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, 2021

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: 001-37471

PIERIS PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Nevada	**EIN 30-0784346**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
255 State Street, 9th Floor Boston, MA United States	**2109**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code
857-246-8998

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

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.001 per share	**PIRS**	**The Nasdaq Stock Market LLC**

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 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) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

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

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

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

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

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant on June 30, 2021, the last business day of the registrant's most recently completed second fiscal quarter, based on the closing price on that date of $3.83, was $170,606,113.

As of February 24, 2022, the registrant had 74,077,417 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the Registrant's Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission.

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Forward-Looking Statements

This annual report on Form 10-K for the year ended December 31, 2021, or this Annual Report on Form 10-K, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve risks and uncertainties, principally in the sections entitled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." All statements other than statements of historical fact contained in this Annual Report on Form 10-K, including statements regarding future events, our future financial performance, expectations for growth and revenues, anticipated timing and amounts of milestone and other payments under collaboration agreements, business strategy and plans, objectives of management for future operations, timing and outcome of legal and other proceedings and our ability to finance our operations are forward-looking statements. We have attempted to identify forward-looking statements by terminology including "anticipates," "approach," "believes," "can," "contemplate," "continue," "look forward," "ongoing," "could," "estimates," "expects," "intends," "may," "appears," "suggests," "future," "likely," "goal," "plans," "potential," "possibly," "projects," "predicts," "seek," "should," "target," "would" or "will" and other similar words or expressions or the negative of these terms or other comparable terminology. Although we do not make forward-looking statements unless we believe we have a reasonable basis for doing so, we cannot guarantee their accuracy. These statements are only predictions and involve known and unknown risks and uncertainties and other factors that may cause our or our industry's actual results, levels of activity, performance or achievements expressed or implied by these forward-looking statements, to differ materially. The description of our Business set forth in Item 1, the Risk Factors set forth in Item 1A and our Management's Discussion and Analysis of Financial Condition and Results of Operations set forth in Item 7 as well as other sections in this report, discuss some of the factors that could contribute to these differences. These forward-looking statements include, among other things, statements about:

- *the accuracy of our estimates regarding expenses, future revenues, uses of cash, capital requirements and the need for additional financing;*
- *the initiation, cost, timing, progress and results of our development activities, preclinical studies and clinical trials;*
- *the timing of and our ability to obtain and maintain regulatory approval of our existing product candidates, any product candidates that we may develop, and any related restrictions, and/or limitations;*
- *our plans to research, develop and commercialize our current and future product candidates and Anticalin platform;*
- *our collaborators' election to pursue or continue research, development and commercialization activities;*
- *our ability to obtain future reimbursement and/or milestone payments from our collaborators;*
- *our ability to attract collaborators with development, regulatory and commercialization expertise;*
- *our ability to obtain and maintain intellectual property protection for our product candidates;*
- *our ability to successfully commercialize our product candidates;*
- *the size and growth of the markets for our product candidates and our ability to serve those markets;*
- *the rate and degree of market acceptance of any future products;*
- *the success of competing drugs that are or may become available;*
- *regulatory developments in the United States and other countries;*
- *the performance of our third-party suppliers and manufacturers and our ability to obtain alternative sources of raw materials;*
- *the potential impact of the coronavirus disease, or COVID-19, pandemic on our clinical trials and other business operations;*
- *our ability to obtain additional financing;*
- *our use of the proceeds from our securities offerings;*

- *any restrictions on our ability to use our net operating loss carryforwards; and*

- *our ability to attract and retain key personnel.*

Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time and it is not possible for us to predict all risk factors, nor can we address the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause our actual results to differ materially from those contained in any forward-looking statements. Actual results could differ materially from our forward-looking statements due to a number of factors, including, without limitation, risks related to: the results of our research and development activities, including uncertainties relating to the discovery of potential drug candidates and the preclinical and ongoing or planned clinical testing of our drug candidates; the early stage of our drug candidates presently under development; our ability to obtain and, if obtained, maintain regulatory approval of our current drug candidates and any of our other future drug candidates; our need for substantial additional funds in order to continue our operations and the uncertainty of whether we will be able to obtain the funding we need; our future financial performance; our ability to retain or hire key scientific or management personnel; our ability to protect our intellectual property rights that are valuable to our business, including patent and other intellectual property rights; our dependence on third-party manufacturers, suppliers, research organizations, testing laboratories and other potential collaborators; the success of our collaborations with third parties; our ability to meet milestones; our ability to successfully market and sell our drug candidates in the future as needed; the size and growth of the potential markets for any of our approved drug candidates and the rate and degree of market acceptance of any of our approved drug candidates; competition in our industry; regulatory developments in the United States and foreign countries, including the U.S. Food and Drug Administration's, or FDA's, views as to the outcome of, the additional in-use and compatibility study for cinrebafusp alfa, (PRS-343), as requested by the FDA in July 2020, and the resolution of the partial clinical hold relating to that drug candidate; the expected impact of new accounting standards; and the length and severity of the pandemic relating to SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), or coronavirus, which causes coronavirus disease 2019, or COVID-19, which could continue to have an impact on our research, development, supply chain and clinical trials.

You should not place undue reliance on any forward-looking statement, each of which applies only as of the date of this Annual Report on Form 10-K. Before you invest in our securities, you should be aware that the occurrence of the events described in the section entitled "Risk Factors" and elsewhere in this Annual Report on Form 10-K could negatively affect our business, operating results, financial condition and stock price. All forward-looking statements included in this document are based on information available to us on the date hereof, and except as required by law, we undertake no obligation to update or revise publicly any of the forward-looking statements after the date of this Annual Report on Form 10-K to conform our statements to actual results or changed expectations.

We have registered trademarks for Pieris®, Anticalin® and Duocalin®. All other trademarks, trade names and service marks included in this Annual Report on Form 10-K are the property of their respective owners. Use or display by us of other parties' trademarks, trade dress or products is not intended to and does not imply a relationship with, or endorsements or sponsorship of, us by the trademark, trade dress or product owner.

As used in this Annual Report on Form 10-K, unless the context indicates or otherwise requires, "our Company", "the Company", "Pieris", "we", "us" and "our" refer to Pieris Pharmaceuticals, Inc., a Nevada corporation, and its consolidated subsidiary, Pieris Pharmaceuticals GmbH (formerly known as Pieris AG), a company organized under the laws of Germany, Pieris Australia Pty Ltd., a company organized under the laws of Australia that is a consolidated subsidiary of Pieris Pharmaceuticals GmbH and Pieris Pharmaceuticals Securities Corporation, a Massachusetts securities corporation, a consolidated subsidiary of Pieris Pharmaceuticals, Inc. Effective as of August 26, 2015 and with notification from the Amtsgericht München as of September 29, 2015, Pieris AG was transformed to Pieris Pharmaceuticals GmbH as a result of a change in the legal entity.

Currency Presentation and Currency Translation

Unless otherwise indicated, all references to "dollars," "$," "US $" or "U.S. dollars" are to the lawful currency of the United States. All references in this Report to "euro" or "€" are to the currency introduced at the start of the third stage of the European Economic and Monetary Union pursuant to the Treaty establishing the European Community, as amended. We prepare our financial statements in U.S. dollars.

The functional currency for our operations is primarily the euro. With respect to our financial statements, the translation from the euro to U.S. dollars is performed for balance sheet accounts using exchange rates in effect at the balance sheet date and for

revenue and expense accounts using a weighted average exchange rate during the period. The resulting translation adjustments are recorded as a component of accumulated other comprehensive loss.

Where in this Report we refer to amounts in euros, we have for your convenience also, in certain cases, provided a conversion of those amounts to U.S. dollars in parentheses. Where the numbers refer to a specific balance sheet account date or financial statement account period, we have used the exchange rate that was used to perform the conversions in connection with the applicable financial statement. In all other instances, unless otherwise indicated, the conversions have been made using the noon buying rate of €1.00 to U.S. $1.13249 based on Thomson Reuters as of December 31, 2021.

PART I

Item 1. BUSINESS

Corporate History

General

Pieris Pharmaceuticals, Inc. was incorporated in the State of Nevada in May 2013 under the name "Marika Inc." Pieris Pharmaceuticals, Inc. began operating the business of Pieris Pharmaceuticals GmbH, or Pieris GmbH, through a reverse acquisition on December 17, 2014. Pieris GmbH (formerly Pieris AG, a German company which was founded in 2001) continues as an operating subsidiary of Pieris Pharmaceuticals, Inc.; Pieris Pharmaceuticals, Inc. is the sole stockholder of Pieris GmbH.

Pieris Pharmaceuticals, Inc.'s corporate headquarters are located at 255 State Street, 9th Floor, Boston, Massachusetts 02109. The research facilities of Pieris GmbH are located in Hallbergmoos, Germany. Pieris Australia Pty Ltd., a wholly-owned subsidiary of Pieris GmbH, was formed on February 14, 2014 to conduct research and development activities in Australia. Pieris Pharmaceuticals Securities Corporation, a wholly-owned subsidiary of Pieris Pharmaceuticals, Inc., was formed on December 14, 2016 to buy, sell, deal in, or hold securities on its own behalf and not as a broker, and will engage in its activities exclusively for investment purposes.

Business Overview

We are a clinical-stage biotechnology company that discovers and develops Anticalin-based drugs to target validated disease pathways in unique and transformative ways. Our clinical pipeline includes an inhaled IL-4Rα antagonist Anticalin protein to treat uncontrolled asthma, an immuno-oncology, or IO, bispecific targeting HER2 and 4-1BB, and an IO bispecific targeting PD-L1 and 4-1BB. Proprietary to us, Anticalin proteins are a novel class of therapeutics validated in the clinic and through partnerships with leading pharmaceutical companies.

