some of our research and preclinical studies. If these third parties do not satisfactorily carry out their contractual duties or fail to meet expected deadlines, our development programs may be delayed or subject to increased costs, each of which may have an adverse effect on our business and prospects.

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. As a result, we are and expect to remain dependent on third parties to conduct our ongoing clinical trials and any future clinical trials of our investigational products. The timing of the initiation and completion of these trials will therefore be partially controlled by such third parties and may result in delays to our development programs. Specifically, we expect CROs, clinical investigators, and consultants to play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, we will not be able to control all aspects of their activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCP requirements, which

are regulations and guidelines controlling how clinical trials should be conducted and are applicable to all of our investigational products in clinical development. The FDA and comparable foreign regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical trial investigators and clinical trial sites. If we or any of our CROs or clinical trial sites fail to comply with applicable GCP requirements, the data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications.

There is no guarantee that any such CROs, clinical trial investigators or other third parties on which we rely will devote adequate time and resources to our development activities or perform as contractually required. Many of these third parties have and continue to suffer from personnel constraints resulting from the COVID-19 pandemic and other economic factors which may impact their ability to perform their contractual obligations. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, otherwise performs in a substandard manner, or terminates its engagement with us, the timelines for our development programs may be extended or delayed or our development activities may be suspended or terminated. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in such clinical trials unless we are able to transfer those subjects to another qualified clinical trial site, which may be difficult or impossible. In addition, clinical trial investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA or comparable foreign regulatory authorities concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any marketing application we submit by the FDA or any comparable foreign regulatory authority. Any such delay or rejection could prevent us from commercializing our investigational products.

Furthermore, these third parties may also 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 investigational products and will not be able to, or may be delayed in our efforts to, successfully commercialize our products.

We contract with third parties for the manufacturing and supply of investigational products for use in preclinical testing and clinical trials and for the supply of standard-of-care drugs or comparator agents in our clinical trials, which supply may become limited or interrupted or may not be of satisfactory quality and quantity.

We do not have any manufacturing facilities. We produce in our laboratory relatively small quantities of compounds for evaluation in our research programs. We rely, and expect to continue to rely, on third parties for the manufacture and supply of our investigational products for preclinical and clinical testing, as well as for commercial manufacture if any of our investigational products are approved. We currently have limited manufacturing arrangements for our investigational products and expect that each of our investigational products will only be covered by single source suppliers for the foreseeable future. In particular, we have an exclusive relationship with WuXi Biologics, located in China, for the manufacture of zimberelimab drug substance. Our contract manufacturers are subject to import and export rules and restrictions, which may impact their ability to acquire materials used in the manufacturing of our investigational product or export our manufactured investigational products to the countries where our clinical trials are conducted. Our reliance on limited manufacturing arrangements increases the risk that we will not have sufficient quantities of our investigational products for use in our clinical trials or, if approved, quantities of product at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We further rely on third parties to procure sufficient quantities of standard-of-care drugs and comparator agents that we use in our clinical trials. We closely monitor the inventory for each of our investigational products, standard of care drugs and/or comparator agents to prevent or minimize the impact of potential disruptions. Supply chain delays can affect all aspects of our manufacturing, supply and distribution to clinical sites, including increased lead times to obtain raw materials used in the manufacturing of our investigational products, longer timeframes to procure standard-of-care drugs and comparator agents, and transit delays in providing the investigational products, standard-of-care drugs or comparator agents to clinical trial sites, each of which could delay, prevent or impair our development efforts.

Furthermore, all entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for our investigational products, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in clinical trials must be manufactured in accordance with cGMP requirements. These regulations govern manufacturing processes and procedures, including record keeping, and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants, or to inadvertent changes in the properties or stability of our investigational products that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of an NDA or Biologics License Application (BLA) on a timely basis and must adhere to the FDA's Good Laboratory Practice regulations and cGMP regulations enforced by the FDA through its facilities inspection program. Comparable foreign regulatory authorities may require compliance with similar requirements. The facilities and quality systems of our third-party contractor manufacturers must pass a pre-approval inspection for compliance with the applicable regulations as a condition of marketing approval of our investigational products. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMP regulations.

In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on commercially reasonable terms, if at all. In particular, any replacement of our manufacturers could require significant effort and expertise because there may be a limited number of qualified replacements. In some cases, the technical skills or technology required to manufacture our investigational products may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our investigational products. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop investigational products in a timely manner or within budget. Our or a third party's failure to execute on our manufacturing requirements, to do so on commercially reasonable terms and comply with cGMP could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of our investigational products under development;
- delay in submitting regulatory applications, or receiving marketing approvals, for our investigational products;
- loss of the cooperation of an existing or future collaborator, including option exercises by Gilead or Taiho under the Gilead Collaboration Agreement or Taiho Agreement, respectively;
- subjecting third-party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease development or to recall batches of our investigational products; and
- in the event of approval to market and commercialize our investigational products, an inability to meet commercial demands for our product or any other future investigational products.

We, or our third-party manufacturers, may be unable to successfully produce or scale-up manufacturing of our investigational products in sufficient quality and quantity, which would delay or prevent us and/or our third-party collaborators from conducting clinical trials and developing our investigational products.

We, or our third-party manufacturers, will need to manufacture and supply large quantities of our investigational products to support our clinical development plans. With respect to investigational products from optioned programs, we, or our third-party manufacturers, may need to produce additional quantities to support the scope of our joint clinical development program with Gilead, Gilead's additional evaluations with its own proprietary products or Taiho's independent clinical development plans. We are also a party to various collaboration and supply arrangements, such as our clinical trial collaboration with AstraZeneca to evaluate domvanalimab in combination with durvalumab in patients with unresectable Stage 3 NSCLC. Furthermore, the COVID-19 pandemic has increased the lead time to

obtain raw materials used in the manufacturing of our investigational products. Accordingly, we, or our manufacturing partners, may be unable to successfully increase the manufacturing capacity for any of our investigational products in a timely or cost-effective manner, or at all, to support these collective needs. In addition, quality issues may arise during scale-up activities. If we or our manufacturing partners are unable to successfully produce or scale up the manufacture of our investigational products in sufficient quality and quantity, the development, testing and clinical trials of that investigational product may be delayed or become infeasible, and marketing approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business.

Changes in methods of investigational product manufacturing or formulation may result in additional costs or delay.

As investigational products progress through preclinical to late-stage clinical trials to marketing approval and commercialization, it is common that various aspects of the development program, such as the investigational product's specifications, manufacturing methods and formulation, are altered along the way in an effort to optimize yield and manufacturing batch size, minimize costs and achieve consistent quality and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our investigational products to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our investigational products and jeopardize our ability to commercialize our investigational products and generate revenue.

Our employees, clinical trial investigators, CROs, consultants, vendors, collaboration partners and any potential commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, clinical trial investigators, CROs, consultants, vendors, collaboration partners and any potential commercial partners. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (i) FDA laws and regulations or those of comparable foreign regulatory authorities, including those laws that require the reporting of true, complete and accurate information, (ii) manufacturing standards, (iii) federal and state health and data privacy, security, fraud and abuse, government price reporting, transparency reporting requirements, and other healthcare laws and regulations in the United States and abroad, or (iv) laws that require the true, complete and accurate reporting of financial information or data. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, as well as a disclosure program and other applicable policies and procedures, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Even if we receive marketing approval, we may not be successful in commercializing our investigational products.

We have no sales, marketing or distribution capabilities or experience. If any of our investigational products ultimately obtains regulatory approval, we, whether alone or in collaboration with Gilead for programs that we commercialize together, may not be able to effectively or successfully market the product due to a number of factors, including:

- the imposition by regulatory authorities of significant restrictions on a product's indicated uses, marketing or distribution;
- the imposition by regulatory authorities of costly and time-consuming post-approval studies, post-market surveillance or additional clinical trials;
- our failure to establish sales and marketing capabilities;

- the failure of our products to achieve the degree of market acceptance by physicians, patients, hospitals, cancer treatment centers, healthcare payors and others in the medical community necessary for commercial success;
- unfavorable pricing regulations or third-party coverage and reimbursement policies; and
- inaccuracies in our estimates of the addressable patient population resulting in a smaller market opportunity than we believed.

If any of our investigational products for which we have or retain sales and marketing responsibilities are approved, we must either develop a sales and marketing organization, which would be expensive and time consuming, or outsource these functions to other third parties. We may be unable to recruit and retain adequate numbers of effective sales and marketing personnel, and if we enter into arrangements with third parties to perform sales, marketing and distribution services our product revenue or the profitability of these product revenue to us are likely to be lower than if we were to market and sell any medicines that we develop ourselves.

Our or our collaborators' inability to successfully market and sell any of our investigational products, if approved, could have a material adverse effect on our business and our overall financial condition.

Even if we receive marketing approval for one or more of our investigational products, our commercial success is dependent on obtaining coverage and reimbursement approval for a product from a government or other third-party payor, which coverage may be delayed or may not be sufficient to cover our costs.

Our commercial success is dependent on obtaining coverage and reimbursement approval for a product from a government or other third-party payor, which is a time-consuming and costly process that could require us and any collaborators to provide supporting scientific, clinical and cost effectiveness data for the use of our products to the payor. There may be significant delays in obtaining such coverage and reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a product 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 products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with branded therapeutics and therapeutics administered under the supervision of a physician. Additionally, our collaborators will be required to obtain coverage and reimbursement for any related companion diagnostics tests they develop separate and apart from the coverage and reimbursement we seek for our investigational products, once approved.

Reimbursement may also impact the demand for, and the price of, any product for which we obtain marketing approval. Assuming we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with those medications. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of our products. Therefore, coverage and adequate reimbursement is critical to new product acceptance and we expect to experience pricing pressures in connection with the sale of any of our investigational products due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes.

Our ability to obtain coverage and reimbursement approval for any of our investigational products, if approved, could have a material adverse effect on the demand for that investigational product, and on our business and our overall financial condition.

Even if our investigational products are approved by the FDA, they may never be approved or commercialized outside the United States, which would limit our ability to realize their full market potential.

In order to market any products outside the United States, we or our collaborators must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. For example, the approval of zimberelimab for the treatment of recurrent or refractory classical Hodgkin's Lymphoma in China by Gloria

Biosciences does not improve the chances of FDA approval for any BLA that we may submit for zimberelimab in the United States in any indication. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us or our collaborators and may require additional preclinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our or our collaborators' failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any investigational products approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we or our collaborators fail to comply with regulatory requirements in international markets or fail to obtain and maintain required approvals, our ability to realize the full market potential of our products will be harmed.

Any investigational products for which we intend to seek approval as biologic products may face competition sooner than anticipated.

The Biologics Price Competition and Innovation Act of 2009 (BPCIA) created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until twelve years from the date on which the reference product was first licensed. During this twelve-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The law is complex and is still being interpreted and implemented by the FDA. As a result, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

Zimberelimab and domvanalimab are biological products and we may develop additional biological products in the future. We believe that any of our current and future investigational products approved as a biological product under a BLA should qualify for the twelve-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to Congressional action or otherwise, or that the FDA will not consider our investigational products to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, could be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products will depend on a number of marketplace and regulatory factors that are still developing.

Risks Related to our In-Licenses and Other Strategic Agreements

We are currently party to several in-license agreements under which we acquired rights to use, develop, manufacture and/or commercialize certain of our investigational products. If we breach our obligations under these agreements, we may be required to pay damages, lose our rights to these investigational products or both, which would adversely affect our business and prospects.

We rely, in part, on license and other strategic agreements, which subject us to various obligations, including diligence obligations with respect to development and commercialization activities, reporting and notification obligations, payment obligations for achievement of certain milestones and royalties on product sales, negative covenants and other material obligations. We may need to devote substantial time and attention to ensuring that we are compliant with our obligations under these agreements. If we fail to comply with the obligations under our license agreements or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and our licensors may have the right to terminate the license. If our license agreements are terminated, we may not be able to develop, manufacture, market or sell the products covered by our agreements and those being tested or approved in combination with such products. Such an occurrence could materially adversely affect the value of the investigational product being developed under any such agreement and any other investigational products being developed or tested in combination. For example, zimberelimab, which we in-licensed from WuXi Biologics, is intended to be used as the cornerstone of our combination strategy. Domvanalimab, which we in-licensed from Abmuno Therapeutics, is being evaluated in four registrational studies: ARC-10, PACIFIC-8 (in collaboration with AstraZeneca), STAR-121 (being operationalized by Gilead) and STAR-221. In the event we breach our license agreement with WuXi Biologics and/or Abmuno Therapeutics, and our license agreements are terminated, we would be unable to pursue our intra-portfolio combination strategy, or we would have to negotiate a new or reinstated agreement, which may not be available to us on equally favorable terms, or at all.

In addition, the agreements under which we license intellectual property or technology to or from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our collaborations or other strategic partnerships on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected investigational products.

We may not realize the benefits of any acquisitions, in-license or other collaborations or strategic alliances that we enter into.

We have entered into in-license agreements with multiple licensors and option agreements to enable the development and commercialization of our investigational products worldwide. In the future, we may seek to enter into acquisitions or additional licensing arrangements with third parties to expand our pipeline or that we believe will complement or augment our development and commercialization efforts with respect to our investigational products and any future investigational products that we may develop. These transactions can entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management's time and attention in order to manage a collaboration or develop acquired products, investigational products or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business. As a result, if we enter into in-license, acquisition or collaboration agreements, or strategic partnerships, 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, which could delay our timelines or otherwise adversely affect our business.

We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction or such other benefits that led us to enter into the arrangement. For example, under the Gilead Collaboration Agreement, for each additional clinical program that Gilead exercises its option to, it will pay an option fee of $150 million per program, and for each research collaboration program that Gilead exercises its option to at the IND-enabling stage, it will pay an option fee of $60 million per program. Furthermore, we and Gilead will equally share global co-development costs for the joint development program, as well as profits and losses for the United States, subject to opt-out rights applicable to certain programs, and expense caps on our spending and true-up adjustments. If Gilead does not exercise its option to develop a program, our capital requirements relating to that development program will significantly increase and we may need to seek a new partner in order to develop and commercialize our investigational products from that program. Failure to realize the benefits of any collaborations or strategic alliances may further cause us to curtail the development of an investigational product, 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 planned sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we will need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our investigational products or bring them to market and generate product sales revenue, which would harm our business prospects, financial condition and results of operations.

We may wish to acquire rights to future assets through in-licensing or may attempt to form collaborations in the future with respect to our investigational products, but may not be able to do so, which may cause us to alter or delay our development and commercialization plans.

The development and potential commercialization of our investigational products may require substantial additional capital to fund expenses. Pursuant to the Gilead Collaboration Agreement, Gilead has an exclusive option to acquire an exclusive license to all of our then current and future clinical programs during the 10-year collaboration term. Given the breadth of the collaboration, our ability to form new collaborations in the future will be limited. If Gilead declines to exercise its option to a program, we may need to enter into new collaborations for such programs with companies that have more resources and experience than us. We may not be successful in these efforts because third parties may not view our investigational products as having the requisite potential to demonstrate safety and efficacy. If and when we collaborate with a third party for development and commercialization of an investigational product, we can expect to relinquish some or all of the control over the future success of that investigational product to the third party. Our ability to 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 following:

- the design or results of clinical trials;
- the likelihood of approval by the FDA or comparable foreign regulatory authorities;
- the potential market for the investigational product;
- the costs and complexities of manufacturing and delivering such investigational product to patients;
- the potential of competing products;
- the existence of uncertainty with respect to our ownership of technology or other rights, which can exist if there is a challenge to such ownership without regard to the merits of the challenge; and
- industry and market conditions generally.

The collaborator may also consider alternative investigational products or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our investigational product. We may also be restricted under any license agreements by one or more negative covenants or otherwise. For example, we may be restricted from entering into agreements on certain terms or at all with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators and changes to the strategies of the combined company. As a result, 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 such investigational product, reduce or delay one or more of our other development programs, delay the potential commercialization or reduce the scope of any planned sales or marketing activities for such investigational product, or increase our expenditures and undertake development, manufacturing or commercialization activities at our own expense and may be prevented from or limited in forming additional strategic collaborations. If we elect to increase our expenditures to fund development, manufacturing 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 investigational products or bring them to market and generate product revenue.

Risks Related to Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for our investigational products, or if the scope of the intellectual property protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our products may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our investigational products and research programs. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel discoveries and technologies that are important to our business, however, we cannot predict:

- if and when patents may issue based on our patent applications;
- the scope of protection of any patent issuing based on our patent applications;
- whether the claims of any patent issuing based on our patent applications will protect our investigational products and their intended uses or prevent others from commercializing competitive technologies or products;
- whether or not third parties will find ways to invalidate or circumvent our patent rights;
- whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications; and/or
- whether we will need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose.

Obtaining and enforcing patents 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. Even if we successfully file and prosecute a patent application, we may not be able to maintain and/or enforce the issued patent. We may determine that filing or maintaining such a patent or any action to enforce a patent may be too high or not in the best interest of our company or our stockholders. It is also possible that we will fail to identify patentable aspects of our research and development results before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach these agreements and disclose such results before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

We also cannot be certain that the claims in our pending patent applications directed to our investigational products and/or technologies will be considered patentable by the U.S. Patent and Trademark Office (USPTO) or by patent offices in foreign countries. One aspect of the determination of patentability of our inventions depends on the scope and content of the "prior art," information that was or is deemed available to a person of skill in the relevant art prior to the priority date of the claimed invention. There may be prior art of which we are not aware that may affect the patentability of our patent claims or, if issued, affect the validity or enforceability of a patent claim. Even if the patents do issue based on our patent applications, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, patents in our portfolio may not adequately exclude third parties from practicing relevant technology or prevent others from designing around our claims. If the breadth or strength of our intellectual property position with respect to our investigational products is threatened, it could dissuade companies from collaborating with us to develop and threaten our ability to commercialize our investigational products. In the event of litigation or

administrative proceedings, we cannot be certain that the claims in any of our issued patents will be considered valid by courts in the United States or foreign countries.

In the future, we may need to obtain additional licenses of third-party technology that may not be available to us or are available only on commercially unreasonable terms, and which may cause us to operate our business in a more costly or otherwise adverse manner that was not anticipated.

From time to time we may be required to license technology from additional third parties to further develop or commercialize our investigational products. Should we be required to obtain licenses to any third-party technology, including any such patents required to manufacture, use or sell our investigational products, such licenses may not be available to us on commercially reasonable terms, or at all. The inability to obtain any third-party license required to develop or commercialize any of our investigational products could cause us to abandon any related efforts, which could seriously harm our business and operations.

We may become involved in lawsuits alleging that we have infringed the intellectual property rights of third parties or to protect or enforce our patents or other intellectual property, which litigation could be expensive, time consuming and adversely affect our ability to develop or commercialize our investigational products.

The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our products candidates. Third parties may assert infringement claims against us based on existing or future intellectual property rights. For example, we are aware of certain patents owned or licensed by Bristol-Myers Squibb having claims directed broadly to treating cancer with anti-PD-1 antibodies (the BMS Patents), which expire in 2023 and 2024. The BMS Patents have been and may in the future be the subject of litigation. In addition, we are aware of certain patents held by Genentech relating to methods of using an anti-PD-1 or anti-PD-L1 antibody in combination with an anti-TIGIT antibody for the treatment of cancer (the Genentech Patents), which expire in 2034. Merck has challenged the Genentech Patents in proceedings before the USPTO. If the validity of the BMS Patents and Genentech Patents are upheld following all challenges, and if we receive regulatory approval for zimberelimab prior to expiration of the BMS Patents or domvanalimab or AB308 in combination with zimberelimab prior to expiration of the Genentech Patents, then we may need to delay commercialization or we may need to obtain a license, which license may not be available on commercially reasonable terms, or at all. If we were sued for patent infringement, we would need to demonstrate that our investigational products, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity may be difficult. For example, in the United States, proving invalidity in court requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing investigational product or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing investigational product. However, we may not be able to obtain any required license on commercially reasonable terms or at all. 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. 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 investigational products or force us to cease some of our business operations, which could materially harm our business.