Anticalin proteins are a class of low molecular-weight therapeutic proteins derived from lipocalins, which are naturally occurring proteins typically found in human blood plasma and other bodily fluids. Anticalin proteins function similarly to monoclonal antibodies by binding tightly and specifically to a diverse range of targets. An antibody is a large protein used by the immune system to recognize a target molecule, called an antigen. We believe Anticalin proteins possess numerous advantages over antibodies in certain applications. For example, Anticalin proteins are relatively small in size and comprised of a single polypeptide chain whereas antibodies are much bigger and comprised of four polypeptide chains. The potentially greater stability and smaller size of Anticalin proteins as compared to antibodies potentially enable unique routes of Anticalin protein drug administration such as inhaled delivery. Higher-molecular-weight entities, such as antibodies, are often too large to be delivered effectively through these methods. Our Anticalin technology is modular, which allows us to design multimeric Anticalin-based bi- and multi- specific proteins to bind with specificity to two or more targets at the same time. This multispecificity offers advantages in biological settings where binding to multiple targets can enhance the ability of a drug to achieve its desired effects, such as facilitating the killing of cancer cells. Moreover, unlike antibodies, the pharmacokinetic, or PK, profile of Anticalin proteins can be adjusted to potentially enable program-specific optimal drug exposure. Such differentiating characteristics suggest that Anticalin proteins have the potential, in certain cases, to become best-in-class drugs.

We have intellectual property rights directed to various aspects of our Anticalin technology platform, allowing for further development and advancement of both our platform and drug candidates. We believe that our ownership or exclusive license of intellectual property related to the Anticalin platform provides us with a strong intellectual property position, particularly in cases where we are seeking to address targets and diseases in a novel way and for which there is existing antibody intellectual property. We also believe that the drug-like properties of the Anticalin drug class have been demonstrated in various clinical trials with different Anticalin-based drug candidates, including PRS-060/AZD1402, cinrebafusp alfa and others.

Our core Anticalin technology and platform were developed in Germany, and we have collaborations with multiple major pharmaceutical and biotechnology companies.

- We entered into a license and collaboration agreement, or the Servier Collaboration Agreement, with Les Laboratoires Servier and Institut de Recherches Internationales Servier, or Servier, in January 2017 in IO.
- In May 2017, we entered into an alliance with AstraZeneca AB, or AstraZeneca, to treat respiratory diseases. On March 29, 2021, we and AstraZeneca entered into the first amendment to the Non-exclusive Anticalin Platform License Agreement dated May 2, 2017 and the second amendment to the License and Collaboration Agreement dated May 2, 2017. Under the amendments, the parties agreed to restructure certain commercial economics for the PRS-060/AZD1402 program by adjusting various milestones and royalty provisions, while fundamentally maintaining the overall value split between AstraZeneca and the Company. In connection with the amendments, we achieved a $13.0 million milestone in connection with the initiation of the phase 2a study for this program and we and AstraZeneca

entered into a subscription agreement pursuant to which we have agreed to issue to AstraZeneca, 3,584,230 shares of our common stock for a total purchase price of $10.0 million in a private placement transaction.

- In February 2018, we entered into a license and collaboration agreement, or the Seagen Collaboration Agreement, with Seagen Inc. (formerly Seattle Genetics, Inc.), or Seagen, in IO. On March 25, 2021 we announced an amendment to the Seagen Collaboration Agreement whereby our option to co-develop and co-commercialize the second of three programs in the collaboration was converted to a co-promotion option in the United States, with Seagen solely responsible for the development and overall commercialization of that program. Under the co-promotion option, we will be entitled to increased royalties from that program in the event that we choose to exercise the option. In addition, we entered into a clinical trial and supply agreement with Seagen to evaluate the safety and efficacy of combining cinrebafusp alfa with Seagen's TUKYSA® (tucatinib), a small-molecule tyrosine kinase HER2 inhibitor, for the treatment of gastric cancer patients expressing lower HER2 levels (IHC2+/ISH- & IHC1+) as part of the initiated phase 2 study. Finally, as part of this transaction, we entered into a subscription agreement pursuant to which we agreed to issue to Seagen 3,706,174 shares of our common stock for a total purchase price of $13.0 million in a private placement transaction.
- On April 24, 2021, the Company and BP Asset XII, Inc., or Boston Pharmaceuticals, a subsidiary of Boston Pharma Holdings, LLC, entered into an exclusive product license agreement, or the BP Agreement, to develop PRS-342, a 4-1BB/GPC3 preclinical immuno-oncology Anticalin-antibody bispecific fusion protein.
- On May 19, 2021, the Company and Genentech, Inc., or Genentech, entered into a research collaboration and license agreement, or the Genentech Agreement, to discover, develop and commercialize locally delivered respiratory and ophthalmology therapies that leverage the Company's proprietary Anticalin technology.

In connection with our efforts to develop multispecific Anticalin-based proteins designed to engage immunomodulatory targets, we have gained non-exclusive access to antibody building blocks that can be utilized to develop multispecific Anticalin-antibody fusion proteins.

Our current development plans focus on two core pillars, respiratory diseases and IO. The lead respiratory Anticalin-based drug candidate, PRS-060/AZD1402, antagonizes IL-4Rα, thereby inhibiting IL-4 and IL-13, two cytokines, which are small proteins mediating signaling between cells within the human body, known to be key mediators in the inflammatory cascade that drive the pathogenesis of asthma and other inflammatory diseases. We believe that the small size and biophysical stability of PRS-060/AZD1402 facilitates direct delivery to the lungs through the use of an inhaler, which may enable relatively high pulmonary concentrations of the drug candidate to be achieved. PRS-060/AZD1402 was tested in a nebulized formulation and an IV arm for PK assessment in 54 healthy volunteers at nominal dose levels ranging from 0.25 mg to 400 mg in a phase 1 single-ascending dose, or SAD, study. Data from that study were presented at the American Thoracic Society International Conference in May 2019 showing that PRS-060/AZD1402 was well-tolerated when given as a single inhaled or intravenous doses to healthy volunteers and there was systemic target engagement (as measured by pSTAT6 inhibition) at doses greater than 2 mg. PRS-060/AZD1402 was also tested in a phase 1 multiple-ascending dose, or MAD, study in 30 patients that were randomized to receive delivered doses via nebulizer ranging from 2 mg to 60 mg (5 mg to 150 mg nominal dose) twice daily for nine consecutive days and one final dose on the 10th day, and 12 patients were randomized to receive placebo at the same intervals, We presented interim data from the PRS-060/AZD1402 phase 1 MAD study at the European Respiratory Society International Congress in October 2019 and reported that PRS-060/AZD1402 was safe and well-tolerated at all doses, led to a statistically significant reduction in fractional exhaled nitric oxide, or FeNO, a validated biomarker for pulmonary eosinophilic airway inflammation, and showed dose-dependent systemic target engagement in patients with mild asthma and elevated levels of FeNO (≥ 35ppb). Inhibition of FeNO levels was seen at doses of 2 mg and above. At 2 mg there was minimal systemic target engagement supporting the concept that pulmonary target engagement by the drug is sufficient to reduce airway inflammation. Following the addition of 4 new cohorts, the phase 1 MAD study has now concluded.

We sponsored the phase 1 SAD/MAD studies for PRS-060/AZD1402, after which AstraZeneca took responsibility for further clinical development of PRS-060/AZD1402. The phase 2a asthma study is ongoing in multiple sites globally. This phase 2a study is a two-part, multi-center, placebo-controlled clinical study of PRS-060/AZD1402 that will evaluate PRS-060/AZD1402 at three dose levels, 1, 3 and 10 mg, using a dry powder formulation administered twice daily. In part 1a of the study, 31 asthma patients, controlled on standard of care (medium dose inhaled corticosteroids (ICS) with long-acting beta agonists (LABA)), were randomized to receive PRS-060/AZD1402 at 1 mg or 3 mg, or to receive a placebo twice daily over four weeks to establish the safety profile and pharmacokinetics of the dry powder formulation of PRS-060/AZD1402. The safety review following completion of part 1a included an evaluation, compared to placebo, of the incidence of adverse events, changes in laboratory markers (immuno-biomarkers, clinical chemistry, and hematology), and forced expiratory volume in one second (FEV1). AstraZeneca has begun enrollment of part 2a of the study to evaluate efficacy, safety, and pharmacokinetics of PRS-060/AZD1402. In part 2a, asthma patients, uncontrolled on medium dose ICS LABA, that have a blood eosinophil count of ≥ 150 cells/μL and FeNO ≥ 25 ppb are being randomized to receive PRS-060/AZD1402 administered at 1 or 3 mg twice daily or a placebo. Following a four-week run-in period, patients will be dosed and monitored over four weeks. FEV1 improvement compared to placebo will be the primary endpoint in this portion of the study. AstraZeneca has also begun

enrollment of part 1b of the study to evaluate the safety of the high dose, 10 mg, of PRS-060/AZD1402 compared to placebo in asthma patients controlled on standard of care. The 10 mg dose or placebo is administered twice daily over four weeks. Although we expect to announce topline data from the phase 2a study this year, we are actively evaluating the feasibility of study timelines in the current geopolitical environment and will update guidance in the orderly course of business, if needed.
Upon receipt of the topline data and notice from AstraZeneca, including a product development plan and budget, the Company will have 30 days to opt into co-development of the program with AstraZeneca at one of two levels, neither of which includes an option exercise fee. If we do not choose to participate in co-development, we would still be entitled to potential sales milestones and royalties. At the first opt-in level, Pieris would be responsible for 25% of the cost-share with a predetermined cost cap for an increased amount of potential sales milestones and royalties compared to not opting-in. At the second opt-in level, we would be responsible for 50% of the cost-share without a cost cap which would result in a gross margin share. The Company also has a separate option to co-commercialize PRS-060/AZD1402 with AstraZeneca in the United States independent of the co-development opt-in decision.

Of the four respiratory programs initially included in the AstraZeneca alliance beyond PRS-060/AZD1402, three are in the discovery stage, the targets and disease areas of which are undisclosed. In January 2022, the Company and AstraZeneca jointly discontinued one discovery-stage program as they were not able to validate an exploratory target. Pieris retains co-development and co-commercialization options for two of the three remaining active discovery programs.

The Company also continues to advance other proprietary discovery-stage respiratory programs. Our lead fully proprietary respiratory asset, PRS-220, an oral inhaled Anticalin protein targeting connective tissue growth factor, or CTGF, is being developed as a local treatment for idiopathic pulmonary fibrosis, or IPF, and has passed the drug candidate nomination stage. We received a €14.2 million grant from the Bavarian Ministry of Economic Affairs, Regional Development and Energy supporting research and development of the program for post-acute sequelae of SARS-CoV-2 infection (PASC) pulmonary fibrosis, or PASC-PF, also known as post-COVID-19 syndrome pulmonary fibrosis, or “long COVID”.