In addition, we may find that competitors are infringing our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving

our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against which we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks. Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of shares of our common stock. Moreover, we cannot assure you that we will have sufficient financial or other resources to defend or pursue such litigation, which typically last for years before they are concluded. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on our business and operations. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other confidential information of former employers or competitors. Although we try to ensure that our employees and consultants do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may become subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor.

While we may litigate to defend ourselves against these claims, even if we are successful, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our investigational products, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition.

We may not be able to protect our intellectual property rights outside of the U.S.

Patents are of national or regional effect, and filing, prosecuting and defending patents on all of our investigational products throughout the world would be prohibitively expensive. As such, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Further, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals or biologics, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. In addition, certain developing countries, including China and India, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. Further, we file patent applications in Russia and the Eurasian patent office, which is headquartered in Moscow. Sanctions against Russia may make it difficult to file and maintain patents in these countries, and Russia has begun taking actions against "unfriendly" countries, including the U.S., which may adversely affect the scope of and/or our ability to enforce our intellectual property rights. In any of these countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. 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.

Changes in patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our investigational products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. However, the patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation, resulting in court decisions, including Supreme Court decisions, that have increased uncertainties as to the ability to obtain and enforce patent rights in the future. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries could increase the uncertainties and costs. For example, in September 2011 the Leahy-Smith America Invents Act (the America Invents Act) was signed into law and included a number of significant changes to U.S. patent law as then existed. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. After March 2013, under the America Invents Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. However, the America Invents 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, financial condition, results of operations and prospects.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We may rely on trade secret and proprietary know-how which can be difficult to trace and enforce and, 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 investigational products, we may also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. Elements of our investigational product, including processes for their preparation and manufacture, may involve proprietary know-how, information, or technology that is not covered by patents, and thus for these aspects we may consider trade secrets and know-how to be our primary intellectual property. Any disclosure, either intentional or unintentional, by our employees, third parties with which we share our facilities or third-party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

Trade secrets and know-how can be difficult to protect. We require our employees to enter into written employment agreements containing provisions of confidentiality and obligations to assign to us any inventions generated in the course of their employment. We and any third parties with which we share facilities enter into written agreements that include confidentiality and intellectual property obligations to protect each party's property, potential trade secrets, proprietary know-how, and information. We further seek to protect our potential trade secrets, proprietary know-how, and information in part, by entering into non-disclosure and confidentiality agreements with parties who are given access to them, such as our corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. With our consultants, contractors, and outside scientific collaborators, these agreements typically include invention assignment obligations. 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 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 or other third party, we would have no right to prevent them 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 or other third party, our competitive position would be harmed.

We may become subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our investigational products or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. 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. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Patent terms may be inadequate to protect our competitive position on our investigational products for an adequate amount of time.

Patent rights are of limited duration. Given the amount of time required for the development, testing and regulatory review of new investigational products, patents protecting such candidates might expire before or shortly after such investigational products are commercialized. Even if patents covering our investigational products are obtained, once the patent life has expired for a product, we may be open to competition from biosimilar or generic products. A patent term extension based on regulatory delay may be available in the United States. However, only a single patent can be extended for each marketing approval, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the patent term extension does not extend to the full scope of the claim, but instead only to the scope of the product as approved. Laws governing analogous patent term extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. 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 will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

Risks Related to our Business Operations

We expect to expand our business operations and, as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to grow our business operations, including, if any of our investigational products receives marketing approval, adding employees in sales and marketing. To manage our anticipated future growth, we must:

- identify, recruit, integrate, maintain and motivate additional qualified personnel;
- manage our development efforts effectively, including the initiation and conduct of clinical trials for our investigational products; and
- improve our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to develop, manufacture and commercialize our investigational products will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert financial and other resources, and a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time, to managing these growth activities.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize our investigational products and, accordingly, may not achieve our research, development and commercialization goals.

Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.

Our ability to compete in the highly competitive biopharmaceuticals industry depends upon our ability to attract, retain and motivate highly skilled and experienced personnel with scientific, medical, regulatory, manufacturing and management skills and experience. We conduct our operations in the San Francisco Bay Area, a region that is home to many other biopharmaceutical companies as well as many academic and research institutions, resulting in fierce competition for qualified personnel and rapidly increasing wages. Our industry also has experienced a high rate of turnover in recent years, which has worsened during the COVID-19 pandemic. While we have expanded a number of our in-office roles to permit remote work arrangements, allowing us to seek talent from outside the San Francisco Bay Area, we still may not be able to attract or retain qualified personnel in the future due to the intense competition for a limited number of qualified personnel among biopharmaceutical companies. Many of the other biopharmaceutical companies against which we compete have greater financial and other resources, different risk profiles and a longer history in the industry than we do. Our competitors may provide higher compensation, more diverse opportunities and/or better opportunities for career advancement. Any or all of these competing factors may limit our ability to continue to attract and retain high quality personnel, which could negatively affect our ability to successfully develop and commercialize our investigational products and to grow our business and operations as currently contemplated.

We are highly dependent on the services of our founders, Terry Rosen, Ph.D., who serves as our Chief Executive Officer, and Juan Jaen, Ph.D., who serves as our President.

We are highly dependent on the services of our founders, Terry Rosen, Ph.D., who serves as our Chief Executive Officer, and Juan Jaen, Ph.D., who serves as our President. Although we have entered into employment agreements with them, they are not for a specific term and each of them may terminate their employment with us at any time, though we are not aware of any present intention of either of these individuals to leave us.

Drs. Rosen and Jaen have significant experience identifying and developing biopharmaceuticals. We believe that their drug discovery and development experience, and overall biopharmaceutical company management experience, would be difficult to replace. However, the historical results, past performance and/or acquisitions of companies with which they were affiliated do not necessarily predict or guarantee similar results for our company. Further, Drs. Rosen and Jaen have certain other business and personal commitments outside of serving as the Chief Executive Officer and President of Arcus, including serving on the boards of other companies and foundations, which may result in diversion of their focus and attention on our company.

We face substantial competition, which may result in others discovering, developing or commercializing products more quickly or marketing them more successfully than us. If their investigational products are shown to be safer or more effective than ours, then our commercial opportunity will be reduced or eliminated.

We compete in the segments of the pharmaceutical, biotechnology and other related markets that develop immunotherapies for the treatment of cancer, which is highly competitive with rapidly changing standards of care. As such, 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 or that would render any products that we may develop obsolete or non-competitive. Our competitors also may obtain marketing 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.

We are aware of several pharmaceutical companies developing products in the same class as our investigational products some of which are further along in development than our corresponding assets. See “Item 1. Business—Competition” for additional information regarding our competitors.

As more investigational products within a particular class of drugs proceed through clinical development to regulatory review and approval, the amount and type of clinical data that may be required by regulatory authorities may increase or change. Consequently, the results of our clinical trials for investigational products in that class will

likely need to show a risk benefit profile that is competitive with or more favorable than those products and investigational products in order to obtain marketing approval or, if approved, a product label that is favorable for commercialization. If the risk benefit profile is not competitive with those products or investigational products, or if the approval of other agents for an indication or patient population significantly alters the standard of care with which we tested our investigational products, we may have developed a product that is not commercially viable, that we are not able to sell profitably or that is unable to achieve favorable pricing or reimbursement. In such circumstances, our future product revenue and financial condition would be materially and adversely affected.

Our internal information technology systems, and those of our third-party CROs and other third parties upon which we rely, are subject to failure, security breaches and other disruptions, which could result in a material disruption of our investigational products' development programs, jeopardize sensitive information, prevent us from accessing critical information or result in a loss of our assets, and potentially expose us to notification obligations, loss, liability or reputational damage and otherwise adversely affect our business.

We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we collect, store and transmit confidential information, including but not limited to intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the confidentiality, integrity and availability of such confidential information. We also have outsourced elements of our operations to third parties, and as a result we manage a number of third-party contractors who have access to our confidential information.

Despite the implementation of security measures, given their size and complexity and the increasing amounts of confidential information that they maintain, our internal information technology systems and those of our third-party CROs and other third parties upon which we rely are vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners, and/or other third parties, or from cyberattacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information and other assets), which may compromise our system infrastructure, lead to data leakage, impair key business processes or other critical business operations, delay our development programs, or result in the loss of assets or other liability. We have monitoring systems in place and have detected at least one intrusion into our computer systems and attempts to exfiltrate our data. Although our investigation in each case indicates that it did not have a material adverse effect on our operations nor result in any compromise of our information, there can be no assurance of a similar result in the future. The COVID-19 pandemic and our reliance on internet technology and the number of our employees who are working remotely has increased the opportunities for cybercriminals to exploit vulnerabilities. Overall, there has been a significant increase in fraud schemes, including a successful social engineering attack against us through one of our employees. We cannot assure you that our data protection efforts and our investment in information technology will prevent breakdowns, data leakages, breaches in our systems or other cyber incidents that could have a material adverse effect upon our reputation, business, operations or financial condition.

Furthermore, as the cyber threat landscape evolves, these attacks are growing in frequency, sophistication and intensity, and becoming increasingly difficult to detect. There can be no assurance that we and our third-party CROs and other third parties upon which we rely will be successful in detecting, preventing or fully recovering systems or data from all breakdowns, service interruptions, attacks or breaches of systems that could adversely affect our business and operations and/or result in the loss or disclosure of critical or sensitive data or other assets, which could result in financial, legal, business or reputational harm to us. Ransomware attacks have risen dramatically and we may be forced to pay to unlock our data and information, re-access our systems and resume our ability to conduct business operations. The loss of clinical trial data for our investigational products could significantly increase our costs to recover or reproduce the data and result in delays in our development programs, impair our ability to obtain marketing approval and reduce the commercial opportunity for our investigational products.

Moreover, significant disruptions of our internal information technology systems or security breaches could result in the loss, misappropriation, and/or unauthorized access, use, or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information, and personal information), which could result in financial, legal, business, and reputational harm to us. In particular, any such event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal

and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business.

Although we maintain insurance coverage to insure against losses suffered as a result of malicious intrusions and cyberattacks, such coverage may be insufficient to fully compensate us for the loss or there may be disputes with our insurers about the availability of insurance coverage for our claims. Cyber insurance may become increasingly difficult to maintain and we may not be able to maintain coverage at a reasonable cost or in an amount adequate to compensate for any loss or satisfy any liability that may arise.

Unfavorable global economic, political and trade conditions could adversely affect our business, financial condition or results of operations and may exacerbate the effects of the risks described herein.

Current global economic conditions are highly volatile due to a number of reasons, including the COVID-19 pandemic and geopolitical instability arising from the ongoing military conflict between Russia and Ukraine and the imposition of sanctions against Russia by the U.S. and EU, which has contributed to rising inflation that has increased our operating expenses and disruptions in the capital and credit markets that may reduce our ability to raise additional capital when needed on acceptable terms, if at all. While we do not have any clinical studies ongoing in Russia, Ukraine or Belarus, we do file patent applications in Russia and the Eurasian patent office, which is headquartered in Moscow. Sanctions may make it difficult to file and maintain patents in these countries, and Russia has begun taking actions against "unfriendly" countries, including the U.S., which may adversely affect the scope of and/or our ability to enforce our intellectual property rights.

Emerging international trade relations may also adversely impact our operations and/or financial condition by limiting or preventing the activities of third parties that we engage or increasing the cost of our operations. For example, WuXi Biologics, located in China, is our sole manufacturer of our investigational biologics, including zimberelimab, domvanalimab and AB308. In addition, if tariffs were to be imposed on the investigational products they manufacture for us, such tariffs would have an adverse impact on our operating results and financial condition.

Furthermore, the current inflationary environment related to increased aggregate demand and supply chain constraints have increased our operating expenses and may continue to affect our operating expenses. Economic conditions may also strain our suppliers, possibly resulting in supply disruptions that impact our ongoing clinical trials and other operations. A significant worsening of global economic conditions could materially increase these risks we face.

Any new or prolonged downturn of global economic conditions could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Our future growth may depend, in part, on our ability to operate in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability may depend, in part, on our ability to commercialize our investigational products in foreign markets for which we may rely on collaboration with third parties. We are not permitted to market or promote any of our investigational products before we receive marketing approval from the applicable regulatory authority in that foreign market, and we may never receive such marketing approval for any of our investigational products. To obtain marketing approval in many foreign countries, we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our investigational products, and we cannot predict success in these jurisdictions. If we obtain approval of our investigational products and ultimately commercialize our investigational products in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for our investigational products in foreign markets;
- our inability to directly control commercial activities because we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;

- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- the existence of additional potentially relevant third-party intellectual property rights;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of our investigational products could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

We or the third parties upon which we depend may be adversely affected by earthquakes, fires or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our headquarters and main research facility are located in the San Francisco Bay Area, which in the past has experienced severe earthquakes and fires. In addition, fires and other natural disasters may increase in frequency and severity over time due to climate change. If these earthquakes, fires, other natural disasters, terrorism and similar unforeseen events beyond our control prevented us from using all or a significant portion of our headquarters or research facility, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. We do not have a disaster recovery or business continuity plan in place and may incur substantial expenses as a result of the absence or limited nature of our internal or third-party service provider disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business. Furthermore, integral parties in our supply chain are operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our ability to conduct our clinical trials, our development plans and business.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history and our ability to generate profits in the future is uncertain. Unused net operating loss carryforwards (NOLs) for the tax year ended December 31, 2017 and prior tax years will carry forward to offset future taxable income, if any, until such unused NOLs expire. Unused NOLs generated after December 31, 2017, under current tax law, will not expire. Our NOLs may be carried forward indefinitely. In addition, the future deductibility of such NOLs will be limited to 80% of current year taxable income in any given year.

Both our current and our future unused losses (and tax credit carryforwards) may be subject to further limitation under Sections 382 and 383 of the Internal Revenue Code (IRC) of 1986, as amended, if we undergo an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period. We performed an analysis under IRC Section 382 and 383 through October 31, 2020 with respect to our net operating loss and credit carryforwards. We concluded that an ownership change, as defined under IRC Section 382, occurred in previous years but that such ownership change did not result in the expiration of our net operating loss or credit carryforwards prior to utilization. We may incur additional ownership changes in the future in connection with any equity issuance, including any additional issuances to Gilead. If we experience any such ownership change, we may be limited in our ability to use our net operating loss and credit carryforwards and be required to make material cash tax payments.

Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited. For example, while California recently enacted a franchise tax law restoring the usability of California state NOLs to offset taxable income for tax years beginning on January 1, 2022, previous law significantly limited the use of California state NOLs for taxable years 2020 and 2021. Similar laws in the future could accelerate or permanently increase state taxes owed.

Therefore, even if we attain sustained profitability, we may be unable to use all or a material portion of our NOLs and other tax attributes, which could adversely affect our future cash flows.

Changes in tax laws and regulations or exposure to additional tax liabilities could adversely affect our financial results.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, or IRS, and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, beginning in 2022, the Tax Cuts and Jobs Act of 2017 eliminates the option to currently deduct research and development expenditures and requires taxpayers to capitalize and amortize U.S. based and non-U.S. based research and development expenditures over five and fifteen years, respectively, pursuant to IRC Section 174. We cannot predict whether, when, in what form, or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or issued, which could result in an increase in our or our stockholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law.

Risks Related to Our Industry

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

We face an inherent risk of product liability exposure related to the testing of our investigational products 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 investigational products or products caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, product liability claims may result in:

- delay or termination of clinical trials;
- decreased demand for any investigational products or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial subjects;
- initiation of investigations by regulators;
- significant costs to defend the related litigation and diversion of management's time and our resources;
- substantial monetary awards to study subjects or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage as our investigational products advance through clinical trials and if we successfully commercialize any products. 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.

Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.

We and any potential collaborators may be subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the FTC Act), that govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our collaborators. In addition, we may obtain health information from third

parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH). Depending on the facts and circumstances, we could be subject to significant penalties if we violate HIPAA.

The legislative and regulatory landscape for privacy and data security continues to evolve, and we expect that there will continue to be new proposed laws, regulations and industry standards relating to privacy and data security in the United States, the EU and other jurisdictions. This increased focus on privacy and data security issues may negatively affect our operating results and our business. For example, the California Consumer Privacy Act of 2018 (CCPA), which took effect on January 1, 2020, gives California residents expanded rights to access and require deletion of their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. In addition, the CCPA authorizes private lawsuits to recover statutory damages for certain data breaches. While it exempts some data regulated by HIPAA and certain clinical trials data, the CCPA may increase our compliance costs and potential liability with respect to other personal information we collect about California residents. Some observers note that the CCPA could mark the beginning of a trend toward more stringent privacy legislation in the U.S., which could increase our potential liability and adversely affect our business.

International data protection laws also apply to health-related and other personal data obtained outside the United States. In the European Union, Regulation (EU) 2016/679 (General Data Protection Regulation) took effect in May 2018 and imposes, in some cases, stricter obligations than data protection laws in the United States on the use of health-related and other personal data. These requirements include the obligation to appoint data protection officers in certain circumstances, rights for individuals to be "forgotten" and to data portability, and the obligation to make public notification of significant data breaches. Under the General Data Protection Regulation, data protection authorities can also impose administrative fines of up to 4% of our total worldwide turnover or up to €20 million (whichever is higher). In addition, the General Data Protection Regulation only permits the transfer of personal data outside the European Economic Area (EEA) to countries that offer a level of data protection deemed adequate by the European Commission, unless an approved data transfer mechanism is in place. One such mechanism was invalidated by the European Court of Justice, adding to the complexity of transferring personal data outside the EEA. The General Data Protection Regulation increases our responsibility and liability in relation to personal data that we process, and we must put in place additional mechanisms to ensure compliance with the new EU data protection rules.

Failure to comply with U.S. and international data protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

Our business operations expose us to broadly applicable fraud and abuse, transparency, government price reporting, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Our operations are subject, either directly or indirectly through our customers and third-party payors, to various U.S. federal and state health care laws, including fraud and abuse, transparency and other healthcare laws and regulations, and similar laws in other jurisdictions in which we conduct our business. These laws may impact, among other things, our research and proposed sales, marketing and education programs and constrain the business of financial arrangements and relationships with healthcare providers, physicians and other parties through which we market, sell and distribute our products for which we obtain marketing approval. The laws that may affect our ability to operate include, but are not limited to the federal Anti-Kickback Statute; federal civil and criminal false claims laws, such as the False Claims Act (FCA); HIPAA; federal and state consumer protection and unfair competition laws; the federal transparency requirements under the Physician Payments Sunshine Act; state and foreign law equivalents of each of these federal laws; and state and foreign laws that require pharmaceutical companies to implement compliance programs. Many of these laws are discussed in detail in "Item 1. Business—Government Regulation—Other U.S. Healthcare Laws and Compliance Requirements" for additional information.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. Federal and state enforcement bodies have continued their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Responding to investigations can be time-and resource-consuming and can divert management's attention from the business. Any such investigation or settlement could increase our costs or otherwise have an adverse effect on our business.

Ensuring that our business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. We have entered into consulting and advisory board arrangements with physicians and other healthcare providers, including some who could influence the use of our investigational products, if approved. Because of the complex and far-reaching nature of these laws, regulatory agencies may view these transactions as prohibited arrangements that must be restructured, or discontinued, or for which we could be subject to other significant civil, criminal and administrative penalties such as fines, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, diminished profits and future earnings, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could substantially disrupt our operations. If any of the physicians or other healthcare providers or entities with which 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 healthcare programs.

Changes in healthcare law and implementing regulations, as well as changes in healthcare policy, may impact our business in ways that we cannot currently predict, and may have a significant adverse effect on our business and results of operations.

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of investigational products, restrict or regulate post-approval activities, and affect the ability to profitably sell investigational products for which marketing approval is obtained. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, on August 16, 2022, President Biden signed into law the Inflation Reduction Act of 2022 (IRA), which, among other things, (1) directs the U.S. Department of Health and Human Services to negotiate the price of certain single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in Affordable Care Act marketplaces through plan year 2025 and eliminates the "donut hole" under the Medicare Part D program by significantly lowering the beneficiary maximum out-of-pocket cost and through a newly established manufacturer discount program. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. We expect that other healthcare reform measures may be adopted in the future, and that any such health reform measures could have an adverse effect on our business and/or results of operation. For additional detail regarding health care reform activities that may impact our business, see "Item 1. Business—Government Regulation—Healthcare Reform" for additional information.

We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for violations.

U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations (collectively, Trade Laws) prohibit, among other things, companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We also expect our non-U.S. activities to increase over time. We expect to rely on third parties for

research, preclinical studies, and clinical trials and/or to obtain necessary permits, licenses, patent registrations, and other marketing approvals. We can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

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 have a material adverse effect on the success of our business.

We, and the third parties with which we share our facilities, 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. Each of our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Each of our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. We could be held liable for any resulting damages in the event of contamination or injury resulting from the use of hazardous materials by us or the third parties with which we share our facilities, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, 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 connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research and development. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Owning our Common Stock

The stock price of our common stock has been and may continue to be volatile or may decline regardless of our operating performance.

The market price of our common stock has fluctuated and may fluctuate significantly in response to numerous factors, many of which are beyond our control, including:

- overall performance of the equity markets;
- our operating performance and the performance of other similar companies;
- results from our ongoing clinical trials and future clinical trials with our current and future investigational products or of our competitors;
- changes in our projected operating results that we provide to the public, our failure to meet these projections or changes in recommendations by securities analysts that elect to follow our common stock;
- regulatory, trade or legal developments in the United States and other countries, including changes in tariffs or other trade restrictions and the changes in the structure of healthcare payment systems;
- the level of expenses related to future investigational products or clinical development programs;
- our failure to achieve product development goals in the timeframe we announce;
- announcements of acquisitions, strategic alliances or significant agreements by us or by our competitors;
- recruitment or departure of key personnel;
- the economy as a whole and market conditions in our industry;
- trading activity by a limited number of stockholders who together beneficially own a majority of our outstanding common stock;
- the size of our market float; and
- any other factors discussed in this report.

In addition, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many immuno-oncology companies. Stock prices of many immuno-oncology companies have fluctuated in a manner unrelated or disproportionate to the operating performance of those companies. In the past, stockholders have filed securities class action litigation following periods of market volatility. If we were to become involved in securities litigation, it could subject us to substantial costs, divert resources and the attention of management from our business and adversely affect our business.

The amount of our future losses is uncertain and our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

Our quarterly and annual operating results may fluctuate significantly in the future due to a variety of factors, many of which are outside of our control and may be difficult to predict, including the following:

- the timing and success or failure of clinical trials for our investigational products or competing investigational products, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- our progress towards the achievement of any product development goals or milestones we announce, including any delays or failures which lead to the suspension or termination of any clinical trial or development program;
- the timing and cost of, and level of investment in, research and development activities relating to our investigational products, which may change from time to time;
- option fees received by us in connection with option exercises by Gilead and/or Taiho pursuant to their respective option agreements and/or payments received by us from Gilead or Taiho in connection with the achievement of certain development and/or regulatory milestones;
- amounts payable by us in connection with the achievement of development, regulatory and commercial milestones under our in-license and other strategic agreements;
- our ability to attract, hire and retain qualified personnel;
- expenditures that we will or may incur to develop additional investigational products;
- our ability to obtain marketing approval for our investigational products, and the timing and scope of any such approvals we may receive;
- the changing and volatile U.S. and global economic environments; and
- future accounting pronouncements or changes in our accounting policies.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

The concentration of our stock ownership will likely limit our stockholders' ability to influence corporate matters, including the ability to influence the outcome of director elections and other matters requiring stockholder approval.

Based upon shares outstanding as of December 31, 2022, our executive officers, directors and the holders of more than 5% of our outstanding common stock, in the aggregate, beneficially owned approximately 47.6% of our common stock. In particular, Gilead owns approximately 18.9% of our outstanding common stock, and we have appointed its two designees to our board of directors pursuant to the terms of our investor rights agreement. As a result, these stockholders, acting together, will have significant influence over all matters that require approval by our stockholders, including the election of directors and approval of significant corporate transactions. Corporate actions

might be taken even if other stockholders oppose them. This concentration of ownership might also have the effect of delaying or preventing a change of control of our company that other stockholders may view as beneficial.

Delaware law and provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make a merger, tender offer or proxy contest difficult, thereby depressing the trading price of our common stock.

Our status as a Delaware corporation and the anti-takeover provisions of the Delaware General Corporation Law may discourage, delay or prevent a change in control by prohibiting us from engaging in a business combination with an interested stockholder for a period of three years after the person becomes an interested stockholder, even if a change of control would be beneficial to our existing stockholders. In addition, our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may make the acquisition of our company more difficult, including the following:

- a classified board of directors with three-year staggered terms, which could delay the ability of stockholders to change the membership of a majority of our board of directors;
- the ability of our board of directors to issue shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of our board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by a majority vote of our entire board of directors, the chairman of our board of directors or our chief executive officer, which could delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors;
- the requirement for the affirmative vote of holders of at least 66⅔% of the voting power of all of the then-outstanding shares of the voting stock, voting together as a single class, to amend the provisions of our amended and restated certificate of incorporation relating to the management of our business or our amended and restated bylaws, which may inhibit the ability of an acquirer to effect such amendments to facilitate an unsolicited takeover attempt; and
- advance notice procedures with which stockholders must comply to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

In addition, as a Delaware corporation, we are subject to Section 203 of the Delaware General Corporation Law. These provisions may prohibit large stockholders, in particular those owning 15% or more of our outstanding voting stock, from merging or combining with us for a certain period of time. A Delaware corporation may opt out of this provision by express provision in its original certificate of incorporation or by amendment to its certificate of incorporation or bylaws approved by its stockholders. However, we have not opted out of this provision.

These and other provisions in our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by our then-current board of directors, including delay or impede a merger, tender offer or proxy contest involving our company. The existence of these provisions could negatively affect the price of our common stock and limit opportunities for our stockholders to realize value in a corporate transaction.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation and our bylaws provide 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, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our bylaws or any action asserting a claim against us that is governed by the internal affairs doctrine. In addition, to prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our bylaws provide that the federal district courts of the United States will be the exclusive forum for resolving 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 it finds favorable for disputes with us or our directors, officers or other employees and may discourage these types of lawsuits. While the Delaware courts have determined that these types of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of these provisions, which may require significant additional costs associated with resolving such action in other jurisdictions, and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

General Risk Factors

Sales of substantial amounts of our outstanding shares may cause the price of our common stock to decline.

The price of our common stock could decline if there are substantial sales of our common stock, particularly sales by our directors, executive officers and significant stockholders, or if there is a large number of shares of our common stock available for sale and the market perceives that sales will occur. We have also registered shares of common stock that we have issued and may issue under our employee equity incentive plans. These shares can be sold freely in the public market upon issuance, subject to vesting conditions and, in the case of our affiliates, volume limitations under Rule 144 under the Securities Act of 1933, as amended.

If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could result in sanctions or other penalties that would harm our business.

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act and the rules and regulations of the New York Stock Exchange. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal controls over financial reporting.

Our 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 in accordance with generally accepted accounting principles. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected. Accordingly, we cannot assure you that we will not in the future identify one or more material weaknesses in our internal control over financial reporting, which may have a negative impact on our ability to timely and accurately produce financial statements, may result in a material misstatement of our Consolidated Financial Statements or may negatively impact the confidence level of our stockholders and other market participants with respect to our reported financial information.

Ensuring that we have adequate internal controls over financial reporting is a costly and time-consuming effort that needs to be re-evaluated frequently. Remote work arrangements as a result of the COVID-19 pandemic have led to changes in work patterns that can make it more difficult to properly perform our controls and may create risks that result in deficiencies in the design of our controls. To the extent necessary, implementing any changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

As of December 31, 2022, our corporate headquarters, which includes executive offices and research and development and business operations, consist of approximately 151,000 square feet of leased office and laboratory space in an office park in Hayward, California. We also lease approximately 109,000 square feet of office space in Brisbane, California. The lease terms for both facilities expire in 2031, subject to options for us to extend the lease term. In October 2022, we entered into an agreement to sublease approximately 31,000 unfinished square feet of our Brisbane office to another company, which is expected to commence in 2023 and extends through 2028, with the sublessee having options to extend the lease term and/or to lease additional space within the building.

Item 3. Legal Proceedings

We are not currently a party to any material legal proceedings. From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity, reputational harm and other factors.

Item 4. Mine Safety Disclosures

None.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information and Stockholders

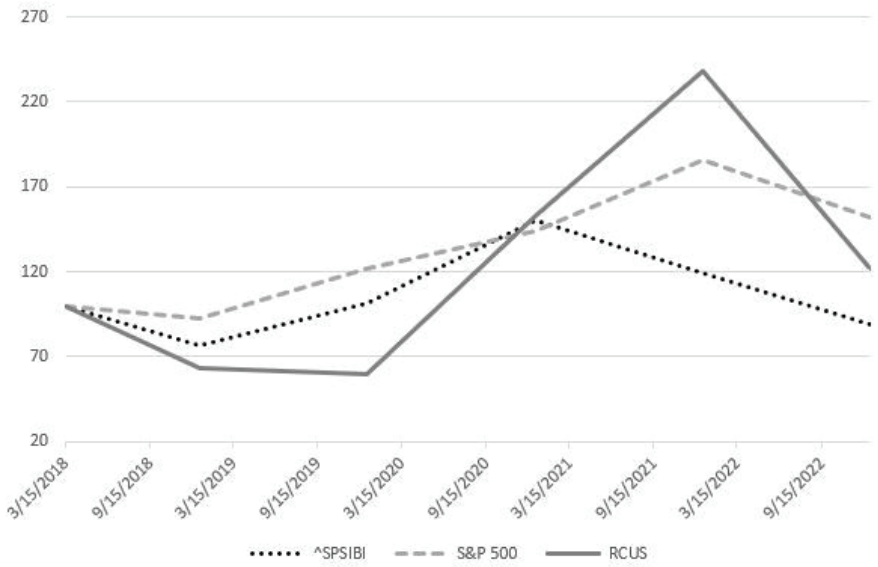
Our common stock trades on the New York Stock Exchange under the symbol "RCUS." As of February 17, 2023, we had 38 stockholders of record as reported by our transfer agent. This does not include beneficial owners whose shares are held in street name.

Dividend Policy

We have never declared or paid cash dividends on our stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors.

Performance Graph

The following graph compares the cumulative stockholders returns from March 15, 2018 (first day of trading of our common stock), through December 31, 2022 for (i) our common stock, (ii) the S&P Biotechnology Index and (iii) S&P 500 Index, assuming $100 invested on March 15, 2018, and reinvestment of dividends if paid. The stockholder return shown on the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns. This graph shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.



$100 investment in stock or index	Ticker	3/15/2018	12/31/2018	12/31/2019	12/31/2020	12/31/2021	12/31/2022
Arcus Biosciences, Inc.	RCUS	$ 100	$ 63	$ 59	$ 153	$ 238	$ 122
S&P Biotechnology Index	SPSIBI	$ 100	$ 77	$ 101	$ 150	$ 120	$ 89
S&P 500 Index	S&P 500	$ 100	$ 93	$ 122	$ 144	$ 186	$ 152

Issuer Purchases of Equity Securities

None.

Item 6. Reserved

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

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes included in this Annual Report. This discussion and other parts of this report contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations, and intentions. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section of this report titled "Risk Factors."

Overview

We are a clinical-stage biopharmaceutical company focused on creating best-in-class therapies. Using our robust and highly efficient drug discovery capability, we have created a significant portfolio of investigational products which are in clinical development, with our most advanced molecule, an anti-TIGIT antibody, now in four Phase 3 registrational studies targeting lung and gastrointestinal cancers. Our deep portfolio of novel small molecules and enabling antibodies allows us to create highly differentiated therapies, which we are developing to treat multiple large indications. We expect our clinical-stage portfolio to continue to expand and to include molecules targeting immuno-oncology, cancer cell-intrinsic and immunological pathways. Our vision is to create, develop and commercialize highly differentiated therapies that have a meaningful impact on patients.

Recent Developments

Following is a summary of recent significant developments affecting our business:

- In November 2022, we announced the amended study design of ARC-10. Under the amended study design, we are comparing domvanalimab and zimberelimab to pembrolizumab and the study will no longer include a chemotherapy arm.
- In November 2022, we announced that we had initiated ARC-20, a Phase 1/1b study of HIF-2α inhibitor AB521 in cancer patients.
- In December 2022, we announced positive results from the fourth interim analysis of the ARC-7 study in patients with first-line, metastatic NSCLC with PD-L1 tumor proportion score (TPS) ≥50% without epidermal growth factor receptor or anaplastic lymphoma kinase (EGFR/ALK) mutations. ARC-7 is a Phase 2, multicenter, three-arm, randomized, open-label study evaluating the combinations of Fc-silent anti-TIGIT monoclonal antibody domvanalimab plus anti-PD-1 monoclonal antibody zimberelimab (doublet) and domvanalimab plus zimberelimab and etrumadenant, an adenosine A2a/A2b receptor antagonist (triplet), versus zimberelimab monotherapy.
- In the third quarter of 2022, together with Gilead, we initiated two new registrational Phase 3 trials including STAR-121 and STAR-221. STAR-121 is being operationalized by Gilead and is evaluating domvanalimab plus zimberelimab plus chemotherapy against the standard of care (pembrolizumab) in first line, PD-l all-comers NSCLC. STAR-221, which we are operationalizing, is evaluating domvanalimab plus zimberelimab and chemotherapy versus the standard of care (nivolumab) plus chemotherapy in first-line, locally advanced unresectable or metastatic gastric, esophageal and gastrointestinal junction adenocarcinomas. During the fourth quarter 2022, Taiho opted to participate in both studies.

Strategic Partnerships

Gilead

In 2020, we and Gilead entered into the Gilead Collaboration Agreement, the Stock Purchase Agreement, and Investor Rights Agreement. The Gilead Collaboration Agreement and the Stock Purchase Agreement were amended in 2021, and the Investor Rights Agreement was amended in 2022.

Under the Gilead Collaboration Agreement, Gilead obtained an exclusive license to zimberelimab and time-limited exclusive options to all of our then-current and future programs during the 10-year collaboration term. In 2021, Gilead obtained rights to an additional four of our investigational products: domvanalimab, etrumadenant, quemliclustat and AB308. For each program to which Gilead exercised or exercises its option, the parties will co-develop globally and co-commercialize the program in the U.S., subject to certain exceptions, and Gilead will have

the right to commercialize the program outside of the United States, subject to the rights of our existing partners in certain territories.

Under the Stock Purchase Agreement Gilead has the right, at its option until July 2025, to purchase up to a maximum ownership of 35% of our then-outstanding voting common stock, and the Investor Rights Agreement provides for a three-year standstill, three-year lockup and the right to designate two individuals to be appointed to our Board of Directors. As of December 31, 2022, Gilead held approximately 18.9% of our outstanding common stock.

Taiho

In 2017, we entered into an Option and License Agreement (Taiho Agreement) with Taiho Pharmaceutical Co., Ltd. (Taiho) pursuant to which Taiho was granted time-limited options to exclusively license for Japan and certain other territories in Asia (excluding China) the development and commercialization rights to each of our programs that arose over a five-year period ending in September 2022. As of December 31, 2022, Taiho has licenses to our (i) adenosine receptor antagonist program (including etrumadenant); (ii) anti-PD-1 program (including zimberelimab); and (iii) our anti-TIGIT program (including domvanalimab and AB308).

Other Licenses, Collaborations, and R&D Arrangements

We in-licensed rights to zimberelimab and CD39 from WuXi Biologics Ireland Limited (WuXi Biologics), and in-licensed rights to domvanalimab from Abmuno Therapeutics LLC (Abmuno). We also have a clinical collaboration agreement with AstraZeneca for the PACIFIC-8 trial evaluating domvanalimab and durvalumab in Stage 3 NSCLC, and BVF Partners L.P. (BVF) to support the discovery and development of compounds for the treatment of inflammatory diseases.

Financial Overview

Since commencing operations in 2015, we have devoted substantially all of our efforts and financial resources to building our research and development capabilities, advancing our investigational product pipeline, and establishing our corporate infrastructure.

We expect to incur substantial expenditures in the foreseeable future as we expand our pipeline and advance our investigational products through clinical development, the regulatory approval process and, if approved, commercial launch activities. For example, in the near term we expect to incur substantial expenses relating to our ongoing and planned clinical trials, the development and validation of our manufacturing processes, and other preclinical, research and discovery development activities. These expenditures will be partially offset by reimbursements for shared expenses from our collaborations, primarily the Gilead collaboration, for certain expenses incurred on their optioned programs. At this time, we cannot reasonably estimate the nature, timing or aggregate amount of costs for our development, potential commercialization, and internal research and development programs.

We have no internal manufacturing facilities, and thus all of our manufacturing activities are contracted to third parties. We also utilize third-party clinical research organizations to manage and execute various aspects of our clinical development and trials.

To date, we have financed our operations primarily from the sale of our equity securities and revenue through research, collaboration and license agreements with our strategic partners including Gilead. We will need substantial additional funding to support our continuing operations and pursue our development strategy. Until such time that we can generate significant revenue from sales of our investigational products, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including existing or potential collaborations with other companies or other strategic transactions. Adequate funding may not be available to us on acceptable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back, or discontinue the development and commercialization of our investigational products or delay our efforts to expand our product pipeline.

As of December 31, 2022, we had $1.14 billion of cash, cash equivalents and marketable securities, which we believe will be sufficient to fund our planned operations into 2026. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect.

Components of Operating Results

Revenues

We have not generated any revenue from product sales and do not expect to generate any revenue from product sales for the foreseeable future. All revenue recognized to date has been through research, collaboration and license arrangements with strategic partners.

License and Development Services Revenue

Our license and development services revenue consists of amounts recognized from the portions of the nonrefundable upfront and milestone payments received from Gilead and Taiho and allocated to performance obligations for licenses or R&D activities performed by us as we develop our investigational products under the terms of our collaboration agreements. License and development services revenues are recognized based upon the timing of the delivery of a license or service if delivery is complete, or based on estimates of each performance obligation's percentage of completion at the period end if it is still in process. We calculate percentage of completion as a ratio of effort incurred to date on each performance obligation to the total estimated effort to be incurred to satisfy that performance obligation.

Other Collaboration Revenue

Other collaboration revenue consists of amounts recognized from the portions of the nonrefundable upfront payments received from Gilead and Taiho and allocated to performance obligations relating to the customer's access to our investigational pipeline over the collaboration period. Other collaboration revenues are recognized throughout the collaboration period.

Operating Expenses

Research and Development Expenses

Our research and development expenses consist of expenses incurred in connection with the research and development of our pipeline programs. These expenses include preclinical and clinical expenses, payroll and personnel expenses, including stock-based compensation for our employees, laboratory supplies, product licenses, consulting costs, contract research, and depreciation. Shared facility expenses are allocated to functional groups proportionally based on usage. Under certain collaboration agreements we agree to share research and development expenses with our partners. Such cost sharing arrangements may result in receiving reimbursement from our partners or require that we reimburse our partners for qualified expenses. We expense both internal and external research and development costs as they are incurred. We record advance payments for services that will be used or rendered for future research and development activities as prepaid expenses and recognize them as an expense as the related services are performed. We recognize reimbursement for shared costs incurred by us and reimbursed by our partners as a reduction in research and development expense.