PRS-220 is progressing in all activities required to support a regulatory submission for clinical evaluation. We presented initial preclinical data for PRS-220 at the European Respiratory Society International Congress 2021, or ERS, demonstrating a more potent and durable target engagement profile compared to a clinical-stage, systemically delivered anti-CTGF antibody benchmark. Additionally, the targeting of CTGF locally in the lung showed increased attenuation of fibrotic lung remodeling *in vivo* compared to the antibody. This outcome correlates with superior lung tissue exposure of PRS-220 compared to that of the antibody in head-to-head studies, where intratracheally administered PRS-220 efficiently penetrates the fibrotic, interstitial lung tissue of mice. Clinical development for the program in IPF is expected to begin in 2022 once regulatory clearance is obtained.

We have also entered into a multi-program research collaboration and license agreement with Genentech, a member of the Roche Group, to discover, develop and commercialize locally delivered respiratory and ophthalmology therapies. We have initiated joint discovery activities in each of the two committed programs.

The lead IO Anticalin-based drug candidate in our pipeline, cinrebafusp alfa, is designed to target the immune receptor 4-1BB and the tumor target HER2. Cinrebafusp alfa is a genetic fusion of a HER2-targeting antibody with an Anticalin protein specific for 4-1BB. The proposed mode of action of this 4-1BB/HER2 bispecific is to promote 4-1BB clustering by bridging 4-1BB-positive T cells with HER2-positive tumor cells, thereby providing a potent co-stimulatory signal to tumor antigen-specific T cells. Cinrebafusp alfa is intended to localize 4-1BB activation in the tumor, and to thereby both increase efficacy and reduce systemic toxicity compared to 4-1BB-targeting antibodies.

The phase 1 study, a multicenter, open-label, dose escalation study, was designed to determine the safety, tolerability, and potential anti-cancer activity of cinrebafusp alfa in patients with advanced or metastatic HER2-positive solid tumors for which standard treatment options are not available, are no longer effective, or are not tolerated, or in patients that have refused standard therapy. Elevated HER2 expression is associated with multiple cancers, including gastroesophageal, bladder, breast and a range of other tumor types. We presented interim data from the phase 1 study at the Society for Immunotherapy of Cancer, or SITC, annual meeting in November 2019. At SITC, we reported that cinrebafusp alfa was well-tolerated and had a favorable safety profile at all doses and schedules tested, demonstrated anti-tumor activity in a heavily pre-treated patient population across multiple tumor types and showed a potent increase in CD8+ T cell numbers in the tumor microenvironment in patients, indicative of 4-1BB agonism on T cells. We also reported initial data from a phase 1 escalation study of cinrebafusp alfa in combination with atezolizumab in November 2019. We reported that cinrebafusp alfa in combination with atezolizumab was well-tolerated and had a favorable safety profile at all doses tested, demonstrated anti-tumor activity in a heavily pre-treated patient population across multiple tumor types and showed a potent increase in CD8+ T cell numbers in the tumor microenvironment in patients demonstrating a clinical benefit, indicative of 4-1BB agonism on T cells and a mode of action distinct from atezolizumab alone.

We presented additional interim data from the phase 1 monotherapy study and atezolizumab combination study of cinrebafusp alfa at the European Society for Medical Oncology, or ESMO, Virtual Congress in September 2020. Data showed that cinrebafusp alfa had an acceptable safety profile at all doses and schedules tested in each clinical study, demonstrated anti-

tumor activity in a heavily pre-treated patient population across multiple tumor types and showed a potent increase in CD8+ T cell numbers in the tumor microenvironment in patients, indicative of 4-1BB agonism on T cells. Additionally, a significant expansion of CD8+ T cells in the tumor microenvironment of responders and a substantial increase of peripheral soluble 4-1BB were observed in the active dose cohorts, suggesting 4-1BB-mediated target engagement. In the monotherapy study, out of 33 response-evaluable patients at the time of the data cutoff, one patient with stage 4 rectal adenocarcinoma achieved a confirmed complete response at the 18 mg/kg Q2W dose (cohort 13b), three patients achieved a partial response at the 8 mg/kg Q2W dose (cohort 11b), and stable disease was observed in 13 patients as best response. In the atezolizumab combination trial, four patients achieved a confirmed partial response at active dose levels.

In January 2022, the first patient was dosed in the two-arm phase 2 study for cinrebafusp alfa in gastric cancer in the United States. Supported by additional data we presented from the phase 1 monotherapy study of cinrebafusp alfa in an oral presentation at the American Association for Cancer Research Virtual Congress, or AACR, in April 2021, the first arm of the phase 2 study includes the combination with ramucirumab and paclitaxel in HER2-high gastric cancer, while the second arm is in combination with tucatinib in HER2-low gastric cancer. Collaboration partners Lilly and Seagen are supplying ramucirumab and tucatinib, respectively. The criteria for advancement of this program will evaluate a composite of measures, including a minimum target of 50% ORR in the HER2-high arm and a minimum target of 40% ORR in the HER2-low arm, duration of response, and safety. The Company expects to report data from the arm evaluating cinrebafusp alfa in combination with tucatinib in HER2-low gastric cancer in 2022. The Company expects to report data from the arm evaluating cinrebafusp alfa in combination with ramucirumab and paclitaxel in HER2-high gastric cancer in 2023. In June 2021, FDA granted orphan drug designation to cinrebafusp alfa for the treatment of HER2-high and HER2-low expressing gastric cancers.

The supporting data presented at AACR included an evaluation of 78 patients who had been enrolled in the monotherapy study as of the February 2021 cutoff date, including four additional patients enrolled in the active dose cohorts (≥2.5 mg/kg) since the data were presented at the ESMO Virtual Congress in September 2020. Out of 42 response-evaluable patients at the time of the data cutoff of February 25, 2021, according to RECIST 1.1, one patient with stage 4 rectal adenocarcinoma achieved a confirmed complete response at the 18 mg/kg Q2W dose (cohort 13b), four patients achieved a partial response (three at the 8 mg/kg Q2W dose (cohort 11b)) and one at the 18 mg/kg Q2W dose (cohort 13b)), and stable disease was observed in 17 patients as best response out of 42 evaluable patients across the predicted active dose ranges (cohorts 9-13b), translating to an ORR of 12% and a DCR of 52%. Consistent with the mechanism of action of cinrebafusp alfa, dose-dependent immune activation was demonstrated by showing an increase in CD8+, T cell, NK cells and cytotoxic activity in the tumor microenvironment and an increase of soluble 4-1BB in the blood, indicating target engagement of 4-1BB and activation of immune cells. Cinrebafusp alfa demonstrated durable anti-tumor activity in a heavily pre-treated patient population. Additionally, clinical benefit was observed in patients with “cold” tumors as well as those with low HER2 expression who were enrolled into the study on the basis of archived HER2-status and were later re-assessed on the basis of a pre-treatment biopsy. Cinrebafusp alfa also showed an acceptable safety profile at all doses and schedules tested in the clinical study with no dose-limiting toxicities. The totality of response data generated in cohorts 11b (8 mg/kg Q2W) and 13b support the recommended phase 2 dose of a two-cycle loading dose of 18 mg/kg (Q2W), following by an 8 mg/kg dose (Q2W) in subsequent cycles.

The last update of the atezolizumab combination study of cinrebafusp alfa was presented at the ESMO Virtual Congress in September 2020. As of the July 2020 cutoff date, 41 patients had been enrolled and seven dose cohorts have been evaluated at a Q3W dosing schedule ranging from 0.05 mg/kg to 8 mg/kg in combination with a fixed 1200 mg dose of atezolizumab. In that trial, under RECIST 1.1, four patients achieved a confirmed partial response at active dose levels and an acceptable safety profile was observed at all doses and schedules tested in the clinical study.

In January 2017, we initiated a strategic collaboration with Servier to discover and develop multiple Anticalin-based bispecific therapeutics in IO. The lead program in the alliance is PRS-344, also known as S095012, a 4-1BB/PD-L1 Anticalin-antibody bispecific and preclinical data for the PRS-344/S095012 program were presented at the SITC 2018 Annual Meeting. We achieved two preclinical milestones under the program, one in December 2018 and another in February 2019 in addition to a clinical development milestone as the first patient was dosed in a global phase 1/2 in patients with solid tumors in November 2021. We also executed our option to opt into co-development and U.S. commercialization of PRS-344/S095012 during the first quarter of 2019. We hold exclusive commercialization rights for PRS-344/S095012 in the United States and will receive royalties on ex-U.S. sales from Servier for this program. The second active program in this alliance is PRS-352, a preclinical-stage program addressing undisclosed targets for immuno-oncology. We successfully completed non-GLP preclinical work in 2020 and PRS-352 is currently under further development at Servier.

In February 2018, we initiated a strategic collaboration with Seagen to discover and develop up to three Anticalin-based tumor-targeted bispecific therapeutics in IO. As part of the alliance, we have achieved a key preclinical milestone for one of the programs in the Seagen collaboration, a bispecific tumor-targeted costimulatory agonist, triggering a $5 million milestone. We have handed the program over to Seagen, which is responsible for further advancement and funding of the asset. The program is one of up to three potential programs in the Seagen alliance, and we believe the achieved milestone further validates our approach and leadership in immuno-oncology bispecifics, complementing the encouraging clinical data seen with cinrebafusp

alfa. During the third quarter of 2021, we initiated the second program within the collaboration with Seagen. We retain a co-promotion option for one of the programs in the United States.

We continue to explore opportunities to develop additional differentiated multispecific therapeutics in IO. We are performing proof of concept and proof of mechanism studies on additional fully proprietary programs to support drug candidate nomination. Additionally, we have several academic collaborations that support our research and development objectives, including collaborations to assist in target and biomarker identification and validation as well as translational research related to our drug candidates in IO.