We do not allocate our costs by investigational product, as a significant amount of research and development expenses include internal costs, such as payroll and other personnel expenses, and certain external costs that are not recorded at the investigational product level. In particular, with respect to internal costs, several of our departments support multiple research and development programs, and we do not allocate those costs by investigational product.

The level of our future research and development investment will depend on a number of factors and uncertainties, including the breadth of the joint development program agreed to with Gilead for the optioned programs, the outcome of our efforts, and the amount of cost reimbursements or milestone payments we receive from our collaborators. We expect our research and development expenses to increase substantially during the next few years as we pursue joint development programs with Gilead for our five optioned molecules and advance these programs towards regulatory approval. We also expect to advance new programs into the clinic. All of this will require significant growth in our development capabilities and infrastructure. In addition, our joint development programs with Gilead for the optioned molecules are anticipated to include a significant number of later-stage clinical trials, which typically include a larger number of subjects, are of a longer duration and include more geographic regions. As we advance our clinical-stage programs and prepare to seek regulatory approval, we will also need to increase our late-stage manufacturing activities. As a result, we expect our preclinical, clinical, and contract manufacturing expenses to increase significantly relative to what we have incurred to date.

In addition, under our arrangements with WuXi Biologics, Abmuno, AstraZeneca and BVF, we may incur additional clinical and regulatory milestone payments based on the development progress of our investigational products. We may also be required to pay royalties in the event of a successful product launch and our receipt of commercial revenues. Therefore, we are unable to predict the timing or the final cost to complete our clinical programs or validation of our manufacturing and supply processes and delays may occur due to numerous factors. Factors that could cause or contribute to delays or additional costs include, but are not limited to, those discussed in "Item 1A. Risk Factors."

General and Administrative Expenses

General and administrative expenses consist principally of personnel-related costs including payroll and stock-based compensation for personnel in executive, finance, human resources, information technology, business and corporate development, and other administrative functions. Shared facility expenses are allocated to functional groups proportionally based on usage. Our general and administrative expenses also include professional fees for legal, consulting, and accounting services, rent and other facilities costs, fixed asset depreciation, and other general operating expenses not otherwise classified as research and development expenses. We do not receive significant reimbursements of these costs through our collaboration with Gilead.

We anticipate that our general and administrative expenses will increase during the next few years as we support our growing research and development activities, including due to staff expansion, and other costs associated with increased infrastructure needs.

Non-Operating Income, net

Non-operating income, net consists primarily of interest earned on our investments in fixed-income marketable securities and non-cash interest expense incurred under the effective interest method on our liability for sale of future royalties to BVF.

Results of Operations

The following table summarizes our results of operations (in millions):

	Year Ended December 31, 2022	Change	Year Ended December 31, 2021	Change	Year Ended December 31, 2020
Revenues:					
License and development service revenue	$ 74	(79)%	$ 345	*	$ 55
Other collaboration revenue	38	-	38	65%	23
Total revenues	112	(71)%	383	*	78
Operating expenses:					
Research and development	288	12%	257	62%	159
General and administrative	104	44%	72	67%	43
Total operating expenses	392	19%	329	63%	202
Income (loss) from operations	(280)	*	54	(144)%	(124)
Non-operating income, net	14	*	1	-	1
Income (loss) before income taxes	(266)	*	55	(145)%	(123)
Income tax expense	(1)	(50)%	(2)	*	-
Net income (loss)	$ (267)	*	$ 53	(143)%	$ (123)

* Not meaningful

Total Revenues

The decrease in Total revenues for 2022 as compared to 2021 was primarily driven by higher revenues in 2021 due to Gilead's exercise of its options, partially offset by increased revenues from R&D services in 2022 including $4 million in revenue recognized due to changes in the total estimated percentage of completion based on management's estimated total effort for the program to be incurred in the future to satisfy the performance obligations, primarily related to revised clinical trial assumptions for R&D and commercial activities.

The increase in Total revenues for 2021 as compared to 2020 was primarily driven by Gilead's exercise of its options and consisted of increases of $290 million in license and development services revenues and $15 million in collaboration revenues.

See Note 5, Revenues to our Consolidated Financial Statements, in Part II, Item 8 for further discussion of the amount and timing of revenues recognized from our collaboration agreements.

Research and Development Expenses

The increase of 12%, or $31 million, in Research and development expenses for 2022 as compared to 2021 was driven by $167 million in higher costs incurred to support our expanded clinical and development activities partially offset by $136 million in higher reimbursements for shared expenses from our collaborations, primarily the Gilead collaboration which was expanded in December 2021. Our expanding clinical and development activities as we enrolled more patients in our existing and new studies including domvanalimab and zimberelimab combination studies drove increases of $10 million in net manufacturing costs and $9 million in net clinical costs. Our growing headcount drove a $13 million increase in net employee compensation costs. The overall increase was partially offset by a $7 million decrease in net scientific licenses expense.

The increase of 62%, or $98 million, in Research and development expenses for 2021 as compared to 2020 was driven by $119 million in higher costs incurred to support our expanded clinical and development activities partially offset by $21 million in higher reimbursements for shared expenses from our collaborations, primarily the Gilead collaboration which was expanded in December 2021. Our growing headcount and our 2021 stock awards drove a $42 million increase in net employee compensation costs. Net costs for our ongoing clinical studies and related manufacturing increased $33 million and $6 million, respectively, as a result of the increased number of clinical-stage programs and trials compared to the prior year. We incurred increases of $10 million in office facilities and technology expense, $7 million in consulting services, and $5 million in lab supplies and equipment, as we expanded our development efforts. The overall increase was partially offset by a $7 million decrease in net scientific licenses expense.

For 2022 and 2021, we recognized gross reimbursements of $161 million and $25 million, respectively, for shared expenses from our collaborations, primarily the Gilead collaboration which was expanded in December 2021.

General and Administrative Expenses

The increase in General and administrative expenses for 2022 as compared to 2021 was primarily driven by the increased complexity of supporting our expanding clinical pipeline and partnership obligations. Our growing headcount and our 2022 stock awards drove a $15 million increase in employee compensation costs, including $6 million in increased non-cash stock-based compensation. We also incurred a $13 million increase in office facilities expense due to the expansion of our office space to support our higher headcount.

The increase in General and administrative expenses for 2021 as compared to 2020 was primarily driven by the increased complexity of supporting our expanding clinical pipeline and partnership obligations, as well as costs associated with being a public company. Our growing headcount and our 2021 stock awards drove a $24 million increase in employee compensation costs, including $16 million in increased non-cash stock-based compensation. We also incurred a $4 million increase in office facilities expense due to our expanding office space to support our higher headcount and an increase of $2 million in consulting expenses due to corporate development activities.

Non-operating Income, Net

The increase in Non-operating income, net for 2022 as compared to 2021 was primarily due to a larger portfolio of marketable fixed-income securities and higher interest income resulting from increased investment yields as compared to the prior year.

Non-operating income, net was flat for 2021 as compared to 2020.

Income Tax Expense

The decrease in Income tax expense for 2022 as compared to 2021 was due primarily to lower pretax income. The 2022 income tax expense considers the impact of the capitalization of R&D expenses for income tax purposes

due to changes in U.S. legislation. The capitalization of R&D expenses may materially impact income tax expense in future years.

The increase in Income tax expense for 2021 as compared to 2020 was due to an increase in pretax income, primarily resulting from Gilead's exercise of its options to our programs.

Liquidity and Capital Resources

Sources of Liquidity

To date, we have financed our operations primarily from the sale of our equity securities and payments received under our research, collaboration and license agreements with our strategic partners, including Gilead. We expect to incur substantial expenditures in the foreseeable future for the development and potential commercialization of our investigational products and ongoing internal research and development programs. At this time, we cannot reasonably estimate the nature, timing or aggregate amount of costs for our development, potential commercialization, and internal research and development programs.

As of December 31, 2022, we had $1.14 billion of cash, cash equivalents and marketable securities, compared to $681 million as of December 31, 2021. The increase in cash from the prior year end is primarily due to the receipt of $725 million in payments from Gilead in January 2022, related to their option exercises in December 2021. Our cash and investments are held in a variety of interest-bearing instruments, including money market funds, U.S. treasury securities, and corporate securities and commercial paper.

Based on our existing business plan, we believe that our existing cash, cash equivalents, and marketable securities will be sufficient to fund our planned level of operations into 2026.

Our cash flow and financing requirements are determined by analyses of operating and capital spending budgets. It is challenging to predict the nature, timing and estimated long-range costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our investigational products. This is made more challenging by events outside of our control, such as the evolving COVID-19 pandemic. Accordingly, our operating plan may change, including as a result of factors currently unknown to us, and we may need to seek additional funds sooner than planned. Such financing may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may adversely affect our business. 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.

See “Item 1A. Risk Factors” for additional risks associated with our substantial capital requirements.

Cash Flows

The following table summarizes our cash flow activities for each of the periods presented below (in millions):

	Year Ended December 31,		
Net cash provided by (used in):	**2022**	**2021**	**2020**
Operating activities	$ 438	$ (256)	$ 111
Investing activities	(413)	(4)	(434)
Financing activities	33	237	439

Operating Activities

Net cash provided by operating activities for 2022 was $438 million as compared to net cash used in operating activities of $256 million for the prior year. The change in operating cash flows is primarily due to the $725 million received from Gilead in January 2022 under the Gilead Collaboration Agreement, partially offset by increased expenses incurred to support our expanded clinical development activities.

Net cash used in operating activities for 2021 was $256 million as compared to net cash provided by operating activities of $111 million for the prior year. The change in operating cash flows is primarily due to the expenses incurred to support our expanded clinical development activities and general and administrative costs incurred to support our operations, partially offset by our net income of $53 million and the timing of payments from Gilead. The increase in expenses incurred for development activities is partially offset by year-over-year changes in non-cash

items, including $33 million increased expense from stock-based compensation, and changes in our asset and liability balances due to the timing of payments to or from our vendors and collaborators.

Investing Activities

Cash used in investing activities for 2022 was primarily due to net purchases of marketable securities of $404 million as we invested a portion of the $725 million received from Gilead in January 2022 under the Gilead Collaboration Agreement.

Cash used in investing activities for 2021 was primarily due to purchases of property and equipment of $26 million, partially offset by net cash proceeds related to our marketable securities of $22 million.

Cash used in investing activities for 2020 was primarily due to net purchases of marketable securities of $431 million as we invested a portion of the proceeds received from our May 2020 public offering and from Gilead for stock issued under the Stock Purchase Agreement.

Financing Activities

Cash provided by financing activities for 2022 was primarily due to net proceeds of $23 million for stock issued under our equity award plans and $10 million received under the BVF agreement.

Cash provided by financing activities for 2021 was primarily due to proceeds of $220 million from Gilead for stock issued under the Stock Purchase Agreement.

Cash provided by financing activities for 2020 was primarily due to net proceeds of $326 million from our May 2020 public offering and $108 million in net proceeds from Gilead for stock issued under the Stock Purchase Agreement.

Contractual Obligations and Commitments

The following table summarizes our current and noncurrent anticipated cash requirements under contractual obligations as of December 31, 2022 (in millions):

	Total	Current	Noncurrent
Operating lease obligations [1]	$ 159	$ 15	$ 144
Liability for sale of future royalties [2]	17	-	17
Total [3]	$ 176	$ 15	$ 161

(1) Consists of cash payments due to landlord for our leased office and laboratory space. As of December 31, 2022, we had obligations consisting of operating leases for our operating facilities for approximately 260,000 square feet. Under the terms of the agreements, we have lease obligations consisting of $159 million in undiscounted minimum lease payments through 2031. In October 2022, we entered into an agreement to sublease approximately 31,000 unfinished square feet of our Brisbane office to another company through 2028. This sublease includes a tenant improvement allowance to be paid by us of $9 million upon lease commencement and we will receive sublease income of approximately $3 million per year (see Note 13 to our Consolidated Financial Statements in Item 8 for further discussion).

(2) Consists of current balance of estimated contingent milestone and royalty payments under the BVF Agreement (see Note 15 to our Consolidated Financial Statements in Item 8 for further discussion).

(3) We have not included contingent milestone or royalty payments or other contractual payment obligations in the table to the extent the timing and amount of such obligations are unknown or uncertain.

We enter into contracts in the normal course of business with third parties for clinical trial management and execution, non-clinical studies and testing, manufacturing, and other services and products for operating purposes. These contracts are generally cancelable on 30 days' notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

See "Liquidity and capital resources" above for further discussion of our cash requirements.

Critical Accounting Judgments and Estimates

Our Consolidated Financial Statements have been prepared in accordance with U.S. generally accepted accounting principles (GAAP). The preparation of these Consolidated Financial Statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent

assets and liabilities at the date of the Consolidated Financial Statements, as well as the reported revenue and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's significant judgments and estimates.

While our significant accounting policies are described in the notes to our Consolidated Financial Statements, we believe that the following critical accounting estimates are most important to understanding and evaluating our reported financial results.

Revenue Recognition

At the inception of an arrangement, we evaluate if a counterparty to a contract is a customer, if the arrangement is within the scope of revenue from contracts with customers guidance, and the term of the contract. We recognize revenue when a customer obtains control of promised goods or services in a contract for an amount that reflects the consideration we expect to receive in exchange for those goods or services. For contracts with customers, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy each performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. As part of the accounting for contracts with customers, we develop assumptions that require judgment to determine the standalone selling price of each performance obligation identified in the contract. In addition, variable consideration such as milestone payments are evaluated to determine if they are constrained and, therefore, excluded from the transaction price. We then allocate the total transaction price to each performance obligation based on their relative estimated standalone selling prices. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

For the recognition of revenue relating to the Gilead Agreements, as disclosed in Note 5, Revenues, to our Consolidated Financial Statements in Part II, Item 8, we allocated the total transaction price to each performance obligation on a relative standalone selling price basis and determined whether revenue should be recognized at a point in time or over time as services are performed. The estimation of the standalone selling price included estimates for forecasted revenues or costs, development timelines, discount rates, and probabilities of technical and regulatory success. We evaluate each performance obligation to determine if it can be satisfied at a point in time or over time as services are performed, and we measure the services delivered to Gilead, which we periodically review based on the progress of the related program. The effect of any change made to an estimated input component and, therefore revenue or expense recognized, would be recorded as a change in estimate. In addition, variable consideration (e.g., milestone payments) is evaluated to determine if it is constrained and, therefore, excluded from the transaction price.

Revenue related to certain performance obligations that are satisfied over time could be materially impacted as a result of changes in the total estimated effort required to satisfy those obligations. A hypothetical 10% change in the total estimated effort required to satisfy the combined license and R&D activities performance obligations related to the agreement with Gilead would have changed the related revenue recognized during the current year by as much as $7 million. For the year ended December 31, 2022, we recognized $4 million in cumulative catch-up revenues from such changes in estimates. See Results of Operations above for further discussion. These changes in estimate could have a material impact on the revenue recognized in a future period.

For performance obligations that are distinct and determined to be transferred or satisfied at a point in time, the estimated standalone selling price will affect the amount of revenue recognized upon satisfaction of the related performance obligation such as the transfer of control of a license. For the domvanalimab license with Gilead, transfer of the license and satisfaction of the related performance obligation occurred in 2021. The estimated standalone selling price of the domvanalimab license utilized assumptions of discounted cash flows which require judgment. A 10% change in the total estimated cash flows used in determining the estimated standalone selling price of the domvanalimab license would have resulted in a change in the amount of revenue recognized in 2021 of approximately

$20 million with a corresponding change in the transaction price allocated to the remaining performance obligations in the Gilead Collaboration Agreement.

Recent Accounting Pronouncements

See "Recent Accounting Pronouncements" in Note 2 to our Consolidated Financial Statements in Item 8 for a discussion of recently adopted accounting pronouncements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risks that may result from changes in interest rates and foreign currency exchange rates.

Interest Rate Risk

As of December 31, 2022 and 2021, we had cash, cash equivalents and marketable securities of $1.14 billion, and $681 million, respectively. This consisted of interest-bearing money market accounts and investments in corporate notes and U.S. government securities, which create an exposure to interest rate risk. A hypothetical 100 basis point increase in interest rates as of December 31, 2022 and 2021 would not have resulted in a material effect on the fair market value of our cash, cash equivalents and marketable securities. In addition, a hypothetical 100 basis point decrease in interest rates as of December 31, 2022 and 2021 would not result in a material effect on income in the respective ensuing year.

Foreign Currency Exchange Risk

We do not have any foreign currency forward or cross currency swap contracts. We are exposed to foreign currency exchange rate risk inherent in our contracts with research institutions, contract research organizations, and contract manufacturing organizations as certain services are performed by them outside the United States and billed in other currencies. A hypothetical 20% adverse movement in foreign currency exchange rates compared with the U.S. dollar relative to exchange rates as of December 31, 2022 and 2021, respectively would not result in material impact to our financial position or income in the respective ensuing year.

Item 8. Financial Statements and Supplementary Data

ARCUS BIOSCIENCES, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors of Arcus Biosciences, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Arcus Biosciences, Inc. (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations, comprehensive income (loss), 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 "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 28, 2023 expressed an unqualified opinion thereon.

Basis for Opinion

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

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

Critical Audit 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 the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accounting for license and collaboration agreements with Gilead Sciences, Inc.

Description of the Matter

As described in Notes 3 and 5 to the consolidated financial statements, the Company has an ongoing Option, License and Collaboration Agreement with Gilead Sciences, Inc., a related party, referred to as the "Amended Gilead Collaboration Agreement", which resulted in the recognition of $107 million of revenue for the year ended December 31, 2022 and $452 million of deferred revenue at December 31, 2022. Of the revenue recognized under this agreement in 2022, $74 million related to amounts received in prior periods that are recognized as revenue when services are performed, with the amount of revenue recognized based on the level of effort expended in a given period in relation to the total effort expected to be incurred to satisfy the applicable performance obligation. Management periodically updates its estimates of the amount, and timing, of the total effort expected to be incurred to satisfy such performance obligations, with any changes in estimate potentially changing the amount of revenue previously recognized and/or the amount to be recognized in future periods.

Auditing the Company's process for estimating the amount and timing of effort expected to be incurred to satisfy such performance obligations is complex, particularly with regard to the significant judgment applied by the Company when updating clinical trial assumptions, including the cost, timing and duration of such trials. Changes to these assumptions can have a material effect on the amount and timing of revenue recognized.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design, and tested the operating effectiveness of controls addressing the risks of material misstatement relating to the Company's process for estimating the cost, timing, and duration of the total effort expected to be incurred to satisfy the identified performance obligations pursuant to the Amended Gilead Collaboration Agreement. For example, we tested management's controls over the identification of changes in estimates and significant assumptions related to the cost, timing and duration of clinical trial activity and development.

Our audit procedures included, among others, obtaining and reading board and joint steering committee minutes, inquiring of research and development personnel, including program managers, obtaining third-party confirmations for a sample of clinical trial and development activity, and testing the completeness and accuracy of the data used by management. We also performed a sensitivity analysis to evaluate the impact that changes in significant assumptions would have on the revenue recognized during 2022.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2016.

San Mateo, California
February 28, 2023

ARCUS BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(In millions, except per share amounts)

	Years Ended December 31,		
	2022	**2021**	**2020**
Revenues:			
License and development service revenue (Includes $74, $330 and $55 from a related party)	$ 74	$ 345	$ 55
Other collaboration revenue (Includes $33, $31 and $16 from a related party)	38	38	23
Total revenues	112	383	78
Operating expenses:			
Research and development (Net of recoveries of $132, $25 and $3 from a related party)	288	257	159
General and administrative (Net of recoveries of $1, $ - and $ - from a related party)	104	72	43
Total operating expenses	392	329	202
Income (loss) from operations	(280)	54	(124)
Non-operating income (expense):			
Interest and other income, net	16	1	1
Effective interest on liability for sale of future royalties	(2)	-	-
Total non-operating income, net	14	1	1
Income (loss) before income taxes	(266)	55	(123)
Income tax expense	(1)	(2)	-
Net income (loss)	$ (267)	$ 53	$ (123)
Net income (loss) per share:			
Basic	$ (3.71)	$ 0.76	$ (2.24)
Diluted	$ (3.71)	$ 0.71	$ (2.24)
Shares used to compute net income (loss) per share:			
Basic	72.0	69.3	54.8
Diluted	72.0	74.0	54.8

See accompanying notes.

ARCUS BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)
(In millions)

	Years Ended December 31,		
	2022	2021	2020
Net income (loss)	$ (267)	$ 53	$ (123)
Other comprehensive loss	(6)	(1)	-
Comprehensive income (loss)	$ (273)	$ 52	$ (123)

See accompanying notes.

ARCUS BIOSCIENCES, INC.
CONSOLIDATED BALANCE SHEETS
December 31, 2022 and 2021
(In millions, except per share amounts)

	December 31,	
	2022	2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 206	$ 148
Marketable securities	803	351
Receivable from collaboration partners ($39 and $745 from a related party)	39	745
Prepaid and other current assets	19	18
Total current assets	1,067	1,262
Long-term marketable securities	129	182
Property and equipment, net	35	32
Other noncurrent assets ($2 and $ - from a related party)	114	116
Total assets	$ 1,345	$ 1,592
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 20	$ 10
Deferred revenue ($97 and $97 to a related party)	97	102
Other current liabilities	76	54
Total current liabilities	193	166
Deferred revenue, noncurrent ($355 and $462 to a related party)	355	462
Other noncurrent liabilities	140	122
Commitments (Note 16)		
Stockholders' equity:		
Preferred stock: $0.0001 par value per share; 10.0 shares authorized; no shares issued and outstanding	-	-
Common stock and additional paid-in capital: $0.0001 par value per share; 400.0 shares authorized; 72.9 shares in 2022 and 70.8 shares in 2021 issued and outstanding	1,206	1,118
Accumulated deficit	(542)	(275)
Accumulated other comprehensive loss	(7)	(1)
Total stockholders' equity	657	842
Total liabilities and stockholders' equity	$ 1,345	$ 1,592

See accompanying notes.

ARCUS BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
Years ended December 31, 2022, 2021 and 2020
(In millions)

	Number of shares of common stock	Common stock and additional paid-in capital	Accumulated deficit	Accumulated other comprehensive loss	Total stockholders' equity
Balance at December 31, 2019	44.2	$ 369	$ (205)	$ -	$ 164
Issuance of common stock in public offering	12.7	326	-	-	326
Issuance of common stock and rights to purchase additional shares in accordance with Gilead Stock Purchase Agreement	6.0	107	-	-	107
Issuance of common stock in connection with our equity award programs	0.8	6	-	-	6
Stock-based compensation	-	22	-	-	22
Net loss	-	-	(123)	-	(123)
Balance at December 31, 2020	63.7	830	(328)	-	502
Issuance of common stock and rights to purchase additional shares in accordance with Amended and Restated Gilead Purchase Agreement, net of offering costs	5.7	220	-	-	220
Issuance of common stock in connection with our equity award programs	1.4	13	-	-	13
Stock-based compensation	-	55	-	-	55
Other comprehensive loss	-	-	-	(1)	(1)
Net income	-	-	53	-	53
Balance at December 31, 2021	70.8	1,118	(275)	(1)	842
Issuance of common stock in connection with our equity award programs	2.1	23	-	-	23
Stock-based compensation	-	65	-	-	65
Other comprehensive loss	-	-	-	(6)	(6)
Net loss	-	-	(267)	-	(267)
Balance at December 31, 2022	72.9	$ 1,206	$ (542)	$ (7)	$ 657

See accompanying notes.

ARCUS BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In millions)

	Years Ended December 31,		
	2022	**2021**	**2020**
Cash flow from operating activities			
Net income (loss)	$ (267)	$ 53	$ (123)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	65	55	22
Depreciation and amortization	6	4	3
Noncash lease expense	8	3	1
Amortization of premiums on marketable securities	-	5	-
Other items, net	3	-	-
Changes in operating assets and liabilities:			
Receivable from collaboration partners ($704, ($17) and ($1) from a related party)	704	(17)	(1)
Other assets (($2), $ - and $ - from a related party)	2	(3)	(6)
Accounts payable	8	(5)	9
Deferred revenue (($107), ($361) and $195 to a related party)	(112)	(368)	188
Other liabilities	21	17	18
Net cash provided by (used in) operating activities	438	(256)	111
Cash flow from investing activities			
Purchases of marketable securities	(1,241)	(719)	(740)
Proceeds from maturities of marketable securities	694	690	308
Proceeds from sales of marketable securities	143	51	1
Purchases of property and equipment	(6)	(26)	(3)
Purchases of in-process research and development	(6)	-	-
Collaboration reimbursements of in-process research and development from a related party	3	-	-
Net cash used in investing activities	(413)	(4)	(434)
Cash flow from financing activities			
Proceeds from issuance of common stock and rights to purchase additional shares ($ -, $220 and $164 from a related party)	-	220	434
Proceeds from sale of future royalties	10	5	-
Proceeds from issuance of common stock pursuant to equity award plans	23	12	5
Net cash provided by financing activities	33	237	439
Net increase (decrease) in cash, cash equivalents and restricted cash	58	(23)	116
Cash, cash equivalents and restricted cash at beginning of period	151	174	58
Cash, cash equivalents and restricted cash at end of period	$ 209	$ 151	$ 174
Supplemental disclosure of cash flow information			
Income taxes paid	$ 3	$ -	$ -
Non-cash investing and financing activities:			
Unpaid portion of property and equipment purchases included in accounts payable and accrued liabilities	$ 3	$ 1	$ 2
Unpaid portion of other assets included in accrued research and development	$ -	$ 1	$ -
Vesting of early exercised stock options and restricted stock	$ -	$ 1	$ 1

See accompanying notes.

Note 1. Organization, liquidity and capital resources

Organization

Arcus Biosciences, Inc. (referred to as "Arcus," "we," "our," "us," or the "Company") is a clinical-stage biopharmaceutical company focused on creating best-in-class therapies. Using our robust and highly efficient drug discovery capability, we have created a significant portfolio of investigational products which are in clinical development, with our most advanced molecule, an anti-TIGIT antibody, now in four Phase 3 registrational studies targeting lung and gastrointestinal cancers. Our deep portfolio of novel small molecules and enabling antibodies allows us to create highly differentiated therapies, which we are developing to treat multiple large indications.

We operate and manage our business as one reportable and operating segment, which is the business of developing and commercializing highly differentiated therapies that have a meaningful impact on patients.

Liquidity and Capital Resources

As of December 31, 2022, we had cash, cash equivalents and marketable securities of $1.14 billion, which we believe will be sufficient to fund our planned operations for a period of at least twelve months following the date of filing of this report.

Note 2. Summary of significant accounting policies

Basis of Presentation

The Consolidated Financial Statements, which include the accounts of Arcus as well as its wholly owned subsidiary, have been prepared in accordance with generally accepted accounting principles in the United States of America (U.S. GAAP) and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented. All intercompany transactions and balances have been eliminated in consolidation.

We assess whether we are the primary beneficiary of a variable interest entity ("VIE") at the inception of the arrangement and at each reporting date. This assessment is based on our power to direct the activities of the VIE that most significantly impact the VIE's economic performance and our obligation to absorb losses or the right to receive benefits from the VIE that could potentially be significant to the VIE. We do not have any significant interests in any variable interest entities of which we are the primary beneficiary.

Use of Estimates

The preparation of the Consolidated Financial Statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses and related disclosures. We base our estimates on historical experience and on various market-specific and other relevant assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Estimates are assessed each period and updated to reflect current information. Actual results may differ materially from those estimates.

Collaborative Arrangements

We assess whether our licensing and other agreements are collaborative arrangements based on whether they involve joint operating activities and whether both parties have active participation in the arrangement and are exposed to significant risks and rewards. For arrangements that we determine are collaborations, we identify each distinct performance obligation, and then determine whether a customer relationship exists for that distinct performance obligation. If we determine a performance obligation within the collaborative arrangement to be with a customer, we apply our revenue accounting policy. If a portion of a distinct bundle of goods or services within the collaborative arrangement is not with a customer, we apply recognition and measurement based on an analogy to authoritative accounting literature or, if there is no appropriate analogy, a reasonable, rational, and consistently applied accounting policy election.

Revenues

We recognize revenue when a customer obtains control of promised goods or services in a contract for an amount that reflects the consideration we expect to receive in exchange for those goods or services. For contracts with customers, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy each performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. As part of the accounting for contracts with customers, we develop assumptions that require judgment to determine the standalone selling price of each performance obligation identified in the contract. In addition, variable consideration such as milestone payments are evaluated to determine if they are constrained and, therefore, excluded from the transaction price. We then allocate the total transaction price proportionally to each performance obligation based on their estimated standalone selling prices. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

We currently do not have product sales and our revenues are derived from arrangements for the development of our investigational products. Such arrangements may require us to deliver various rights, services and/or goods, including intellectual property rights/licenses, R&D services, manufacturing services and/or commercialization services. The underlying terms of these arrangements may generally include consideration to Arcus in the form of one or more of the following: (i) nonrefundable, up-front license fees; (ii) milestone payments related to the achievement of developmental, regulatory, or commercial goals; (iii) royalties on net sales of licensed products; (iv) fees attributable to options to intellectual property; and (v) profit sharing.

In arrangements involving more than one performance obligation, each performance obligation is evaluated to determine whether it qualifies as distinct based on whether (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available and (ii) the good or service is separately identifiable from other promises in the contract. The consideration under the arrangement is then allocated to each separate distinct performance obligation based on its respective relative stand-alone selling price. The estimated selling price of each deliverable reflects our best estimate of what the selling price would be if the deliverable was regularly sold by us on a stand-alone basis or by using an adjusted market assessment approach if selling price on a stand-alone basis is not available. The consideration allocated to each distinct performance obligation is recognized as revenue when control of the related goods is transferred or services are performed. We evaluate each performance obligation to determine if it can be satisfied at a point in time or over time as services are performed. For performance obligations that are determined to be satisfied over time we determine an appropriate method of measuring progress for purposes of recognizing revenue.

Consideration associated with at-risk substantive performance milestones is recognized as revenue when it is probable that a significant reversal of the cumulative revenue recognized will not occur.

For arrangements that include sales-based royalties, including milestone payments based on sales thresholds, and for which the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any royalty revenue resulting from any of our arrangements.

The accounting for these arrangements requires us to develop estimates and assumptions that require judgment. These estimates may include items such as forecasted revenues or costs, development timelines, discount rates, and probabilities of technical and regulatory success. Actual results may differ materially from those estimates.

See Note 5, Revenues, for more information.

Research and Development Expenses

Research and development ("R&D") costs are expensed as incurred and primarily include: salaries, benefits and other staff-related costs; facilities and overhead costs; third-party service provider costs for preclinical and clinical studies; laboratory supplies and equipment maintenance costs; consulting; payments under collaborative and other arrangements including milestone payments, licenses and fees; expense reimbursements to collaboration partners; and other related expenses. Under certain collaborative arrangements, we are reimbursed for a portion of the research and development expenses, including costs of drug supplies. When these R&D expenses are incurred under a reimbursement or cost sharing model with a collaboration partner, we record the related reimbursements as a reduction of R&D expense in our Consolidated Statements of Operations. Acquired in-process research and development projects with no alternative future use are recorded in R&D expense upon acquisition.

Net payment or reimbursement of R&D costs is recognized when the obligations are incurred or as we become entitled to the cost recovery. See Note 4, License and collaboration agreements, for more information.

Clinical study costs are a significant component of R&D expenses. Our clinical studies are primarily performed by third-party contract research organizations ("CROs"). We monitor levels of performance under each significant contract including the extent of patient enrollment and other activities and accrue costs for clinical studies performed over the service periods specified in the contract. We adjust our estimates, if required, based upon our ongoing review of the level of effort and costs actually incurred by the CROs. All of our material CRO contracts are terminable by us upon written notice, and we are generally only liable for actual services completed by the CRO and certain noncancelable expenses incurred at termination.

General and Administrative Expenses

General and administrative ("G&A") expenses relate to: finance; human resources; legal and other administrative activities which consist primarily of personnel costs; facilities and overhead costs; legal expenses; and other general and administrative costs. G&A expenses also include cost recoveries associated with collaborative R&D arrangements.

Stock-Based Compensation

We provide share-based compensation in the form of various types of equity-based awards, including restricted stock units ("RSU"s) and stock options. The fair values of RSU's and stock options, which are subject to service conditions and vesting, are recognized as compensation expense on a straight-line basis over the service period net of forfeitures as they occur. See Note 8, Stock-based compensation, for more information.

Income Taxes

We provide for income taxes under the asset and liability method. Current income tax expense or benefit represents the amount of income taxes expected to be payable or refundable for the current year. Deferred income tax assets and liabilities are determined based on differences between the financial statement reporting and tax bases of assets and liabilities and net operating loss and credit carryforwards, measured using the enacted tax rates and laws that will be in effect when such items are expected to reverse. Deferred income tax assets are reduced, as necessary, by a valuation allowance when we determine it is more likely than not that some or all of the tax benefits will not be realized.

We recognize the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained upon examination by tax authorities. We assess all material positions taken in any income tax return, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. As of each balance sheet date, unresolved uncertain tax positions must be reassessed, and we will determine whether (i) the factors underlying the sustainability assertion have changed and (ii) the amount of the recognized tax benefit is still appropriate.

We include any penalties and interest expense related to income taxes as a component of other expense and interest income, net, as necessary.

See Note 6, Income taxes, for more information.

Cash Equivalents

Cash equivalents consist of marketable securities having an original maturity of three months or less at the time of purchase.

Marketable securities

We consider our interest-bearing securities investment portfolio as available-for-sale, and accordingly, these investments are recorded at fair value, with unrealized gains and losses recorded in Accumulated Other Comprehensive Income (AOCI). See Note 10, Cash, cash equivalents and marketable securities, and Note 15, Fair value measurements, for more information.

Property and Equipment

Property and equipment is recorded at cost and depreciated using the straight-line method over the estimated useful lives of the assets, ranging from three to ten years. Leasehold improvements are amortized over the shorter of their estimated useful lives or the related lease term. We review property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. See Note 11, Property and equipment, for more information.

Leases

We determine whether an arrangement is or contains a lease at contract inception. Operating lease right-of-use assets and lease liabilities are recognized at the commencement date based on the present value of the lease payments over the lease term, which is the non-cancelable period stated in the contract adjusted for any options to extend or terminate when it is reasonably certain that we will exercise that option. Right-of-use assets are adjusted for prepaid lease payments, lease incentives and initial direct costs incurred. Operating lease expense for the minimum lease payments is recognized on a straight-line basis over the lease term. When our operating leases do not provide an implicit interest rate, we generally utilize our incremental borrowing rate, based on the information available at the commencement date to determine the lease liability. We do not recognize the right-of-use assets and liabilities for leases with lease terms of one year or less with payments recognized as operating expenses on a straight-line basis over the lease term. See Note 13, Leases, for more information.

Fair Value of Financial Instruments

We apply fair value accounting for all financial and non-financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis. We define fair value as the price that would be received from selling an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. When determining the fair value measurements for assets and liabilities which are required to be recorded at fair value, we consider the principal or most advantageous market in which we would transact and the market-based risk measurements or assumptions that market participants would use in pricing the asset or liability, such as risks inherent in valuation techniques, transfer restrictions and credit risks. See Note 15, Fair value measurements, for more information.

Other Significant Accounting Policies

Our other significant accounting policies are described in the remaining appropriate notes to the Consolidated Financial Statements.

Recent Accounting Pronouncements

There have been no new accounting pronouncements issued or adopted during the year ended December 31, 2022 with a significant impact to our financial statements.

Note 3. Related party - Gilead Sciences, Inc.

In 2020, we and Gilead Sciences, Inc. (Gilead) entered into an Option, License and Collaboration Agreement (the Gilead Collaboration Agreement), Common Stock Purchase Agreement (the Stock Purchase Agreement), and Investor Rights Agreement (Investor Rights Agreement). In 2021, we amended the Gilead Collaboration Agreement (the Amended Gilead Collaboration Agreement) and the Stock Purchase Agreement (the Amended Stock Purchase Agreement) and in 2022, we amended the Investor Rights Agreement (Amended Investor Rights Agreement). We refer to these agreements collectively as the Gilead Agreements.

Stock Purchase Agreement and Investor Rights Agreement

In 2020, under the Stock Purchase Agreement, Gilead purchased 5,963,029 shares for a total cost of $200 million, of which $91 million was allocated to the revenue related performance obligations (See Note 5, Revenues for more information) created by the Gilead Collaboration Agreement.

In 2021, under the Amended Stock Purchase Agreement, Gilead purchased 5,650,000 shares for a total cost of $220 million.

Gilead has the right, at its option until July 2025, to purchase up to a maximum of 35% of the Company's then-outstanding voting common stock, at a purchase price equal to the greater of a 20% premium to market (based on a trailing five-day average closing price at option exercise) or the $33.54 initial purchase price. Based on the value of our common stock at each contract closing, the right to purchase additional shares had no value.

Under the Investor Rights Agreement, Gilead has the right, which they have exercised, to designate two members of our Board of Directors. This agreement also includes a three-year standstill, included a two-year lockup, provided Gilead with registration rights commencing at the end of the lockup period and provides Gilead with pro rata participation rights in certain future financings. In October 2022, we registered Gilead's shares and the agreement was amended, primarily to extend the two-year lockup period to three-years expiring July 13, 2023.

As of December 31, 2022, Gilead held approximately 18.9% of the Company's outstanding common stock arising from purchases in our May 2020 public offering and purchases under the Stock Purchase Agreement and Amended Stock Purchase Agreement.

Collaboration Agreements

In 2020, we entered into the Gilead Collaboration Agreement, which gave Gilead an exclusive license to develop and commercialize zimberelimab (the anti PD-1 program) in certain markets and time-limited options to acquire exclusive licenses to develop and commercialize any of our then-current and future clinical programs arising during the 10-year collaboration term, contingent upon $100 million option continuation payments payable on each of the second, fourth, sixth and eighth anniversaries of the agreement. Upon closing of the transaction in July 2020, Gilead made an upfront payment of $175 million.

In 2021, we entered into the Amended Gilead Collaboration Agreement pursuant to which Gilead exercised its option to three programs—providing Gilead with exclusive licenses to develop and commercialize domvanalimab and AB308 (collectively, the anti-TIGIT program), etrumadenant (the adenosine receptor antagonist program) and quemliclustat (the CD73 program), in certain markets—for a total payment of $725 million that was received in 2022. The amendment also (i) provided for a slight reduction in the royalties for these three programs, such that Gilead will pay us tiered royalties as a percentage of revenues ranging from the mid-teens to the low twenties; and (ii) removed the $100 million option continuation payment that was otherwise due on the second anniversary of the Gilead Collaboration Agreement.

Gilead's option, on a program-by-program basis, will expire after a prescribed period following the achievement of a clinical development milestone in such program and our delivery to Gilead of the requisite data package. Gilead may exercise its option to any program at any time prior to expiration of the option and will pay Arcus an option fee of $150 million per program. With respect to domvanalimab, we are also eligible to receive up to $500 million in potential U.S. regulatory approval milestones.