Strategy

Our corporate vision is to become a fully-integrated biotechnology company by discovering and developing Anticalin-based therapeutics to target validated disease pathways in unique and transformative ways with the ultimate goal of commercializing our therapeutic products. We intend to engage with partners for many of our programs in a combination of geographic and program-based arrangements to maximize our business opportunities. We also intend to retain certain development and commercial rights on selected products as our experience in late-stage drug development grows. Key elements of our strategy include:

- ***Collaborating with AstraZeneca on the execution of the PRS-060/AZD1402 phase 2 studies.*** We previously reported promising data from our phase 1 SAD and MAD studies of PRS-060/AZD1402. We achieved a $13.0 million milestone in connection with the initiation of patient enrollment in the phase 2a study of PRS-060/AZD1402 in the first quarter of 2021. The efficacy portion (part 2a) of this phase 2a study is currently ongoing following a successful sponsor evaluation of safety data from part 1a (1 and 3 mg dose compared to placebo) of the study. Successful development of PRS-060/AZD1402 would both further validate our platform and could provide a convenient and effective option for uncontrolled asthma patients as a potential first-in-class inhaled biologic.
- ***Advancing cinrebafusp alfa into a phase 2 study to evaluate the drug candidate in combination with ramucirumab and paclitaxel in HER2-high expressing gastric cancer and in combination with tucatinib in HER2-low expressing gastric cancer.*** In January 2022, we dosed the first patient in the two-arm phase 2 study for cinrebafusp alfa in gastric cancer in the United States. Supported by additional data we presented from the phase 1 monotherapy study of cinrebafusp alfa in an oral presentation at the American Association for Cancer Research Virtual Congress, or AACR, in April 2021, the first arm of the phase 2 study includes the combination with ramucirumab and paclitaxel in HER2-high expressing gastric cancer, while the second arm is in combination with tucatinib in HER2-low expressing gastric cancer. Collaboration partners Lilly and Seagen are supplying ramucirumab and tucatinib, respectively. The Company expects to report initial data from the arm evaluating cinrebafusp alfa in combination with tucatinib in HER2-low gastric cancer in 2022. The Company expects to report data from the arm evaluating cinrebafusp alfa in combination with ramucirumab and paclitaxel in HER2-high gastric cancer in 2023. In June 2021, FDA granted orphan drug designation to cinrebafusp alfa for the treatment of HER2-high and HER2-low expressing gastric cancers, indications with high unmet medical need.
- ***Advancing PRS-344/S095012 through phase 1/2 study.*** Together with Servier, we dosed the first patient in the phase 1/2 study for PRS-344/S095012 in November 2021.
- ***Advancing PRS-220 to initiation of phase 1 study.*** We continue developing PRS-220 as a CTGF-targeting, inhaled treatment of idiopathic pulmonary fibrosis (IPF), an indication of high unmet medical need. In addition, we are exploring PRS-220 in another type of pulmonary fibrosis, post-acute sequelae of COVID-19 pulmonary fibrosis (PASC-PF). We completed the drug candidate nomination stage in 2021, followed by chemistry, manufacturing, and control, or CMC, activities such as the development of a robust process for large-scale manufacturing and the development of a nebulized formulation. We are now conducting clinical-enabling activities including the non-clinical safety assessment of the drug and plan to enter phase 1 study in 2022.
- ***Continuing to build our platform by entering into new partnerships and license and collaborative arrangements and advancing our currently partnered programs.*** We have entered into partnership and collaborative arrangements with pharmaceutical companies in a diverse range of therapeutic areas and geographies. We have active strategic partnerships with the global pharmaceutical companies Servier, AstraZeneca, Seagen and Genentech. Together with our partners, we intend to advance multiple drug candidates through preclinical studies and to select further drug candidates for clinical development in the future. We will also continue to seek to engage with new pharmaceutical partners that can contribute funding, experience and marketing ability for the successful development and commercialization of our current and future drug candidates.
- ***Pursuing additional opportunities for our Anticalin technology.*** The flexibility of our Anticalin platform presents a unique opportunity to adapt and develop Anticalin proteins with therapeutic potential across a broad range of

indications. We intend to continue to identify, vet and pursue opportunities to develop novel Anticalin-based therapeutics for respiratory diseases, oncology and additional diseases.

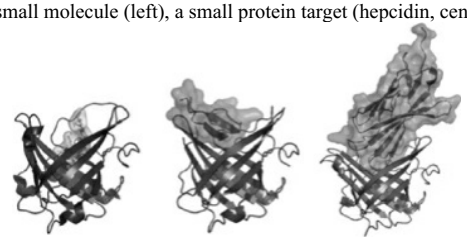
- ***Pursuing other platform development activities.*** We continue to make investments in our Anticalin platform, including in display and other technologies used to discover and optimize Anticalin proteins against targets of interest to increase speed, throughput and caliber of the selection process. In addition, we continue to make investments in our platform for the characterization and manufacturing of Anticalin proteins to develop drug candidates with excellent drug-like properties that can be efficiently produced.

Anticalin Platform Technology

Our platform technology focuses on low molecular-weight Anticalin proteins that can bind tightly and specifically to a diverse range of targets. Anticalin proteins are derived from human proteins called lipocalins, which are naturally occurring low-molecular weight human proteins of approximately 17 to 21 kDa molecular mass typically found in blood plasma and other bodily fluids. The lipocalin class of proteins defines a group of specific extracellular binding proteins that, collectively, exhibit extremely high structural homology, yet have a low amino acid sequence identity (less than 20%), making them attractive "templates" for amino acid diversification. Lipocalins naturally bind to, store and transport a wide spectrum of molecules. The defining attributes of the human lipocalin class and, by extension, Anticalin proteins, engineered from the lipocalin class of proteins, are a rigidly conserved beta-barrel backbone with four flexible loops, which, together, form a cup-like binding pocket. The graphic below shows the tear lipocalin (left) and neutrophil gelatinase-associated lipocalin, or NGAL (right).

We currently develop our Anticalin proteins from two scaffolds, namely the tear lipocalin, found primarily in human tear fluid as well as the lung epithelium, and NGAL, a protein involved in the innate immune system, by selection from diverse libraries with mutations in the genetic code of the ligand binding regions and regions of the proteins that are amenable for amino acid exchanges. These mutations have the potential to lead to highly specific, high-affinity binding proteins for both small and large molecular targets. Mutations are introduced at pre-defined positions, creating exponentially diverse pools of Anticalin proteins, the most potent and well-behaved of which are selected and optimized in a customized manner through *in vitro* selection using techniques such as phage and yeast display, successful techniques in antibody-based drug discovery. The ability to generate highly-diverse and high-quality Anticalin libraries and to select for the best binders among the large pool of Anticalin proteins by display technologies gives us the opportunity to select specific and high affinity Anticalin proteins for a wide variety of targets. The flexibility inherent in the Anticalin proteins' cup-like structure allows us to choose both small-molecule targets that are capable of binding inside the 'cup' as well as larger protein targets that are predominantly bound by the flexible loop region outside of the 'cup'. Our phase 1 studies for PRS-060/AZD1402, our prior phase 1 and 2 studies of PRS-080, our prior phase 1 study of PRS-050, as well as the phase 1 study of a PCSK9-specific Anticalin protein, indicate that these proteins appear to have low immunogenic potential and thereby have the potential to exhibit a favorable safety profile.

The below graphic illustrates Anticalin proteins binding to a small molecule (left), a small protein target (hepcidin, center) and a large protein target (CTLA4, right):



To obtain a specific Anticalin protein, we take advantage of the breadth of our proprietary Anticalin libraries, generated through our protein engineering expertise. We created, and will continue to create, proprietary Anticalin libraries by rationally diversifying certain lipocalin regions, thereby generating Anticalin libraries suitable for identifying binders to different types of targets. By utilizing bacterial and mammalian expression platforms from the earliest stages of drug discovery through current Good Manufacturing Practice, or cGMP, manufacturing, we created seamless platforms that facilitate the selection of high-quality and cost-effective drug candidates. Anticalin-based drug candidates have been proven to be suitable for expression in

standard mammalian expression systems. Thus, Anticalin protein manufacturing is not limited to bacterial systems, and the expression system can be selected on a program-by-program basis. See "—Manufacturing" below.

Anticalin proteins share many of the favorable qualities of antibodies, including:

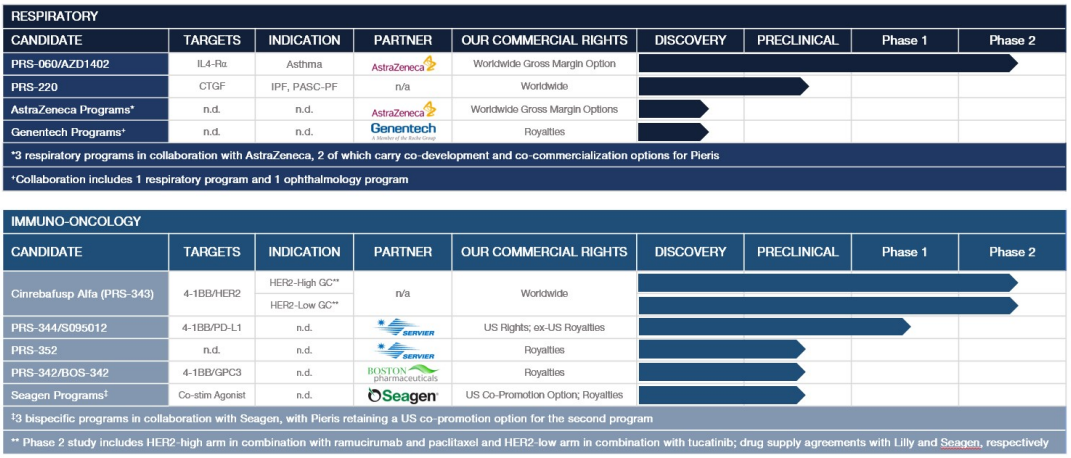
- *High specificity to their targets*. Like antibodies, Anticalin proteins can bind their targets without binding other molecules, even molecules with very similar chemical structures or amino acid sequences, allowing for more effective treatments through, for example, minimizing off-target effects.
- *Tight binding and effective biological activity at their targets.* Like antibodies, Anticalin proteins are able to bind their targets at subnanomolar affinities. Anticalin proteins can potentially achieve desirable biological effects by inhibiting an undesired or inducing a desired cell activity by binding to cell-surface receptors or their ligands.
- *Scalability for large-scale production*. Like antibodies, Anticalin proteins lend themselves to large-scale production, yet can also be produced in a range of expression systems ranging from prokaryotic (bacterial) to eukaryotic (for example, animal and fungal) cells. Anticalin proteins can take advantage of several well-understood and widely-practiced methods of protein production both in small amounts for preclinical testing and at larger scale for clinical trials and commercial production.