For each program that Gilead opts into, both companies will co-develop and equally share global development costs, subject to certain opt-out rights that we have, and caps on our spending and related subsequent adjustments. For each program, provided we have not exercised our opt-out rights, we have the option to co-promote in the United

States with equal sharing of related profits and losses. Gilead has the right to exclusively commercialize outside of the U.S., subject to the rights of our existing partners in any territories.

Under the Amended Gilead Collaboration Agreement, Gilead also has option rights to two research programs for which we will lead discovery and early development activities. With respect to these two research programs, Gilead has the right to exercise its option, on a program-by-program basis, either (i) upon our completion of certain IND-enabling activities for an option payment of $60 million or (ii) following the achievement of a clinical development milestone for an option payment of $150 million. These research programs were not determined to be performance obligations at contract inception, due to the very early stages of the programs.

As of December 31, 2022, Gilead has licenses to domvanalimab, AB308, etrumadenant, quemliclustat and zimberelimab.

For the years ended December 31, 2022, 2021 and 2020; we recognized revenue under this agreement of $107 million, $361 million and $71 million, respectively; and reimbursements from Gilead recognized as reductions in R&D expense of $132 million, $25 million and $3 million, respectively. For the year ended December 31, 2022, we recognized reimbursements from Gilead as reductions in G&A expense of $1 million.

For a more detailed discussion on revenues recognized under this collaboration see Note 5, Revenues.

Note 4. License and collaborations

We enter into licensing agreements, strategic collaborations and other similar arrangements with third parties for the development and commercialization of certain investigational products. These arrangements may be collaborative and involve two or more parties who are active participants in the operating activities of the collaboration and are exposed to significant risks and rewards depending on the commercial success of the activities. These arrangements may include: non-refundable upfront payments; payments for options to acquire certain rights; potential development and regulatory milestone payments and/or sales-based milestone payments; royalty payments; revenue or profit-sharing arrangements; expense reimbursements; and cost-sharing arrangements.

See Note 2, Summary of significant accounting policies, for additional discussion of revenues recognized under these types of arrangements. Operating expenses for costs incurred pursuant to these arrangements are reported in their respective expense line items in the Consolidated Statements of Operations, net of any payments due to or reimbursements due from our collaboration partners, with such reimbursements being recognized at the time the party becomes obligated to pay. Our significant arrangements are discussed below.

Gilead Collaboration

See Note 3, Related party - Gilead Sciences, Inc.

AstraZeneca Collaboration

In 2020, we entered into a collaboration with AstraZeneca to evaluate domvanalimab, our investigational anti-TIGIT antibody, in combination with AstraZeneca's durvalumab in a registrational Phase 3 clinical trial in patients with unresectable Stage 3 non-small cell lung cancer (NSCLC), known as the PACIFIC-8 trial. Under the collaboration, each company will retain existing rights to their respective molecules and any future commercial economics. AstraZeneca will conduct the trial, and each company will supply their respective investigational product to support the trial. Under the terms of the agreement, we will reimburse AstraZeneca for its share of the trial costs upon the achievement of certain milestones or under certain circumstances if the agreement is terminated early. The portion of the costs that we consider to be unavoidable are accrued in advance of the achievement of the milestone.

The PACIFIC-8 trial forms part of the Arcus and Gilead joint development program for domvanalimab and our portion of the trial costs are shared with Gilead. We have recognized a receivable of $2 million from Gilead at December 31, 2022 which is recorded in Other noncurrent assets.

For the years ended December 31, 2022 and 2021, under this arrangement we recognized as R&D expense $4 million and $1 million, respectively, before expected recoveries from our cost-sharing agreement with Gilead. At December 31, 2022 and 2021, we have recognized a liability of $5 million and $1 million, respectively, which is recorded in Other noncurrent liabilities.

Taiho License

In 2017, we entered into an agreement with Taiho Pharmaceutical Co., Ltd (Taiho) under which we granted Taiho exclusive options to programs arising over a five-year period which ended in September 2022 (the Option Period) for an upfront payment of $35 million. Upon an option exercise of a program, Taiho would obtain exclusive development and commercialization rights to investigational products under the program for Japan and certain other territories in Asia (excluding China) (the Taiho Territory).

For each option that Taiho exercises, they will be obligated to make a payment of $3 million to $15 million, depending on the development stage of the optioned program. Upon exercise, Taiho is solely responsible for continued development and commercialization in the Taiho Territory. In addition, for each optioned program we would be eligible to receive clinical and regulatory milestones of up to $130 million and commercial milestone payments of up to $145 million with the achievement of certain sales thresholds in the Taiho Territory. We will also receive royalties ranging from high single-digits to mid-teens on net sales of licensed products in the Taiho Territory. Royalties will be payable by product and country commencing on the first commercial sale and ending upon the later of: (a) 10 years; and (b) expiration of the last-to-expire valid claim of our patents covering the manufacture, use or sale.

As of December 31, 2022, Taiho has exercised its options to (i) etrumadenant (the adenosine receptor antagonist program); (ii) zimberelimab (the anti PD-1 program); and (iii) domvanalimab and AB308 (collectively, the anti-TIGIT program).

For the year ended December 31, 2021, option payments totaling $15 million were recognized as revenue. For the years ended December 31, 2022, 2021 and 2020 we recognized revenue of $5 million, $7 million, and $7 million, respectively, related to the upfront payment. For a more detailed discussion on revenues see Note 5, Revenues.

WuXi Biologics License – anti-PD-1

In 2017, we entered into an agreement with WuXi Biologics Ireland Limited (WuXi Biologics) which, as amended, provides us with exclusive rights to (i) develop, use and manufacture products that include an anti-PD-1 antibody, including zimberelimab, worldwide and (ii) commercialize any such products worldwide, except in Greater China. Under the agreement, as of December 31, 2022 we may incur (i) clinical and regulatory milestone payments, and commercialization milestone payments of up to $375 million, (ii) tiered royalties that range from the high single-digits to low teens on net sales of the licensed products and (iii) fees related to any sublicenses.

During the years ended December 31, 2021 and 2020, we incurred milestones of $10 million and $5 million, respectively, and for the year ended December 31, 2020, we incurred sub-license fees of $10 million in connection with the Gilead Collaboration Agreement. All payments were recorded as R&D expense.

WuXi Biologics License – anti-CD39

In 2020, we entered into an agreement with WuXi Biologics, under which we obtained the exclusive worldwide license to anti-CD39 antibodies discovered under the agreement. We will be responsible for the further development and commercialization of these antibodies. Under the agreement, as of December 31, 2022 we may incur additional clinical and regulatory milestone payments of up to $15 million and royalty payments in the low single digits on net sales of the licensed products.

During the year ended December 31, 2022, we made a milestone payment of $2 million which was recorded as R&D expense.

Abmuno License

In 2016, we entered into an agreement with Abmuno Therapeutics LLC (Abmuno), under which we obtained the exclusive worldwide license to develop, use, manufacture, and commercialize products that include an anti-TIGIT antibody, including domvanalimab. Under the agreement, as of December 31, 2022 we may incur additional clinical, regulatory and commercialization milestone payments of up to $88 million.

During the years ended December 31, 2022, 2021 and 2020, we incurred development milestone expenses of $5 million, $5 million and $3 million, respectively, which were recorded as R&D expense.

Note 5. Revenues

The following table summarizes our revenues by collaboration, category of revenue, and the method of recognition (in millions):

			Year Ended December 31,		
	Over time	Point in time	2022	2021	2020
Gilead Collaboration					
License to domvanalimab		*	$ -	$ 329	$ -
License to zimberelimab		*	-	-	55
License and R&D services	*		74	1	-
Access rights	*		33	31	16
Taiho Collaboration					
License to domvanalimab		*	-	15	-
Access rights	*		5	7	7
Total revenues			$ 112	$ 383	$ 78

Revenues from Gilead accounted for 96%, 94% and 91% of Total revenues for the years ended December 31, 2022, 2021 and 2020, respectively.

The following table summarizes the revenue recognized as a result of changes in the deferred revenue balance (in millions):

	Year Ended December 31,		
	2022	2021	2020
Revenue recognized from amounts in deferred revenue at the beginning of the period	$ 112	$ 202	$ 7

Revenue from the Gilead Collaboration Agreement

We determined that the Amended Gilead Collaboration Agreement (see Note 3, Related party - Gilead Sciences, Inc., for more information) represented a contract modification and at the amendment closing date of December 21, 2021, we allocated the transaction price to the new and remaining performance obligations. The following table summarizes the transaction price and the allocation of the transaction price to the performance obligations (in millions):

Transaction price	Amount
Deferred revenues as of December 21, 2021	$ 165
Option payment for Domvanalimab	275
Option payment for Etrumadenant	250
Option payment for Quemliclustat	200
Total transaction price	$ 890

Allocation to performance obligations	Distinct	Combined	Amount
Domvanalimab - License	*		$ 329
Domvanalimab - R&D services	*		34
Etrumadenant - License and R&D services		*	219
Quemliclustat - License and R&D services		*	176
Zimberelimab - R&D and commercial services	*		11
Access rights	*		84
Option continuation periods	*		37
Total allocated transaction price			$ 890

Our assessment of the transaction price for the Amended Gilead Collaboration Agreement included an analysis of amounts we expected to receive, which at contract inception consisted of the upfront cash payment of $725 million, as well as amounts totaling $165 million deferred from the original Gilead transaction. This excludes the $100 million option continuation payment that was eliminated in the amendment. We determined the entire $890 million to be the allocable transaction price as of the amendment closing date, due to the history of timely payments by Gilead including the receipt of $725 million in January 2022.

We had $452 million and $559 million of deferred revenue remaining on our Consolidated Balance Sheets related to this collaboration at December 31, 2022 and December 31, 2021, respectively, allocated between current and noncurrent based on the expected timing of future recognition. Total revenues recognized during the year ended December 31, 2022 includes cumulative catch-up revenue of $4 million, due to changes in the total estimated percentage of completion and management's estimated total effort to be incurred in the future to satisfy the performance obligations, primarily related to revised clinical trial assumptions for R&D and commercial activities. This cumulative catch-up reduced net loss per share in the year ended December 31, 2022 by $0.06.

We accounted for each performance obligation as follows:

Domvanalimab – License

Under the Gilead Collaboration Agreement, Gilead obtained an option to the exclusive rights to our anti-TIGIT program, including domvanalimab and AB308, in exchange for an option payment of $275 million, if exercised. Prior to the closing of the Amended Gilead Collaboration Agreement, we had $37 million of deferred revenue on our Consolidated Balance Sheet related to this performance obligation.

Effective December 2021, under the Amended Gilead Collaboration Agreement, Gilead exercised the option and obtained an exclusive license to domvanalimab. We determined that this license was distinct based on an evaluation of the delivery of the license, noting that the program was in the later stages of development and it met the criteria for being distinct from the R&D services required under the Amended Gilead Collaboration Agreement. Specifically, the domvanalimab program was in a Phase 3 clinical trial at the time that Gilead acquired the license and the Company concluded that: (i) the R&D services for such later-stage, Phase 3 IP, primarily involved validating the drug’s efficacy, and (ii) the ongoing R&D services do not significantly modify or customize the drug compound such that the IP is not significantly different at the end of the arrangement as a result of the services. We determined the standalone selling price of this license using a discounted cash flow method.

We recognized as revenue the full $329 million of the allocated transaction price in the year ended December 31, 2021.

Domvanalimab – R&D services

We determined that we retain a separate performance obligation to perform further R&D services for Gilead related to domvanalimab. The standalone selling price of this obligation was determined using an expected cost-plus margin approach. We recognize the amounts allocated to these services as the performance obligation is satisfied, calculated as an estimated percentage of completion based on management's estimated total effort for the program.

We recognized $5 million in license and R&D services revenue in the year ended December 31, 2022 and no revenue was recognized in 2021 as the R&D services had not yet commenced. At December 31, 2022 we had $30 million of deferred revenue remaining on our Consolidated Balance Sheet related to this performance obligation.

Etrumadenant – License and R&D services

Under the Gilead Collaboration Agreement Gilead obtained an option to the exclusive rights to our adenosine receptor program, etrumadenant, in exchange for an option payment of $250 million, if exercised. Prior to the closing of the Amended Gilead Collaboration Agreement, we had $127 million of deferred revenue on our Consolidated Balance Sheet related to this performance obligation.

Effective December 2021, under the Amended Gilead Collaboration Agreement, Gilead exercised the option and obtained an exclusive license to etrumadenant and we were also obligated to perform further R&D services for Gilead related to etrumadenant. We determined that the license and R&D services were combined based on an evaluation of the delivery of the license, due to the early stage of the technology and the specialized nature of our know-how. We determined the standalone selling price of the license using a discounted cash flow method and the R&D services

using an expected cost-plus margin approach. We recognize the amounts allocated to the combined license and services as the performance obligation is satisfied, calculated as an estimated percentage of completion based on management's estimated total effort for the program.

We recognized $34 million in license and R&D services revenue in the year ended December 31, 2022 and no revenue was recognized in 2021 as the R&D services had not yet commenced. At December 31, 2022 we had $185 million of deferred revenue remaining on our Consolidated Balance Sheet related to this performance obligation.

Quemliclustat – License and R&D services

Under the Gilead Collaboration Agreement Gilead obtained an option to the exclusive rights to the Company's CD73 program, quemliclustat, in exchange for an option payment of $200 million, if exercised. Prior to the closing of the Amended Gilead Collaboration Agreement, we had no deferred revenue on our Consolidated Balance Sheet related to this performance obligation.

Effective December 2021, under the Amended Gilead Collaboration Agreement, Gilead exercised the option and obtained an exclusive license to quemliclustat and we were also obligated to perform further R&D services for Gilead related to quemliclustat. We determined that the license and R&D services were combined based on an evaluation of the delivery of the license, due to the early stage of the technology and the specialized nature of our know-how. We determined the standalone selling price of the license using a discounted cash flow method and the R&D services using an expected cost-plus margin approach. We recognize the amounts allocated to the combined license and services as the performance obligation is satisfied, calculated as an estimated percentage of completion based on management's estimated total effort for the program.

We recognized $26 million in license and R&D services revenue in the year ended December 31, 2022 and no revenue was recognized in 2021 as the R&D services had not yet commenced. At December 31, 2022 we had $149 million of deferred revenue remaining on our Consolidated Balance Sheet related to this performance obligation.

Zimberelimab – License

Effective July 2020, under the Gilead Collaboration Agreement, Gilead obtained an exclusive license to zimberelimab. We determined that this license was distinct based on an evaluation of the delivery of the license, noting that the program was in the later stages of development and it met the criteria for being distinct from the R&D services required under the Gilead Collaboration Agreement. We determined the standalone selling price of this license using a discounted cash flow method.

We recognized the full $55 million of the allocated transaction price as revenue in the year ended December 31, 2020.

Zimberelimab – R&D and commercialization services

We determined that we retained separate performance obligations to perform further R&D and commercialization services for Gilead related to zimberelimab, as a monotherapy and in combination with other agents. Prior to the closing of the Amended Gilead Collaboration Agreement, we had $10 million of deferred revenue on our Consolidated Balance Sheet, related to these performance obligations. The standalone selling price of these obligations were determined using an expected cost-plus margin approach. We recognize the amounts allocated to these services as the performance obligations are satisfied, calculated as an estimated percentage of completion based on management's estimated total effort for the program.

We recognized $9 million and $1 million for R&D and commercialization services in the year ended December 31, 2022 and 2021, respectively. At December 31, 2022, we had $1 million of deferred revenue remaining on our Consolidated Balance Sheet related to these performance obligations.

Access rights and option continuation periods

Under the Amended Gilead Collaboration Agreement, Gilead has exclusive access to our current programs as well as the future programs for a period of ten years, contingent upon option continuation payments totaling $300 million, consisting of a $100 million payment on each of the fourth, sixth, and eighth anniversaries of the agreement.

Prior to the closing of the Amended Gilead Collaboration Agreement, we had $92 million deferred revenue on our Consolidated Balance Sheet related to this performance obligation.

The standalone selling price of this ongoing R&D pipeline access was determined using an expected cost-plus margin approach. We use a time-elapsed input method to measure progress toward satisfying this obligation, which is the method we believe most faithfully depicts the Company's performance in transferring the promised services during the time period in which Gilead has access to our R&D pipeline. Accordingly, the revenue allocated to this performance obligation is being recognized using this input method over the minimum four-year period. We determined that Gilead is not obligated to pay the remaining $300 million due over the remainder of the term and excluded these payments from the transaction price. Failure to pay the non-obligatory option continuation payments will result in Gilead's loss of certain rights to access and obtain licenses to the programs arising from our R&D pipeline.

We recognized as revenue $33 million, $31 million and $16 million associated with this obligation in the years ended December 31, 2022, 2021 and 2020, respectively under the Gilead Collaboration Agreement and the Amended Gilead Collaboration Agreement. At December 31, 2022, we had $87 million of deferred revenue on our Consolidated Balance Sheet related to this performance obligation.

Capitalized costs to obtain a contract

We incurred $7 million in costs to obtain the Gilead Agreements in 2020, which consisted of consultant and legal fees. We determined that $2 million of these costs were related to the Stock Purchase Agreement which were recognized as offering costs and we allocated the remaining costs to the various performance obligations, to be recognized as the underlying performance obligation is satisfied and revenue is recognized. We incurred $4 million in costs to obtain the Amended Gilead Collaboration Agreement in 2021, which consisted of fees to a third party. These fees were combined with the $4 million of capitalized fees that remained from the original agreement at the amendment closing date, and the total $8 million was allocated to the performance obligations identified under the Amended Gilead Collaboration Agreement, to be recognized as expense as the underlying performance obligation is satisfied and revenue is recognized.

For the years ended December 31, 2022, 2021 and 2020, we recognized expense related to these capitalized costs of $1 million, $4 million and $1 million, respectively, which was recorded in G&A expense. As of December 31, 2022, we had $4 million in capitalized costs to obtain the contract, of which $1 million was recorded as Prepaid and other current assets and $3 million was recorded as Other noncurrent assets in our Consolidated Balance Sheet.

Note 6. Income taxes

Income (loss) before income taxes included the following (in millions):

	Year Ended December 31,		
	2022	2021	2020
Domestic	$ (267)	$ 54	$ (123)
Foreign	1	1	-
Income (loss) before income tax	$ (266)	$ 55	$ (123)

The provision for income taxes included the following (in millions):

	Year Ended December 31,		
	2022	2021	2020
Current			
Federal	$ -	$ 1	$ -
State	1	1	-
Total income tax expense	$ 1	$ 2	$ -

The 2022 income tax expense considers the impact of the capitalization of R&D expenses for income tax purposes due to changes in U.S. legislation.

The reconciliation between the federal statutory income tax rate and our effective tax rate was as follows:

	Year Ended December 31,		
	2022	2021	2020
Federal statutory income tax rate	21.0 %	21.0 %	21.0 %
State taxes, net of federal benefit	(0.1)	0.8	-
Equity investment	0.9	(4.1)	4.2
Research and development credits	3.1	(11.9)	3.1
Change in valuation allowance	(24.5)	(2.6)	(27.4)
Stock based compensation	0.1	(0.8)	(0.2)
Non-deductible expenses and other	(0.6)	0.9	(0.7)
Provision for income taxes	(0.1) %	3.3 %	0.0 %

Deferred income taxes reflect the net tax effects of (a) temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes, and (b) operating losses and tax credit carryforwards.