While often compared to antibodies, we believe Anticalin proteins offer several advantages over antibodies, including:

- *Small size and biophysical stability*. Anticalin proteins are small in size and are monomeric. Therefore, we believe Anticalin proteins are generally more biophysically stable than antibodies, which are composed of four polypeptide chains. This will potentially enable unique routes of administration, such as pulmonary delivery. Higher-molecular-weight entities such as antibodies are often too large to be formulated and delivered effectively through these methods. We believe Anticalin proteins may also be less expensive to manufacture than antibodies due to their lower molecular weight and less bulky structure as well as the ability to leverage the prokaryotic-based manufacturing systems, a less costly manufacturing system than mammalian cell-based manufacturing systems, to create them.
- *Optimization of half-life*. Anticalin proteins can be engineered to have a half-life that is optimal for the indication area and a desired dosing schedule. Antibodies typically have half-lives of two weeks or longer, whereas Anticalin proteins can be engineered to have half-lives from hours to weeks, depending on the half-life extension technology employed, if any. This optionality allows us to exert greater control over the amount of circulating Anticalin protein in the blood and the amount of time such Anticalin proteins circulate in the blood, depending on the underlying biology we are trying to address.
- *Platform for higher-order multispecificity and avoidance of cross-linking.* Our Anticalin technology allows for monovalent or multivalent target engagement, including multispecificity within a single protein. We believe that a monovalent "backbone" is an advantage in situations where pure antagonism of certain cellular receptors is desired. The dual-binding nature of antibodies, which have two "arms," can be a disadvantage when the antibodies bind to and cross-link cell-surface receptors. Such cross-linking often leads to undesirable activation of the cells bearing those receptors. Single-action, or monovalent, Anticalin proteins have only a single binding site and by that do not induce cross-linking. Further, when it is called for by the biology we are addressing, we can create multispecific Anticalin proteins that can simultaneously bind (i) two or more different targets or (ii) different epitopes on the same target by genetically linking Anticalin proteins with distinct specificities or by genetic fusion of an Anticalin protein with an antibody. We believe this multispecificity offers advantages in biological settings where binding to multiple targets can enhance the ability of a drug to achieve its desired effects, such as killing cancer cells. Novel Anticalin proteins genetically fused to each other or to existing antibodies for simultaneous target engagement are expressed as a fusion protein without generally compromising on manufacturability.
- *Flexible formatting facilitates selection of potent T cell engagers.* The molecular architecture of Anticalin proteins as a single polypeptide chain that folds into a stable eight-stranded β-barrel with exposed N- and C-termini, both not part of the binding site, makes them ideal building blocks to generate bispecific and even multispecific fusion proteins offering novel therapeutic modalities. Multispecific Anticalin-based fusion proteins can be used to pursue innovative therapeutic strategies in IO, particularly by addressing the "immunological synapse" that forms at the interface upon contact between an immune cell and a cancer cell. This can drive an efficient activation of tumor-specific T cells in the vicinity of the tumor, thereby avoiding some of the toxicities observed with peripheral T cell activation in healthy tissues. Generally, the formatting flexibility of Anticalin-based biologics offers the ability of modulating valency and geometry of the multispecific compound according to biological needs. For example, Anticalin proteins can be genetically fused to either the N- or C- terminus of the antibody heavy or light chain, thereby resulting in different geometries of the fusion protein with the antibody as well as Anticalin binding sites covering a range of distances with regard to the T cell target on the one hand and the tumor antigen on the other.

Implementation of the Anticalin Platform Technology: Our Drug Candidate Pipeline

Each of our drug candidates is in the early stage of development, and we anticipate that it will likely be several years before any of our drug candidates could be commercialized. The following table summarizes the status of our current drug candidates and programs:



PRS-060/AZD1402 Targeting IL-4Rα in Asthma

PRS-060/AZD1402 is an Anticalin drug candidate targeting IL-4Rα, a cell surface receptor expressed on immune cells in the lung. IL-4Rα is specific for the cytokine IL-4 and the closely related cytokine IL-13, both key drivers of the immune system. PRS-060/AZD1402 is derived from human tear lipocalin, has a 20 pM affinity for human IL-4Rα and has a favorable stability profile. Following the results reported in the "Clinical data" section below, and presented at the American Thoracic Society International Conference in May 2019 and European Respiratory Society International Congress in October 2019, AstraZeneca started a global phase 2a study of PRS-060/AZD1402. We believe that PRS-060/AZD1402 represents a first-in-class inhaled biologic targeting IL-4Rα for the treatment of asthma. PRS-060/AZD1402 is being developed in partnership with AstraZeneca, as further described below.

Asthma market

Asthma is a very common chronic airway disorder affecting approximately 300 million people worldwide according to the Global Initiative for Asthma, including approximately 26 million Americans according to the U.S. Centers for Disease Control. Of these 26 million, approximately 7 million are children. Asthma is responsible for 13 million physician visits per year including approximately 2 million emergency visits in the United States, according to the American Lung Association. In the United States between 2008 and 2013, asthma was responsible for approximately $3 billion in losses due to missed work and school days, approximately $29 billion due to asthma-related deaths, and approximately $50 billion in medical costs. This resulted in a total cost of asthma in the United States of approximately $82 billion in 2013 according to the American Thoracic Society.

In 2016, of the approximately 19 million asthma patients over 12 years of age in the United States, about 41%, or 7.8 million, had moderate-to-severe asthma; of the approximately 47.8 million asthma patients over 12 years of age in Europe, about 45%, or 21.5 million, had moderate-to-severe asthma. About 40% of moderate-to-severe asthma patients have uncontrolled asthma, which amounts to approximately 3.1 million patients with moderate-to-severe uncontrolled asthma in the United States and approximately 8.6 million in Europe according to an analysis prepared by Artisan Healthcare Consulting. There are several biologics approved for moderate-to-severe uncontrolled asthma in the United States and Europe. Omalizumab is an anti-IgE monoclonal antibody marketed by Roche/Genentech and Novartis for moderate-to-severe persistent allergic asthma and chronic idiopathic urticaria; in 2020, Roche/Genentech and Novartis reported total global sales for omalizumab in the amount of $3,306 million. Mepolizumab is an anti-IL5 monoclonal antibody marketed by GlaxoSmithKline, or GSK, for severe eosinophilic asthma; in 2020, GSK reported global sales for mepolizumab in the amount of $1,314 million. Benralizumab is an anti-IL5 receptor monoclonal antibody marketed by AstraZeneca for severe eosinophilic asthma; in 2020 AstraZeneca reported global

sales for benralizumab in the amount of $949 million. Dupilumab is an anti-IL4Rα monoclonal antibody marketed by Sanofi/Regeneron for atopic dermatitis and moderate-to-severe uncontrolled asthma; in 2020, Sanofi/Regeneron reported total global sales of dupilumab in the amount of $3,976 million. Tezepelumab is an anti-TSLP monoclonal antibody marketed by Amgen and AstraZeneca for severe asthma; tezepelumab was approved by the FDA in December 2021.

Challenges in using conventional therapy

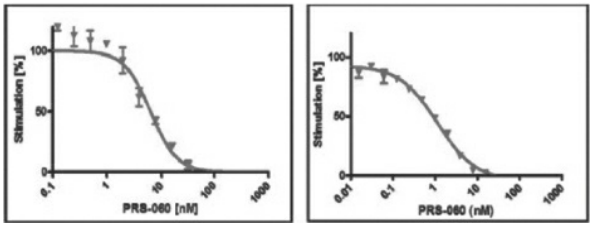
The current standard of care for persistent, moderate-to-severe allergic asthma is high-dose inhaled corticosteroids or ICS often in combination with inhaled long-acting beta-adrenergic agonists, or LABA. In uncontrolled moderate-to-severe allergic asthma, omalizumab is sometimes given to patients in addition to ICS/LABA combinations. Omalizumab was approved for this condition in the United States in 2003. Outside of the United States, omalizumab is approved for severe asthma. Omalizumab works by binding to the immune mediator immunoglobulin E, or IgE, and inhibiting IgE-mediated activation of mast cells and basophils, types of white blood cells. It has also been shown to impact some diseases, such as asthma, which are driven by eosinophils, another important class of immune cells. However, patient response to omalizumab has been shown to be inconsistent, as reported in a publication by McNicholl and Heaney in 2008 in the journal *Core Evidence*, which explained that in only some studies did omalizumab improve lung function. Furthermore, general asthma symptoms are also typically unaffected by omalizumab. Finally, in 2007, the FDA issued a black box warning for omalizumab due to reported cases of anaphylaxis, a potentially life-threatening allergic reaction suffered by some patients who had taken the drug.
Beyond omalizumab, there are five approved biologics, or antibodies, for the treatment of asthma. Three target the IL-5 pathway, one targets IL-4Rα, and one targets thymic stromal lymphopoietin (“TSLP”). GSK's mepolizumab, which targets IL-5, was approved for severe eosinophilic asthma in adults and children older than 12 in 2015. Teva’s reslizumab, also targeting IL-5, was approved in 2016 and AstraZeneca’s benralizumab, which targets IL-5 receptor alpha, or IL-5Rα, was approved in November 2017. Amgen's and AstraZeneca's tezepelumab, which targets TSLP, was approved in December 2021 as an add-on maintenance treatment for adult and pediatric patients ages 12 years and older with severe asthma, Dupilumab is an antibody that targets IL-4Rα that is delivered subcutaneously and was approved for the treatment of moderate-to-severe atopic dermatitis in March 2017. In October 2018, Regeneron and its partner Sanofi announced that the FDA had approved dupilumab as “add-on maintenance therapy in patients with moderate-to-severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid-dependent asthma.” In the phase 3 Liberty Asthma Quest study, dupilumab (300 mg every 2 weeks) in the pre-specified high eosinophilic group (eosinophil blood count of ≥ 300 cells/microliter) demonstrated a reduction in annualized rate of severe exacerbations by 67.4% and an improvement in forced expiratory volume in one second, or FEV1, by 0.24L. The Liberty Asthma Venture trial evaluated dupilumab in oral glucocorticoid-dependent severe asthma patients. In the overall population, the percentage of patients that decreased oral corticosteroid use by 50% or more was 80% in the dupilumab group versus 50% for placebo (or a 60% relative reduction), while decreasing the rate of severe exacerbations by 59% and improving FEV1 by 0.22L versus placebo. In the high eosinophilic group, dupilumab decreased the rate of severe exacerbations by 71% and improved FEV1 by 0.32L versus placebo (Rabe et al., 2018).