Significant components of our deferred tax assets and liabilities were as follows (in millions):

	Year Ended December 31,	
	2022	2021
Deferred tax assets:		
Federal and state net operating loss carryforwards	$ 24	$ 24
Research and development credits carryforwards	22	13
Stock-based compensation	16	10
Depreciation and amortization	6	6
Deferred revenue	19	24
Lease liability	25	25
Capitalized research and development costs	53	-
Other	7	4
Total deferred tax assets	172	106
Deferred tax liabilities:		
Right-of-use assets	(22)	(23)
Total deferred tax liabilities	(22)	(23)
Less valuation allowance	(150)	(83)
Net deferred tax assets (liabilities)	$ -	$ -

The accounting for deferred taxes involves the evaluation of a number of factors concerning the realizability of net deferred tax assets. We considered factors such as our history of operating losses, the nature of our deferred tax assets, and the timing, likelihood and amount, if any, of future taxable income during the periods in which those temporary differences and carryforwards become deductible, including amounts that may arise under the collaboration agreement with Gilead entered into in 2020 and the 2021 program opt-ins. As a result of our evaluation of these factors, including the uncertainty that exists with respect to the option fees and milestone payments, we do not believe that it is more likely than not that the deferred tax assets will be realized. Accordingly, a full valuation allowance has been established and no deferred tax asset is shown in the accompanying Consolidated Balance Sheets. The valuation allowance increased by approximately $67 million for the year ended December 31, 2022 and decreased by approximately $1 million for the year ended December 31, 2021.

The United States enacted the Tax Cuts and Jobs Act in December 2017, which requires companies to capitalize all of their R&D costs for U.S. tax purposes, including software development costs, incurred in tax years beginning after December 21,2021. Beginning in 2022, for tax purposes we began capitalizing and amortizing R&D costs over a five-year period for domestic research and a fifteen-year period for international research rather than expensing these costs immediately.

At December 31, 2022, we had total net operating loss carryforwards (NOLs) of $109 million that have no expiration date and federal research tax credits of approximately $18 million that begin to expire in 2039. We also have state NOLs of approximately $19 million that begin to expire in 2035, and state research tax credits of approximately $12 million that have no expiration date, and foreign research tax credits of approximately $3 million that have no expiration date. Use of the U.S. federal and state NOLs and credit carryforwards may be subject to a substantial annual limitation due to the ownership change provisions of U.S. tax law, as defined in Section 382 and 383 of the Internal Revenue Code of 1986, as amended, and similar state provisions. The annual limitation may result in the expiration of NOLs and credits before use. We have determined that an ownership change, as defined under IRC Section 382, occurred in previous years. While we do not expect these ownership changes to result in the expiration of net operating loss and credit carryforwards prior to utilization, we are subject to an annual limitation on the use of its tax attributes. The limitation on the use of net operating loss and credit carryforwards could reduce our ability to use a portion of the tax attributes to offset future taxable income.

We have not been audited by the Internal Revenue Service, any state or foreign tax authority. We are subject to taxation in the United States and in Australia. Due to net operating loss and research credit carryforwards, all of our tax years, from 2015 to 2022, remain open to U.S. federal and California state tax examinations. In addition, our fiscal years from 2018 to 2022 are open to examination in Australia.

Uncertain Tax Positions

We follow the provisions of FASB Accounting Standards Codification (ASC 740-10), *Accounting for Uncertainty in Income Taxes*. ASC 740-10 prescribes a comprehensive model for the recognition, measurement, presentation and disclosure in financial statements of uncertain tax positions that have been taken or are expected to be taken on a tax return. No liability related to uncertain tax positions is recorded in the Consolidated Financial Statements. The reserve for unrecognized tax benefits was approximately $8 million and $5 million at December 31, 2022, and 2021, respectively.

Due to the full valuation allowance at December 31, 2022 and 2021, current adjustments to the unrecognized tax benefit will have no impact on our effective income tax rate; any adjustments made after the valuation allowance is released will have an impact on the tax rate.

Interest and penalties related to unrecognized tax benefits are included in the provision for income taxes. There were no interest or penalties accrued at December 31, 2022 or 2021.

The following table summarizes the activity related to our unrecognized tax benefits (in millions):

	Year Ended December 31,	
	2022	2021
Beginning balance	$ 5	$ 3
Additions for tax positions taken in current year	3	2
Ending balance	$ 8	$ 5

As of December 31, 2022, the total amount of gross unrecognized tax benefits was $8 million, of which, if recognized, none would impact our effective tax rate. We do not anticipate material changes to our uncertain tax positions through the next 12 months.

Note 7. Net income (loss) per share

The computation of basic net income (loss) per share is based on the weighted-average number of our common shares outstanding during the period. The computation of diluted net income (loss) per share is based on the weighted-average number of our common shares and dilutive potential common shares, which primarily include shares that may be issued under our stock option, restricted stock award, and ESPP programs (collectively, dilutive securities) as determined under the treasury stock method.

The following table sets forth the computation of basic and diluted net income (loss) per share (in millions, except per share data):

	Year Ended December 31,		
	2022	2021	2020
Net income (loss) (Numerator):			
Net income (loss)	$ (267)	$ 53	$ (123)
Weighted-average shares (Denominator):			
Outstanding	72.0	70.3	56.4
Less: Subject to vesting	-	(1.0)	(1.6)
Weighted-average shares for basic EPS	72.0	69.3	54.8
Effect of dilutive securities	-	4.7	-
Weighted-average shares for diluted EPS	72.0	74.0	54.8
Net income (loss) per share			
Basic	$ (3.71)	$ 0.76	$ (2.24)
Diluted	$ (3.71)	$ 0.71	$ (2.24)

The following table summarizes potentially dilutive securities excluded from the computation of diluted net income (loss) per share calculations because they would have been antidilutive (in millions):

	At December 31,		
	2022	2021	2020
Common stock options issued and outstanding	12.0	4.5	9.9
Restricted stock units issued	1.3	-	0.7
Unvested early exercised common stock options	-	-	0.2
Employee Stock Purchase Plan shares	0.2	0.1	-
Unvested restricted stock issued as part of collaboration agreement	-	-	1.3
Total	13.5	4.6	12.1

We have also excluded the effect of Gilead's right to purchase additional shares of our common stock from the calculation as these rights had no intrinsic value at either December 31, 2022, 2021 or 2020.

Note 8. Stock-based compensation

Stock-based compensation expense

The following table reflects the components of stock-based compensation expense recognized in our Consolidated Statements of Operations (in millions):

	Year Ended December 31,		
	2022	2021	2020
Research and development	$ 33	$ 29	$ 11
General and administrative	32	26	11
Total stock-based compensation	$ 65	$ 55	$ 22

As of December 31, 2022, unrecognized compensation costs related to non-vested stock option awards and RSUs totaled $90 million and $37 million, respectively, and is expected to be recognized over a weighted average period of 2.2 years and 2.4 years, respectively.

Stock Plans

We grant awards to employees and nonemployees under a series of equity incentive plans (collectively, the Stock Plans). Awards under our Stock Plans are made with newly issued shares reserved for this purpose.

2020 Stock Plan

In January 2020, we adopted the 2020 Inducement Plan (2020 Stock Plan). Under this plan, an initial 3.0 million shares of our common stock were authorized by the Board of Directors for the award of stock options and other equity-based awards as an inducement to eligible individuals to enter into employment with us. During the years ended December 31, 2021 and 2020, the Board of Directors authorized an increase of 5.0 million shares and 1.0 million shares, respectively. As of December 31, 2022, there were 3.2 million shares available for grant under this plan.

2018 Stock Plan

In March 2018, we adopted the 2018 Equity Incentive Plan (2018 Stock Plan), which replaced the 2015 Stock Plan. Under this plan, an initial 3.6 million shares were reserved together with 0.7 million shares that remained available for issuance at adoption under the 2015 Stock Plan. Any outstanding awards under the 2015 Stock Plan that subsequently expire, lapse unexercised or are forfeited to or repurchased by us are also added to the 2018 Stock Plan. The number of shares reserved for issuance will automatically increase on January 1 of each year by a number equal to or the smaller of (i) 3.6 million shares, (ii) 4% of the shares of common stock outstanding on the last business day of the prior fiscal year, or (iii) an amount as determined by the Board of Directors. As of December 31, 2022, there were 3.6 million shares available for grant under this plan. On January 1, 2023, the number of shares available for issuance under this Plan automatically increased by 2.9 million.

2015 Stock Plan

Our amended 2015 Stock Plan, which was in place prior to our public offering in March 2018, allowed option holders to exercise stock options prior to vesting, subject to certain limitations. Any exercised unvested shares were subject to repurchase by us at the original exercise price in the event the option holder's service with the Company was terminated either voluntarily or involuntarily.

Employee Stock Purchase Plan

In March 2018, we adopted the 2018 Employee Stock Purchase Plan (2018 ESPP). The 2018 ESPP provides eligible employees with the opportunity to purchase shares of common stock through payroll deductions at a price equal to 85% of the lower of the fair market value per share on the first trading day of the applicable 24-month offering period or on the applicable purchase date. Employees are limited to a maximum purchase limit of 3,000 shares on each purchase date or $25,000 of shares purchased in a calendar year. The 2018 ESPP is intended to constitute an "employee stock purchase plan" under Section 423(b) of the Internal Revenue Code of 1986, as amended. The 2018 ESPP may be terminated by our board of directors at any time. Under this plan, an initial 0.7 million shares were reserved for issuance. The number of shares reserved for issuance will automatically increase on January 1 of each year by a number equal to or the smaller of (i) 1.1 million shares, (ii) 1% of the shares of common stock outstanding

on the last business day of the prior fiscal year, or (iii) an amount as determined by the Board of Directors. As of December 31, 2022, there were 2.0 million shares available for purchase under this plan. On January 1, 2023, the number of shares available for purchase under this Plan automatically increased by 0.7 million shares. The number of shares issued under the 2018 ESPP during the years ended December 31, 2022, 2021 and 2020 was 0.3 million, 0.2 million, and 0.2 million, respectively.

Restricted Stock Units

We grant restricted stock units (RSUs) to our employees and directors under the 2018 Plan. The RSUs vest annually or quarterly over four years for employees and annually for directors. The following table summarizes information regarding our RSUs for the year ended December 31, 2022:

	Total Restricted Stock Units (in millions)	Weighted Average Grant Date Fair Value
Nonvested at December 31, 2021	1.1	$ 32.23
RSUs granted	0.9	30.22
RSUs vested	(0.5)	32.27
RSUs forfeited or canceled	(0.2)	30.65
Nonvested at December 31, 2022	1.3	$ 31.09

The total grant date fair value of shares vested during the years ended December 31, 2022, 2021 and 2020 was $15 million, $12 million and $0.1 million, respectively.

Stock Options

The exercise price of stock options is set at the closing price of our common stock on the grant date, and the related number of shares granted is fixed at that point in time. Awards expire 10 years from the date of grant. The following table summarizes information regarding our stock options for the year ended December 31, 2022:

	Shares Subject to Outstanding Options (in millions)	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in millions)
Outstanding at December 31, 2021	12.0	$ 19.46		
Options granted	2.3	$ 30.37		
Options exercised	(1.4)	$ 13.17		
Options forfeited or canceled	(0.9)	$ 25.93		
Outstanding at December 31, 2022	12.0	$ 21.77	7.60	$ 50
Options vested and expected to vest as of December 31, 2022	12.0	$ 21.77	7.60	$ 50
Options exercisable as of December 31, 2022	6.7	$ 18.01	7.01	$ 42

During the years ended December 31, 2022, 2021 and 2020, the intrinsic value of shares exercised was $26 million, $17 million, and $7 million, respectively, and the fair value of shares vested during the same period was $48 million, $40 million, and $17 million, respectively.

Valuation Assumptions for Stock Options and ESPP

We utilize the Black-Scholes pricing model to estimate the fair value of stock options and shares issued under our ESPP. The following table summarizes the key assumptions used to calculate the fair value and the resulting weighted-average grant date fair value of stock options granted:

	Year Ended December 31,		
Stock Options	**2022**	**2021**	**2020**
Weighted average closing price of our common stock on grant date	$ 30.37	$ 33.03	$ 17.36
Risk-free interest rate	2.4% - 4.0%	1.0% - 1.4%	0.4% - 0.5%
Expected term (in years)	6.02	6.02	6.02
Volatility	76.5% - 79.3%	75.3% - 77.6%	76.5% - 78.5%
Dividend yield	0%	0%	0%
Weighted average fair value of stock options granted	$ 20.75	$ 22.05	$ 11.57

	Year Ended December 31,		
ESPP	**2022**	**2021**	**2020**
Risk-free interest rate	1.6% - 4.7%	0.0% - 0.6%	0.1% - 0.2%
Expected term (in years)	0.5 - 2.0	0.5-2.0	0.5-2.0
Volatility	68.9% - 82.5%	61.2% - 95.7%	66.6% - 136.0%
Dividend yield	0%	0%	0%

Closing price of our common stock on grant date — The exercise price of our stock options is set as the closing price of our common stock on the grant date.

Risk-free interest rate — The risk-free rate assumption is based on the U.S. treasury yield in effect at the time of grant for instruments with maturities similar to the expected term of our stock options.

Expected term — We have opted to use the "simplified method" for estimating the expected term of options, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option (generally 10 years).

Volatility — Due to our limited operating history and a lack of company specific historical and implied volatility data, our estimate of expected volatility is based on the historical volatility of a group of similar publicly traded companies. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards.

Dividend yield — We have not issued any dividends in our history and do not expect to issue dividends over the life of the options.

Note 9. Employee benefit plan

We have a 401(k) defined contribution plan for all our employees which allows tax-deferred salary deductions. The Company matches, at its discretion, employee contributions. For the years ended December 31, 2022 and 2021, we made contributions of $2 million and $1 million to the plan. We made no contributions to the plan for the year ended December 31, 2020.

Note 10. Cash, cash equivalents and marketable securities

The following table summarizes amortized cost, gross unrealized gains and losses and the fair value of our cash, cash equivalents and marketable securities, all of which are considered available for sale, by type of securities:

Types of securities as of December 31, 2022	**Amortized Cost**	**Unrealized Gain**	**Unrealized Loss**	**Fair Value**
Money market funds	$ 169	$ -	$ -	$ 169
U.S. treasury securities	317	-	(3)	314
Corporate securities and commercial paper	635	-	(4)	631
U.S. government agency securities	20	-	-	20
Certificate of deposit	4	-	-	4
Total	$ 1,145	$ -	$ (7)	$ 1,138

Types of securities as of December 31, 2021	Amortized Cost	Unrealized Gain	Unrealized Loss	Fair Value
Money market funds	$ 148	$ -	$ -	$ 148
U.S. treasury securities	112	-	-	112
Corporate securities and commercial paper	422	-	(1)	421
Total	$ 682	$ -	$ (1)	$ 681

The following table summarizes the fair values of our cash, cash equivalents and marketable securities by location in the Consolidated Balance Sheets and contractual maturity:

Location in Consolidated Balance Sheets	Contractual Maturity	Year Ended December 31, 2022	2021
Cash and cash equivalents	-	$ 206	$ 148
Marketable securities	Within one year	803	351
Long-term marketable securities	Between one year and three years	129	182
Total		$ 1,138	$ 681

Realized gains or losses recognized on the sale of available-for-sale marketable securities were not material for the years ended December 31, 2022, 2021 and 2020. Realized gains and losses are included in Interest and other income, net, in the Consolidated Statements of Operations. The cost of a security sold is determined using the specific-identification method.

We limit the credit risk associated with our investments by placing them with banks and institutions it believes are highly credit worthy and investing in highly rated investments. We held a total of 219 and 165 positions in securities which were in unrealized loss positions as of December 31, 2022 and 2021, respectively. We do not intend to sell our securities with unrealized loss positions and have concluded we will not be required to sell the securities before recovery of the amortized cost for the investment at maturity. No credit related losses have been recognized for any of the periods presented.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash within the Consolidated Balance Sheets to the total shown in the Consolidated Statements of Cash Flows (in millions):

	As of December 31, 2022	2021
Cash and cash equivalents	$ 206	$ 148
Restricted cash (included in Other noncurrent assets)	3	3
Cash, cash equivalents and restricted cash	$ 209	$ 151

Restricted cash at December 31, 2022 and 2021 represents cash balances held as security in connection with our facility lease agreements.

Note 11. Property and equipment

Property and equipment, net was all located in the United States and consisted of the following (in millions):

	Useful Life (in years)	As of December 31, 2022	2021
Leasehold improvements	10	$ 34	$ 32
Scientific equipment	5	17	14
Furniture and equipment	3-5	3	2
Construction in progress	-	4	2
Total		58	50
Less: Accumulated depreciation and amortization		(23)	(18)
Property and equipment, net		$ 35	$ 32

Note 12. Consolidated balance sheet components

Prepaid and Other Current Assets

Prepaid and other current assets consisted of the following (in millions):

	As of December 31,	
	2022	2021
Prepaids and other assets	$ 15	$ 16
Accrued interest receivable	4	2
Total prepaid and other current assets	$ 19	$ 18

Other Current Liabilities

Other current liabilities consisted of the following (in millions):

	As of December 31,	
	2022	2021
Accrued research and development	$ 45	$ 30
Accrued personnel expenses	25	17
Income taxes payable	-	2
Other	6	5
Total other current liabilities	$ 76	$ 54

Note 13. Leases

We lease our corporate headquarters, which includes approximately 151,000 square feet of executive offices, research and development, and business operations, in Hayward, California. This includes approximately 14,500 square feet of leased space that commenced in April 2022, with related tenant improvement allowances totaling approximately $6 million. We also lease approximately 109,000 square feet in Brisbane, California. Both leases: are non-cancelable; extend through 2031; have two options, at our sole discretion, to extend the lease terms for a period of eight years each; and require monthly lease payments that are subject to annual increases throughout the lease term.

In October 2022, we entered into an agreement to sublease approximately 31,000 unfinished square feet of our Brisbane office to another company. This sublease includes a tenant improvement allowance to be paid by us of $9 million. Under the terms of the agreement, we will receive sublease income of approximately $3 million per year which will be recognized on a straight-line basis over the lease term. This sublease is non-cancelable, is expected to commence in 2023 and extends through 2028, with the sublessee having options to extend the lease term and/or to lease additional space within the building.

At December 31, 2022 and 2021, our lease portfolio had a weighted average remaining term of 9.0 years and 10.0 years, respectively, and a weighted average discount rate of 5.2% and 5.1%, respectively.

The following table summarizes information related to our leases, all of which are classified as operating (in millions):

	As of December 31,	
Location in Consolidated Balance Sheets	2022	2021
Assets:		
Other noncurrent assets - right-of-use assets	$ 100	$ 105
Prepaid expenses and other current assets - net tenant receivable	-	3
Liabilities:		
Other current liabilities - net current operating lease liabilities	3	-
Other noncurrent liabilities	117	117

For the years ended December 31, 2022, 2021 and 2020, the Company incurred lease expense of $18 million, $7 million, and $3 million, respectively. Lease costs include rent expense, which consists primarily of our proportionate share of operating expenses, property taxes, and insurance which we have elected to include in lease costs.

The following table summarizes our cash and non-cash information related to our operating leases (in millions):

	Years Ended December 31,		
	2022	2021	2020
Cash paid for amounts included in measurement of lease liabilities	$ 11	$ 5	$ 2
Cash received from tenant improvement allowances	8	3	-
Right-of-use assets obtained in exchange for new operating lease liabilities	3	95	8
Recognition of tenant improvement allowance receivable included in Other current liabilities	6	11	1

The following table summarizes our future minimum lease payments at December 31, 2022 (in millions):

Year Ending December 31,	Operating Leases
2023	$ 15
2024	16
2025	16
2026	17
2027	18
Thereafter	77
Total undiscounted future minimum lease payments	159
Less: Imputed interest	(33)
Total present value of lease liabilities	$ 126

As of December 31, 2022, we have a tenant allowance receivable of $6 million expected to be received within one year. This amount is included as offset to our lease liability in Other current liabilities on the Consolidated Balance Sheet.

As of December 31, 2022, we have provided deposits for letters of credit totaling $3 million to secure our obligations under our leases, which are included in Other noncurrent assets on the Consolidated Balance Sheet.

Note 14. Stockholders' equity

Common Stock

We are authorized to issue up to 400.0 million shares of common stock.

Public Offering

In 2020, under our shelf registration statement that was filed with the SEC in May 2020, we issued 12.7 million shares of our common stock at $27.50 per share in an underwritten public offering. The total number of shares sold consisted of 11.0 million base shares and an additional 1.7 million shares sold pursuant to the underwriters' option exercise. Proceeds from the public offering were approximately $326 million net of underwriting discounts, commissions and other offering expenses.

Gilead Stock Purchase Agreement

In 2020, we closed a private offering under the Stock Purchase Agreement pursuant to which Gilead purchased 6.0 million shares of our common stock at a price of $33.54 per share for a total investment of approximately $200 million. Approximately $91 million of Gilead's investment was determined to be a premium on the fair value of the common stock and was allocated to the revenue related performance obligations under the Gilead Collaboration Agreement. See Note 3, Related party - Gilead Sciences, Inc., and Note 5, Revenues, for further discussion of these agreements with Gilead. Net proceeds allocated to the equity investment were approximately $108 million after deducting the premium and direct offering expenses of $2 million.

In February 2021, we closed a second private offering under the Amended Stock Purchase Agreement, pursuant to which Gilead made an equity investment of approximately $220 million in the Company by purchasing 5.7 million shares of our common stock at a price of $39.00 per share.

Preferred Stock

We have 10.0 million shares of preferred stock issuable in series. There was no preferred stock outstanding as of December 31, 2022 and 2021.

Note 15. Fair value measurements

We determine the fair value of financial and non-financial assets and liabilities using the fair value hierarchy, which establishes three levels of inputs that may be used to measure fair value, as follows:

- Level 1 inputs include unadjusted quoted prices in active markets for identical assets or liabilities;
- Level 2 inputs include observable inputs other than Level 1 inputs, such as quoted prices for similar assets or liabilities; quoted prices for identical or similar assets or liabilities in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the asset or liability; and
- Level 3 inputs include unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the underlying asset or liability. Our Level 3 assets and liabilities include those whose fair value measurements are determined using pricing models, discounted cash flow methodologies or similar valuation techniques and significant management judgment or estimation.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

The following tables summarizes the types of assets and liabilities measured at fair value on a recurring basis by level within the fair value hierarchy (in millions):

	December 31, 2022			
	Level 1	Level 2	Level 3	Total
Assets				
Money market funds	$ 169	$ -	$ -	$ 169
U.S. treasury securities	-	314	-	314
Corporate securities and commercial paper	-	631	-	631
U.S. government agency securities	-	20	-	20
Certificate of deposit	-	4	-	4
Total assets measured at fair value	$ 169	$ 969	$ -	$ 1,138
Liabilities				
Liability for sale of future royalties	$ -	$ -	$ 17	$ 17
Total liabilities measured at fair value	$ -	$ -	$ 17	$ 17

	December 31, 2021			
	Level 1	Level 2	Level 3	Total
Assets				
Money market funds	$ 148	$ -	$ -	$ 148
U.S. treasury securities	-	112	-	112
Corporate securities and commercial paper	-	421	-	421
Total assets measured at fair value	$ 148	$ 533	$ -	$ 681
Liabilities				
Liability for sale of future royalties	$ -	$ -	$ 5	$ 5
Total liabilities measured at fair value	$ -	$ -	$ 5	$ 5

Liability for sale of future royalties

In 2021, we entered into an agreement with BVF Partners L.P. (BVF), under which BVF will fund the discovery and development of compounds for the treatment of inflammatory diseases (the Program) for $15 million in non-refundable payments paid in 2021 and 2022. In return, we are obligated to perform research and development activities in the Program, to make contingent payments upon the achievement of certain clinical and regulatory milestones of

up to $73 million or $160 million depending on whether the program is solely developed by us or with Gilead if they opt-in pursuant to the Gilead Collaboration Agreement. We will also pay mid- to high-single digit royalties on any net product sales generated by the Program. We account for the BVF Agreement as a liability primarily because we have significant continuing involvement in generating the cash flows due to BVF.

The liability is recorded at fair value by using probability-adjusted discounted cash flows, and we revalue this liability each reporting period until the related contingencies have been resolved. The fair value measurement of this liability is based on significant unobservable inputs reviewed quarterly by management. The inputs include, as applicable, estimated probabilities and the timing of achieving specified development, regulatory and commercial milestones as well as estimated annual sales. Significant changes that increase or decrease the probabilities of achieving the related development, regulatory and commercial events or that shorten or lengthen the time required to achieve such events or that increase or decrease estimated annual sales would result in corresponding increases or decreases in the fair values of the obligations, as applicable. Changes in the fair value of this liability related to interest accretion are recognized in Non-operating income (expense) in the Consolidated Statements of Operations.

The imputed effective interest rate on the unamortized portion of the liability was approximately 20.6% as of December 31, 2022. The liability for sale of future royalties is reported in Other noncurrent liabilities in the Consolidated Balance Sheets and changes were as follows (in millions):

	Year Ended December 31	
	2022	2021
Beginning balance	$ 5	$ -
Cash received	10	5
Interest accretion	2	-
Ending balance	$ 17	$ 5

Note 16. Commitments

Standby Letters of Credit

We have standby letters of credit up to an aggregate of $3 million provided as collateral for our leases. The letters of credit are secured by $3 million in deposits classified as restricted cash and included in Other noncurrent assets on the Consolidated Balance Sheet. At December 31, 2022 the standby letters of credit were not drawn down.

Purchase Commitments

We have contractual arrangements with CROs and suppliers. These contracts are generally cancelable on 30 days' notice and the obligations under these contracts arise as the services are performed.

Indemnification

As permitted under Delaware law and in accordance with our bylaws, we are required to indemnify our officers and directors for certain events or occurrences while the officer or director is or was serving in such capacity. We are also party to indemnification agreements with our directors and officers. We believe the fair value of the indemnification rights and agreements is minimal and accordingly, we have not recorded any liabilities as of December 31, 2022 and 2021.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Securities Exchange Act of 1934 (Exchange Act) reports is recorded, processed, summarized, and reported within the time periods specified in the rules and forms of the Securities and Exchange Commission, and that such information is accumulated and communicated to management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues, if any, within an organization have been detected. Accordingly, our disclosure controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our disclosure control system are met.

As of the end of the period covered by this report, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of our disclosure controls and procedures pursuant to Exchange Act Rule 13a-15. Based upon, and as of the date of, this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15(d)-15(f). Our management, with the participation of our principal executive officer and principal financial officer, conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2022. Our assessment was based on criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control Integrated − Framework (2013).

Our 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. Our 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 our assets;
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 our receipts and expenditures are being made only in accordance with authorizations of our management and board of directors; and
3. provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of our assets that could have a material effect on 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.

Based on our evaluation under the framework in Internal Control − Integrated Framework, management concluded that our internal control over financial reporting was effective as of December 31, 2022.

Our independent registered public accounting firm, Ernst & Young LLP, has audited our Consolidated Financial Statements included in Item 8 of this Annual Report on Form 10-K and have issued a report on our internal control over financial reporting as of December 31, 2022. Their report on the audit of internal control over financial reporting appears below.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors of Arcus Biosciences, Inc.

Opinion on Internal Control Over Financial Reporting

We have audited Arcus Biosciences, Inc.'s internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Arcus Biosciences, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the 2022 Consolidated Financial Statements of the Company and our report dated February 28, 2023 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's 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/ Ernst & Young LLP

San Mateo, California
February 28, 2023

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item will be set forth in our proxy statement to be filed with the Securities and Exchange Commission within 120 days after the end of our fiscal year ended December 31, 2022 (our "Proxy Statement") and is incorporated into this Annual Report on Form 10-K by reference, specifically:

- Information regarding our directors and any persons nominated to become a director, as well as with respect to some other required board matters, is set forth under Proposal 1 entitled "Election of Directors" and under the caption "Corporate Governance."
- Information regarding our audit committee and our designated "audit committee financial expert" is set forth under the caption "Corporate Governance."
- Information regarding Section 16(a) beneficial ownership reporting compliance, if any, will be set forth under the caption "Delinquent Section 16(a) Reports."
- Information regarding procedures by which stockholders may recommend nominees to our board of directors is set forth under the caption "Nominating and Corporate Governance Committee" under "Corporate Governance."
- Information regarding our executive officers is set forth under "Executive Officers."

We have adopted a Code of Conduct and Ethics that applies to all directors, officers and employees of the Company, which is available on our website at www.arcusbio.com. If we make any substantive amendments to our Code of Conduct and Ethics or grant any waivers to our directors or executive officers, we will disclose it on our website or in a Current Report on Form 8-K.

Item 11. Executive Compensation

The information required by this Item will be set forth in our Proxy Statement under the captions "Executive Compensation," "Compensation of Directors" and "Compensation Committee Interlocks and Insider Participation" and is incorporated into this Annual Report on Form 10-K by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item will be set forth in our Proxy Statement under the caption "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" and is incorporated into this Annual Report on Form 10-K by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item will be set forth in our Proxy Statement under the captions "Related Person Transactions" and "Corporate Governance" and is incorporated into this Annual Report on Form 10-K by reference.

Item 14. Principal Accounting Fees and Services

The information required by this Item will be set forth in our Proxy Statement under the Proposal with the caption "Ratification of Appointment of Independent Registered Public Accounting Firm" and is incorporated into this Annual Report on Form 10-K by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this Annual Report on Form 10-K:

(1) Financial Statements

See Index to Consolidated Financial Statements at Item 8 herein.

(2) Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

(3) Exhibits.

See Exhibit Index following Item 16 below.

Item 16. Form 10-K Summary

None.

Exhibit Index

Exhibit Number	Exhibit Description	Incorporated by Reference			
		Form	File No	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation.	10-Q	001-38419	3.1	May 9, 2018
3.2	Amended and Restated Bylaws.	8-K	001-38419	3.1	May 26, 2020
4.1	Reference is made to Exhibits 3.1 and 3.2				
4.2	Description of Common Stock.	10-K	001-38419	4.3	February 25, 2021
10.1[A]	Compensation Program for Non-Employee Directors	8-K	001-38419	10.1	June 16, 2022
10.2[A]	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.	S-1	333-223086	10.1	February 16, 2018
10.3[A]	Arcus Biosciences, Inc. Management Cash Incentive Plan.	S-1	333-223086	10.13	February 16, 2018
10.4[A]	Form of Severance and Change in Control Agreement (for use before September 24, 2018).	S-1	333-223086	10.14	February 16, 2018
10.5[A]	Form of Severance and Change in Control Agreement (for use from September 24, 2018).	10-Q	001-38419	10.2	November 8, 2018
10.6[A]	Amended and Restated Letter Agreement, dated February 14, 2018, between the Registrant and Terry Rosen, Ph.D.	S-1	333-223086	10.5	February 16, 2018
10.7[A]	Amended and Restated Letter Agreement, dated February 14, 2018, between the Registrant and Juan Carlos Jaen, Ph.D.	S-1	333-223086	10.6	February 16, 2018
10.8[A]	Offer letter by and between Arcus Biosciences, Inc. and Jennifer Jarrett dated September 10, 2020.	10-Q	001-38419	10.2	November 5, 2020
10.9[A]	Offer letter by and between Arcus Biosciences, Inc. and Robert C. Goeltz II dated June 30, 2020.	10-Q	001-38419	10.1	November 5, 2020
10.10[A]	Letter Agreement, dated July 25, 2022, between the Registrant and Dimitry S.A. Nuyten, MD., Ph.D.	10-Q	001-38419	10.3	November 2, 2022
10.11[A]	Arcus Biosciences, Inc. 2015 Stock Plan and forms of agreements thereunder.	S-1/A	333-223086	10.2	March 5, 2018
10.12[A]	Arcus Biosciences, Inc. 2018 Equity Incentive Plan (including form agreements for use before January 1, 2021).	S-1/A	333-223086	10.3	March 5, 2018
10.13[A]	Form of Stock Option Notice and Agreement under 2018 Equity Incentive Plan (for use from January 1, 2021).	10-K	001-38419	10.36	February 25, 2021
10.14[A]	Form of RSU Notice and Agreement under 2018 Equity Incentive Plan (for use from January 1, 2021).	10-K	001-38419	10.37	February 25, 2021
10.15[A]	Arcus Biosciences, Inc. 2018 Employee Stock Purchase Plan.	S-1/A	001-38419	10.4	March 5, 2018

10.16[A]	Arcus Biosciences, Inc. Amended and Restated 2020 Inducement Plan.	10-K	001-38419	10.18	February 23, 2022
10.17[A]	Form of Stock Option Grant Notice (2020 Inducement Plan).	10-K	001-38419	10.26	March 5, 2020
10.18[A]	Form of Restricted Stock Unit Grant Notice (2020 Inducement Plan).	10-K	001-38419	10.27	March 5, 2020
10.19	Lease, dated September 30, 2015, between the Registrant and Hayward Point Eden I Limited Partnership, as amended on July 22, 2016 and October 12, 2017.	S-1	333-223086	10.8	February 16, 2018
10.20	Third Amendment dated June 26, 2020 to the Lease agreement dated September 30, 2015 between Arcus Biosciences, Inc. and Hayward Point Eden I Limited Partnership.	10-Q	001-38419	10.4	August 6, 2020
10.21	Fourth Amendment dated October 16, 2020 to the Lease agreement dated September 30, 2015 between Arcus Biosciences, Inc. and Hayward Point Eden I Limited Partnership.	10-Q	001-38419	10.3	November 5, 2020
10.22	Fifth Amendment dated April 1, 2021 to the Lease agreement dated September 30, 2015 between Arcus Biosciences, Inc. and Hayward Point Eden I Limited Partnership.	10-Q	001-38419	10.2	May 5, 2021
10.23[B]	License Agreement, dated December 8, 2016, between Arcus Biosciences, Inc. and Abmuno Therapeutics LLC.	S-1	333-223086	10.10	February 16, 2018
10.24[B]	License Agreement, dated August 16, 2017, between Arcus Biosciences, Inc. and WuXi Biologics (Cayman) Inc.	S-1	333-223086	10.11	February 16, 2018
10.25[C]	Amendment No. 1 dated June 27, 2019 to the License Agreement dated August 16, 2017 between Arcus Biosciences, Inc. and WuXi Biologics (Cayman) Inc.	10-Q	001-38419	10.2	August 6, 2019
10.26[C]	Amendment No. 2 dated March 2, 2020 to the License Agreement dated August 16, 2017 between Arcus Biosciences, Inc. and WuXi Biologics (Cayman) Inc.	10-K	001-38419	10.28	March 5, 2020
10.27[C]	Amendment No. 3 dated May 10, 2021 to the License Agreement dated August 16, 2017 between Arcus Biosciences, Inc. and WuXi Biologics (Cayman) Inc.	10-Q	001-38419	10.2	August 5, 2021
10.28[C*]	Amendment No. 4 dated December 30, 2022 to the License Agreement dated August 16, 2017 between Arcus Biosciences, Inc. and WuXi Biologics (Cayman) Inc.				
10.29	Assignment Agreement dated November 10, 2020 by and among Arcus Biosciences, Inc., WuXi Biologics (Cayman) Inc. and WuXi Biologics Ireland Limited to the License Agreement dated August 16, 2017.	10-K	001-38419	10.35	February 25, 2021
10.30[B]	Option and License Agreement, dated September 19, 2017, between Arcus	S-1	333-223086	10.12	February 16, 2018

	Biosciences, Inc. and Taiho Pharmaceutical Co., Ltd.				
10.31[B]	Amendment No. 1 to Option and License Agreement, dated September 19, 2017, between Arcus Biosciences, Inc. and Taiho Pharmaceutical Co, Ltd.	10-Q	001-38419	10.1	November 8, 2018
10.32[C]	Option, License and Collaboration Agreement dated May 27, 2020 between Arcus Biosciences, Inc. and Gilead Sciences, Inc.	10-Q	001-38419	10.1	August 6, 2020
10.33[C]	Amendment No. 1 dated November 17, 2021 to the Option, License and Collaboration Agreement dated May 27, 2020 between Arcus Biosciences, Inc. and Gilead Sciences, Inc.	10-K	001-38419	10.34	February 23, 2022
10.34[C]	Letter Agreement with Gilead Sciences, Inc., dated July 1, 2022.	10-Q	001-38419	10.2	August 3, 2022
10.35[C]	Common Stock Purchase Agreement dated May 27, 2020 between Arcus Biosciences, Inc. and Gilead Sciences, Inc.	8-K	001-38419	99.1	July 13, 2020
10.36[C]	Amended and Restated Common Stock Purchase Agreement dated January 31, 2021 between Arcus Biosciences, Inc. and Gilead Sciences, Inc.	SC 13D/A	005-90423	99.1	February 2, 2021
10.37[C]	Investor Rights Agreement dated May 27, 2020 between Arcus Biosciences, Inc. and Gilead Sciences, Inc.	8-K	001-38419	99.2	July 13, 2020
10.38	Amendment No. 1 to Investor Rights Agreement, dated October 11, 2022.	8-K	001-38419	10.1	October 11, 2022
21.1*	List of subsidiaries of the registrant.				
23.1*	Consent of independent registered public accounting firm.				
24.1*	Power of Attorney (included on signature page to this Annual Report).				
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.				
101.INS	XBRL Instance Document – The instance document does not appear in the				

	Interactive Data File because its XBRL tags are embedded within the Inline XBRL 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 Data File (formatted as inline XBRL and contained in exhibit 101)

* Filed herewith.

A Indicates management contract or compensatory plan or arrangement.

B The Company has been granted confidential treatment for certain portions of this exhibit. The omitted portions have been filed separately with the Securities and Exchange Commission.

C This exhibit omits certain information the Company deems immaterial and either of the type that it treats as confidential or would be competitively harmful if disclosed.

† This certification is deemed not filed for purposes of section 18 of the Exchange Act, or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act.

SIGNATURES

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

ARCUS BIOSCIENCES, INC.

Date: February 28, 2023

By: /s/ Terry Rosen

Terry Rosen, Ph.D.
Chief Executive Officer
(Principal Executive Officer and Duly Authorized Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS that each person whose signature appears below constitutes and appoints Terry Rosen, Ph.D. and Juan Carlos Jaen, Ph.D., and each of them, his or her true and lawful attorneys-in-fact and agents, each with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that each of said attorneys-in-fact and agents or their substitute or substitutes may lawfully do or cause to be done by virtue hereof. Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Annual Report on Form 10-K 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/ Terry Rosen **Terry Rosen, Ph.D.**	Chief Executive Officer and Director (Principal Executive Officer)	February 28, 2023
/s/ Juan Carlos Jaen **Juan Carlos Jaen, Ph.D.**	President and Director	February 28, 2023
/s/ Jennifer Jarrett **Jennifer Jarrett**	Chief Operating Officer and Director	February 28, 2023
/s/ Robert C. Goeltz II **Robert C. Goeltz II**	Chief Financial Officer (Principal Financial and Accounting Officer)	February 28, 2023
/s/ Kathryn Falberg **Kathryn Falberg**	Director	February 28, 2023
/s/ Linda Higgins **Linda Higgins, Ph.D.**	Director	February 28, 2023
/s/ Yasunori Kaneko **Yasunori Kaneko, M.D.**	Director	February 28, 2023
/s/ David Lacey **David Lacey, M.D.**	Director	February 28, 2023
/s/ Nicole Lambert **Nicole Lambert**	Director	February 28, 2023
/s/ Patrick Machado **Patrick Machado, J.D.**	Director	February 28, 2023
/s/ Merdad Parsey **Merdad Parsey, M.D., Ph.D.**	Director	February 28, 2023
/s/ Andrew Perlman **Andrew Perlman, M.D., Ph.D.**	Director	February 28, 2023
/s/ Antoni Ribas **Antoni Ribas, M.D., Ph.D.**	Director	February 28, 2023