Advantages to inhalation as a route of administration for PRS-060/AZD1402

We believe that local delivery via inhalation may lead to a better tolerability profile than systemically administered antibodies. Since dosing by inhalation is a common route of administration in asthma patients, it could represent a more convenient dosage regimen for patients than dosing of antibodies by injection. PRS-060/AZD1402 was safe and well-tolerated in a SAD phase 1 study, and was evaluated in a MAD phase 1 study with interim data suggesting that PRS-060/AZD1402 was safe and well-tolerated at all doses, led to a statistically significant reduction in FeNO and showed dose-dependent systemic target engagement in patients with mild asthma and elevated levels of FeNO.

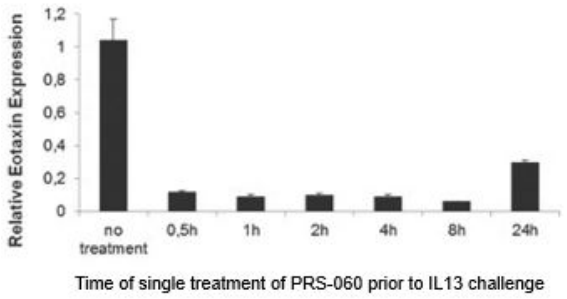
Preclinical data

In *in vitro* assays, PRS-060/AZD1402 specifically bound to immobilized targets such as human IL-4Rα in a concentration-dependent manner. We tested the binding of PRS-060/AZD1402 to various targets in an enzyme-linked immunosorbent assay, or ELISA, a standard *in vitro* assay platform. In these tests, PRS-060/AZD1402 bound to IL-4Rα with subnanomolar affinity and it did not bind to three other human cell-surface interleukin receptors (IL-6R, IL-18Rα, IL-23Rα). Furthermore, the activity of IL-4 and IL-13 was inhibited by PRS-060/AZD1402 in a dose-dependent manner. The charts below show the inhibition of IL-4- (left) or IL-13- (right) induced proliferation in human TF-1 cells *in vitro* by PRS-060/AZD1402.

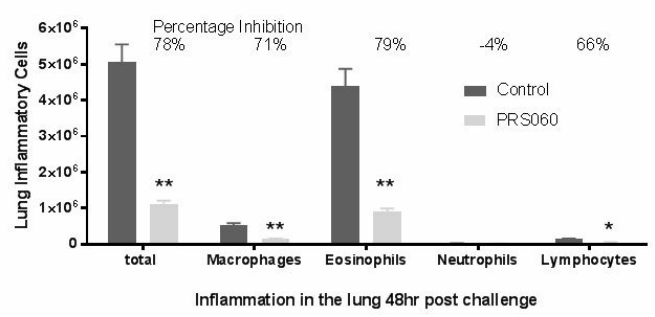


In *in vivo* assays in mice genetically altered to express human IL-4Rα, human IL-4 and IL-13, low doses of lung delivered PRS-060/AZD1402 inhibited the induction of eotaxin protein, a marker of airway inflammation, in lung tissue following pulmonary delivery. We observed this inhibition at both the RNA and protein levels compared both to buffer and to tear lipocalin (control).

The chart below shows the duration of PRS-060/AZD1402-mediated inhibition of eotaxin gene expression in lung tissue by a single pulmonary dose in mice:



When we administered IL-13 into the lung of humanized mice (that express human IL-4, IL-13 and IL-4Rα), inflammation was induced as determined by eotaxin expression, which was not inhibited when phosphate buffered saline, or PBS, or human wild type lipocalin was administered into the lung. In contrast to the PBS or wild-type lipocalin administration, increases in eotaxin expression were prevented when PRS-060/AZD1402 was administered into the lung before IL-13. As demonstrated in the above chart, the model showed the inhibitory potential lasts for up to 24 hours after PRS-060/AZD1402 administration. We have also demonstrated that PRS-060/AZD1402 reduces the inflammation associated with antigen challenge in a mouse asthma model. The chart below shows that pre-treatment with PRS-060/AZD1402 reduces the lung levels of the key inflammatory cells' eosinophils and lymphocytes, a profile that supports the hypothesis that lung delivery of an IL-4Rα antagonist to asthmatics may be viable approach to the treatment of asthma.



Clinical data

PRS-060/AZD1402 was tested in a nebulized formulation in 54 healthy volunteers at nominal dose levels ranging from 0.25 mg to 400 mg in a phase 1 SAD study; the drug candidate was safe and well-tolerated in the volunteers in that study. Data from that

study were presented at the American Thoracic Society International Conference in May 2019 showing that PRS-060/AZD1402 was well-tolerated when given as a single inhaled or intravenous doses to healthy volunteers and there was systemic target engagement (as measured by pSTAT6 inhibition). We presented interim data from the PRS060/AZD1402 phase 1 MAD study at the 2019 European Respiratory Society International Congress in October 2019 and reported that PRS-060/AZD1402 was safe and well-tolerated at all doses, led to a statistically-significant reduction in FeNO, a validated biomarker for eosinophilic airway inflammation and showed dose-dependent systemic target engagement in patients with mild asthma and elevated levels of FeNO (≥ 35ppb). During the treatment period, 30 patients were randomized to receive delivered doses of PRS-060/AZD1402 ranging from 2 mg to 60 mg (5 mg to 150 mg administered through a nebulizer (nominal dose)) twice daily for nine consecutive days and one final dose on the 10^{th} day, and 12 patients were randomized to receive placebo at the same intervals. Statistically significant and pronounced inhibition of FeNO relative to placebo was observed at all doses. When comparing the 20 mg PRS-060/AZD1402 powered cohort (n=12) to placebo, the primary statistical analysis using the emax model demonstrated a 36% relative reduction in FeNO (p-value <0.0001). Systemic target engagement was dose-dependent and closely aligned with systemic exposure of the drug, consistent with results of the phase 1 SAD study. Minimal systemic exposure and target engagement were observed at the 2 mg dose, suggesting that local target engagement by the drug may be sufficient to reduce airway inflammation, as evidenced by FeNO reduction at that 2 mg dose level.

We sponsored the phase 1 SAD/MAD studies for PRS-060/AZD1402, after which AstraZeneca took responsibility for further clinical development of PRS-060/AZD1402. A phase 2a asthma study of PRS-060/AZD1402 is ongoing in multiple sites globally. This phase 2a study is a two-part, multi-center, placebo-controlled clinical study of PRS-060/AZD1402 that will evaluate PRS-060/AZD1402 at up to three dose levels using a dry powder formulation administered twice daily. In part 1a of the study, 31 asthma patients, controlled on standard of care (medium dose inhaled corticosteroids (ICS) with long-acting beta agonists (LABA)), received PRS-060/AZD1402 twice daily over four weeks to establish the safety profile and pharmacokinetics of the dry powder formulation of PRS-060/AZD1402. The safety review following completion of part 1a included an evaluation, compared to placebo, of the incidence of adverse events, changes in laboratory markers (immuno-biomarkers, clinical chemistry, and hematology), and forced expiratory volume in one second (FEV1). AstraZeneca began enrollment of part 2a of the study to evaluate efficacy, safety, and pharmacokinetics of PRS-060/AZD1402 administered twice daily to asthma patients, uncontrolled on medium dose ICS with LABA, that have a blood eosinophil count of ≥ 150 cells/μL and FeNO ≥ 25 ppb in two active arms and a placebo arm. Following a four-week run-in period, patients will be dosed and monitored over four weeks. FEV1 improvement compared to placebo will be the primary endpoint in this portion of the study. AstraZeneca began enrollment of part 1b of the study to evaluate the safety of the high dose in asthma patients controlled on standard of care who will receive PRS-060/AZD1402 twice daily over four weeks. We expect to announce topline data from the phase 2a study this year, although we are actively evaluating the feasibility of study timelines in the current geopolitical environment and will update guidance in the orderly course of business, if needed. Upon receipt of the topline data and notice from AstraZeneca, including a product development plan and budget, the Company will have 30 days to opt into co-development of the program with AstraZeneca. The Company also retains a separate option to co-commercialize PRS-060/AZD1402 with AstraZeneca in the United States.

PRS-220 Targeting Connective Tissue Growth Factor (CTGF) in IPF and PASC-PF

Our lead fully proprietary respiratory asset, PRS-220, an oral inhaled Anticalin protein targeting connective tissue growth factor, or CTGF, is being developed as a local treatment for idiopathic pulmonary fibrosis, or IPF, and has passed the drug candidate nomination stage. The project is currently in the IND-enabling stage and first-in-human ("FIH") trials are planned to begin in 2022. We received a €14.2 million grant from the Bavarian Ministry of Economic Affairs, Regional Development and Energy supporting research and development of the program for post-acute sequelae of SARS-CoV-2 infection (PASC) pulmonary fibrosis, or PASC-PF, also known as post-COVID-19 syndrome pulmonary fibrosis, or “long COVID”.

What is IPF?

Idiopathic pulmonary fibrosis, or IPF, is a devastating and fatal lung disease of unknown cause with median survival of only three to five years after diagnosis. In patients with IPF, fibrotic remodeling and excess deposition of extracellular matrix, or ECM, causes the destruction of lung architecture leading to loss of lung elasticity and lung function, impairment of gas exchange and finally organ failure. To date, there is no cure for IPF. Treatment options for IPF are very limited, with two FDA-approved drugs, Ofev (nintedanib) and Esbriet (pirfenidone), only capable of slowing down disease progression but not arresting the insidious progression of the disease. Moreover, due to gastrointestinal and other drug-related side effects, nintedanib and pirfenidone are not well-tolerated, leading many patients to discontinue treatment. Thus, a high unmet medical need exists for alternative treatment options for IPF that effectively attenuate the lung function decline or arrest the insidious decline of lung function while offering an improved safety profile with fewer side effects and greater tolerability.

What is PASC-PF?

Following COVID-19, a substantial proportion of patients experience persistent impairment of lung function with associated radiographic-detected lung abnormalities. This phenomenon is known as PASC-PF. Acute COVID-19 is known to cause extensive lung inflammation and injury, and studies suggest that approximately 30% of patients hospitalized with severe COVID-19 will develop persistent respiratory symptoms with persistent lung abnormalities. Given the high number of SARS-CoV-2 infections worldwide and the substantial proportion of patients suffering from severe COVID-19, PASC-PF represents a high unmet medical need that is expected to create a substantial burden on patients and the global healthcare systems. Based on similarities between PASC-PF and IPF, anti-fibrotic drugs including nintedanib and pirfenidone are considered to be promising agents for the treatment of PASC-PF and are currently under investigation for this indication. We believe that anti-CTGF therapy might provide a more effective and safer alternative.

Biology of CTGF

CTGF, or CCN2, is a member of the CCN family of proteins, a family of matricellular proteins associated with the ECM involved in intercellular signaling. In adulthood, CTGF is expressed at a low level but can be strongly induced by certain stimuli such as cytokines, growth factors or mechanical stress.

CTGF contributes to the control of various biological processes, such as proliferation, differentiation, adhesion and angiogenesis. CTGF is known to interact with a variety of proteins including receptors, cytokines and ECM proteins. Among the different cytokines and growth factors that interact with CTGF, transforming growth factor β, or TGF-β, is known to play a crucial role in the development of fibrotic diseases. In order to mediate functions such as cell adhesion, motility and tissue remodeling, CTGF interacts with integrins and components of the ECM such as fibronectin, aggrecan and heparan sulfate proteoglycans. Specifically, in the context of cell adhesion, CTGF is thought to play a role as a molecular bridge between the ECM to integral cell surface proteins.

Role and validation of CTGF as a target for IPF

The pathogenesis of fibrosis is considered to be a dysregulated wound healing process in response to repetitive microinjuries leading to excessive deposition of ECM and impairment of tissue function. CTGF has been associated with fibrotic remodeling in various organs and is highly expressed in fibrotic tissues of different origin, including renal fibrosis, scleroderma, cardiac fibrosis and IPF.

CTGF is a key mediator of wound healing and fibrosis through its interaction with several factors regulating cell proliferation, differentiation, motility, adhesion, and ECM deposition. TGF-β and CTGF are widely regarded as universal mediators of fibrogenesis. TGF-β has been identified as a transcriptional regulator of CTGF, and as supported by preclinical studies, both cytokines are thought to promote fibrotic tissue remodeling in a collaborative manner.

In lung tissue from IPF patients, CTGF levels are found to be elevated when compared to donor tissue with epithelial cells and myofibroblasts being the main cell types expressing the protein in diseased lung tissues (Figure 1).

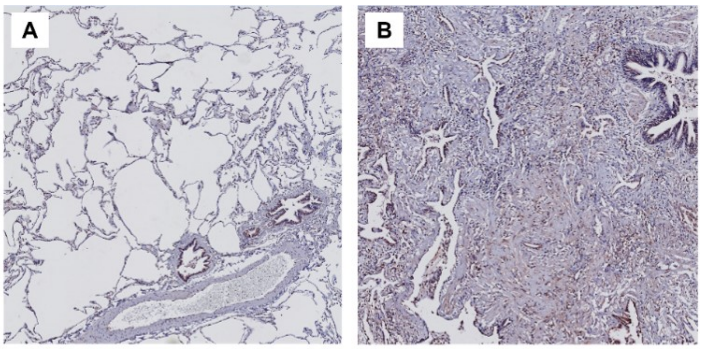


Figure 1 Immunohistochemistry of CTGF in human (A) donor and (B) IPF lung tissues.

Inhibition of CTGF by monoclonal antibodies in preclinical models of lung fibrosis provided evidence supporting its function as a driver of fibrotic lung remodeling *in vivo*. Lung specific overexpression of CTGF in mice demonstrated that CTGF is sufficient to drive fibrotic remodeling of the lung *in vivo*. Moreover, local targeting of CTGF in the lung using an siRNA-based approach attenuated bleomycin-induced lung fibrosis in mice. Based on this evidence, we believe that local targeting of CTGF in the lung is essential to achieve anti-fibrotic activity.

Current approaches to clinical CTGF targeting

In a phase 2 clinical trial (PRAISE), the anti-CTGF monoclonal antibody pamrevlumab/FG-3019 attenuated disease progression in patients suffering from IPF, demonstrating proof of concept for targeting of CTGF for the treatment of IPF. In the PRAISE study, a relative reduction of the decline in percentage of predicted forced vital capacity ("FVC") by 60.3% was observed at week 48, as compared to placebo. Patients in the pamrevlumab group also experienced fewer protocol-defined progression events (defined as death or ≥10 % decline in FVC %-predicted) as compared to the placebo group. In addition, pamrevlumab demonstrated good tolerability with a safety profile similar to placebo. The overall frequency of treatment-emergent adverse events was similar in the treatment and the placebo groups. The safety and efficacy of pamrevlumab will be further evaluated in phase 3 trials (ZEPHYRUS I + II; NCT03955146, NCT04419558) in patients with IPF.

Rationale for local targeting of CTGF

Based on the high expression of CTGF in lung tissue of IPF patients and its reported pro-fibrotic role in the lung in preclinical models, local targeting of CTGF in the lung is considered essential for driving the anti-fibrotic effect. PRS-220 is being developed as a first-in-class inhaled antagonist of the pro-fibrotic mediator CTGF. The inhaled route of administration of PRS-220 offers several advantages over pamrevlumab, the parenterally administered CTGF-targeted monoclonal antibody that is currently in clinical development for IPF.

In comparison to parenteral administration of a monoclonal antibody, inhaled administration of PRS-220 is expected to result in greater exposure of the drug at the site of the disease. Meanwhile, it is known that parenterally administered monoclonal antibodies have a low lung bioavailability with approximately 15% penetrating the lung tissue. Moreover, inhaled administration of PRS-220 is also expected to result in greater lung exposure by avoidance of the CTGF drug “sink” in the peripheral circulation. CTGF is present in the circulation and levels were found to be increased in IPF patients. Another advantage of an inhaled therapy is the convenience of home-based dosing with a portable, handheld nebulizer, as opposed to the office-based injections or intravenous route of delivery of parenteral monoclonal antibodies such as pamrevlumab.

Preclinical data

PRS-220 is a NGAL-based mutant selected from Pieris’ proprietary Anticalin libraries using phage display technology and high-throughput screening. PRS-220 binds to CTGF with high affinity in the picomolar range as measured by surface plasmon resonance, or SPR, and does not show binding to other members of the CCN2 protein family. Compared to the anti-CTGF antibody pamrevlumab, PRS-220 binds with higher affinity and retains a more stable target engagement over a longer period of time (Figure 2).

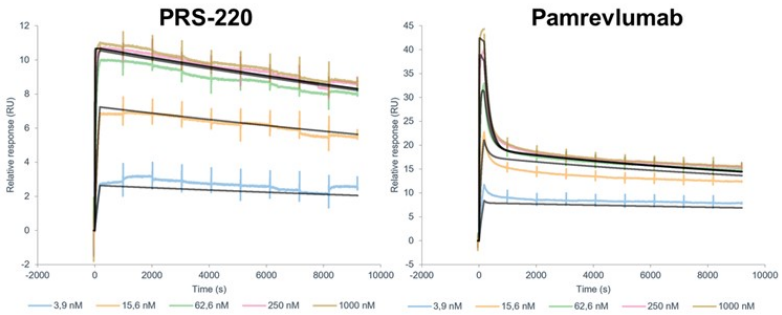
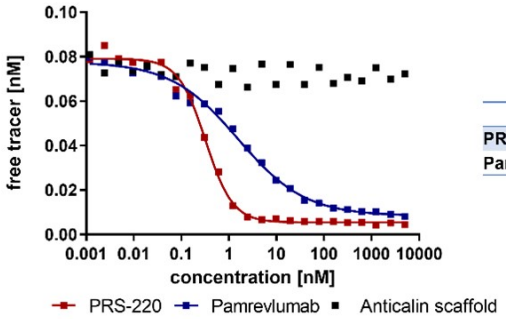


Figure 2 SPR binding experiment showing the binding of PRS-220 (left) and pamrevlumab (right) to CTGF. The 1:1 binding model was used to fit the data of PRS-220. The bivalent analyte model was used to fit the data of the antibody pamrevlumab. CTGF-Fc was immobilized on a CM5 chip, and PRS-220 and pamrevlumab were used as analytes. Pamrevlumab was generated in-house.

PRS-220 targets the functionally active epitope of CTGF as shown by competition ELISA where PRS-220 effectively displaces the clinically active pamrevlumab from CTGF (Figure 3).



	IC50
PRS-220	0.32 nM
Pamrevlumab	1.6 nM

Figure 3 Competition of PRS-220 with pamrevlumab for binding to CTGF and competition of pamrevlumab with itself for binding to CTGF. Competition was assessed in an ELISA-based format using coated pamrevlumab and biotinylated CTGF as tracer.

To assess the lung biodistribution of PRS-220 upon local lung delivery, we challenged mice with bleomycin to induce lung fibrosis. Once fibrosis was established in the animals, fluorescently-labeled PRS-220 was given intratracheally and the distribution of the drug was analyzed using Light Sheet imaging, revealing a favorable lung tissue distribution profile of PRS-220 in the fibrotic lungs. PRS-220 was not only detected in the airways but also penetrated the fibrotic, interstitial lung tissue (Figure 4A). Compared to intravenously administered pamrevlumab, which was analyzed in parallel, PRS-220 showed a higher coverage of the fibrotic tissue (Figure 4B).

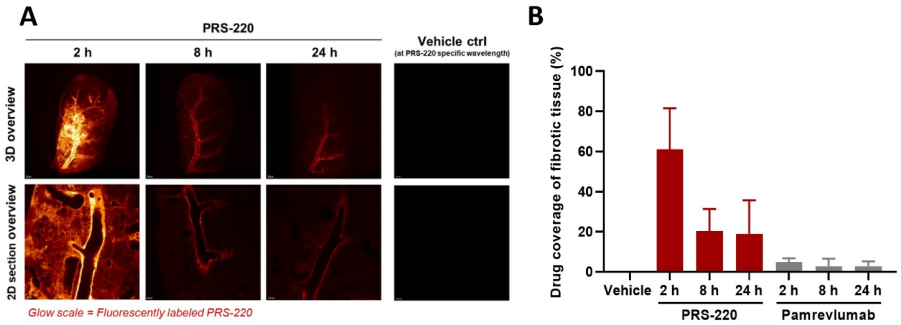


Figure 4 Lung biodistribution of PRS-220 upon intratracheal delivery to fibrotic lungs of mice. (A) Alexa-647 labeled PRS-220 (100 µg/mouse) was administered to the lungs of mice via the intratracheal route at day 21 after bleomycin challenge. The lung tissue distribution was analyzed 2, 8, and 24 hours after PRS-220 administration by Light Sheet imaging of the left lung lobes (630 nm excitation channel). The figure shows representative 3D overview images (scale bars 500 µm) and magnified 2D sections from 3D scanned lungs (scale bars 150 µm). Lungs of saline treated mice imaged at the PRS-220 specific wavelength served as negative controls. (B) Compound accumulation in fibrotic tissue determined by Light Sheet imaging and quantitative analysis (n = 2-5 per group). 100 µg Alexa-647 labeled pamrevlumab was administered intravenously at day 21 after bleomycin challenge.

Developability assessments of PRS-220 showed favorable biophysical properties ensuring robustness and stability for large-scale manufacturing and nebulized inhaled administration. Aerosols generated using vibrating mesh technology show aerodynamic properties suitable for effective lung deposition.

Proprietary Respiratory Platform

We continue to advance other proprietary discovery-stage respiratory programs.

AstraZeneca Respiratory Collaboration beyond PRS-060/AZD1402

As further described below, our license and collaboration agreement with AstraZeneca, or the AstraZeneca Collaboration Agreement, includes three programs beyond PRS-060/AZD1402. We retain co-development and co-commercialization rights to two out of those three programs. Discovery work is ongoing for on all of the additional development candidates under the collaboration. The targets and disease areas of those three programs are undisclosed.

Genentech Collaboration

In May 2021, we and Genentech, a member of the Roche Group, entered into a multi-program Research Collaboration and License Agreement to discover, develop and commercialize locally delivered respiratory and ophthalmology therapies that leverage the Company's proprietary Anticalin-based technology. These two focus areas of the collaboration are uniquely suited to the advantages offered by the small size of Anticalin proteins when delivered locally. The first two programs have been initiated and Pieris is responsible for discovery research and early preclinical development of these programs, and Genentech will be responsible for IND-enabling activities, clinical development, and commercialization of the programs. Genentech will also have the option to select additional targets in return for an option exercise fee.

Cinrebafusp alfa Targeting 4-1BB (CD-137) in Oncology

Cinrebafusp alfa is a bispecific protein targeting the immune receptor 4-1BB and the tumor target HER2. It is generated by genetic fusion of an Anticalin protein specific for 4-1BB to each heavy chain of a HER2-targeting antibody. The mode of action of this 4-1BB/HER2 bispecific is to promote 4-1BB clustering by bridging 4-1BB-positive T cells with HER2-positive tumor cells, and to thereby provide a potent co-stimulatory signal to tumor antigen-specific T cells. Cinrebafusp alfa is intended to localize 4-1BB activation in the tumor, and to thereby both increase efficacy and reduce systemic toxicity compared to 4-1BB-targeting antibodies being developed by third parties in clinical trials. In January 2022, we dosed the first patient in the two-arm phase 2 cinrebafusp alfa study.

Biology of the co-stimulatory immune receptor 4-1BB

4-1BB is a co-stimulatory immune receptor and a member of the tumor necrosis factor receptor, or TNFR, super-family. It is mainly expressed on activated CD4+ and CD8+ T cells, activated B cells, and natural killer, or NK, cells. 4-1BB plays an important role in the regulation of immune responses and thus is a target for cancer immunotherapy. 4-1BB ligand, or 4-1BBL, is the only known natural ligand of 4-1BB and is constitutively expressed on several types of antigen-presenting cells, or APC. 4-1BB-positive T cells are activated by engaging a 4-1BBL-positive cell. The induced 4-1BB clustering leads to activation of the receptor and downstream signaling. In a T cell pre-stimulated by the T cell receptor, or TCR, binding to a cognate major histocompatibility complex, or MHC, target, co-stimulation via 4-1BB leads to further enhanced activation, survival and proliferation, as well as the production of pro-inflammatory cytokines and an improved capacity to kill.

Clinical validation of 4-1BB targeting therapies

The demonstration of the potential therapeutic benefit of 4-1BB co-stimulation in nonclinical models has spurred the development of therapeutic antibodies targeting 4-1BB, utomilumab and urelumab.

Utomilumab is a humanized IgG2 antibody that binds 4-1BB in a manner that blocks the binding of endogenous 4-1BBL to 4-1BB, and that according to publicly available data is well-tolerated as a monotherapy and in combination with rituximab.

Urelumab is an IgG4 antibody that, in contrast to utomilumab, binds 4-1BB in a manner that does not interfere with the 4-1BB / 4-1BBL interaction. While an initial study reported manageable toxicity with doses up to 10 mg/kg, a follow-up monotherapy phase 2 study was reported to have been stopped due to an "unusually high incidence of grade 4 hepatitis." Prior clinical trials with urelumab were focused on safety and efficacy at lower doses as monotherapy or in combination, for example, with rituximab (NCT01775631).

Rationale for bispecific targeting of 4-1BB

We believe that the natural mode of activation of 4-1BB, which requires receptor clustering, demonstrates that an ideal 4-1BB-targeting agent should firstly lead to clustering of 4-1BB, and secondly do so in a tumor-localized fashion on TILs. The antibodies currently in clinical development are not ideal in that respect, as 4-1BB clustering can only be induced by binding to Fcg receptor-positive cells, which are not selectively tumor-localized but distributed throughout the body for Fcg-dependence of TNFR targeting. The toxicity data of urelumab indicates that such a non-selective activation leads to unacceptable toxicity, potentially making it impossible to find a therapeutic window for such 4-1BB-targeting antibodies.

We therefore hypothesized that to obtain an ideal 4-1BB-targeting agent, a bispecific molecule should be designed to target 4-1BB on one end and a differentially expressed tumor target on the other end. A visualization of the general concept is provided in Figure 5, below. HER2/4-1BB bispecific is envisioned to promote 4-1BB clustering by bridging T cells with HER2-positive tumor cells, and to thereby provide a potent co-stimulatory signal to tumor antigen-specific T cells, further enhancing its TCR-mediated activity and leading to tumor destruction.

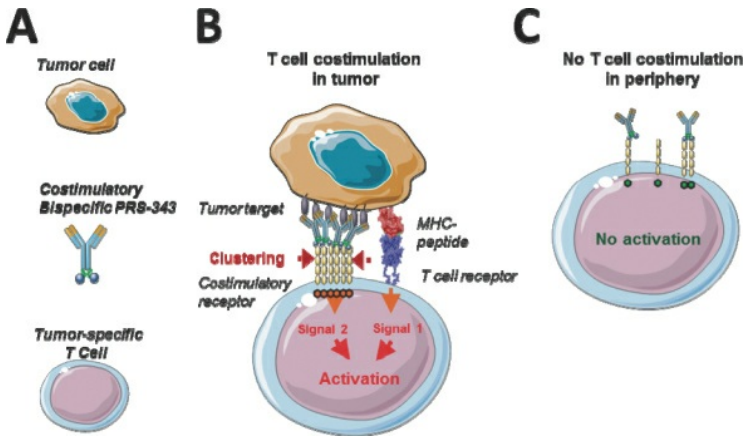


Figure 5 Concept of co-stimulatory T cell engagement. (A) The elements of the system are a target-positive tumor cell, a T cell with a TCR that is specific for an HLA/peptide combination on the tumor, and a co-stimulatory bispecific. (B) Within a patient's tumor, tumor-specific T cells are bridged with tumor cells by a co-stimulatory bispecific. The resulting clustering of the co-stimulatory TCR provides a local co-activating signal to the T cell, further enhancing its TCR-mediated activity and leading to tumor destruction. (C) Toxic side effects are expected to be manageable, as target-negative cells do not lead to co-stimulation of T cells due to a lack of target-mediated receptor clustering, and healthy tissue is spared by tumor-co-stimulated T cells due to the absence of a primary, TCR-mediated signal. Design and Generation of HER2/4-1BB bispecific cinrebafusp alfa.

To obtain a molecule that would work by the mode of action of co-stimulatory T cell engagement, we generated the HER2/4-1BB bispecific cinrebafusp alfa. The molecule consists of two different building blocks binding to the two targets HER2 and 4-1BB. To generate the 4-1BB-specific building block of cinrebafusp alfa, we utilized Anticalin technology. A 4-1BB-binding Anticalin protein was generated based on a re-design of the natural binding pocket of NGAL using mutant Anticalin libraries and a selection and screening process. The resulting 4-1BB targeting Anticalin protein binds human 4-1BB with an affinity of 2 nM as determined by surface plasmon resonance, or SPR, and is capable of co-stimulating human T cells when immobilized on a plastic dish together with an anti-CD3 antibody.

To generate the bivalent HER2/4-1BB bispecific cinrebafusp alfa, we constructed a genetic fusion of a 4-1BB-specific Anticalin protein to the C-terminus of each heavy chain of a HER2-binding antibody, connected by a flexible, non-immunogenic linker.

We utilized a sandwich ELISA experiment to investigate whether cinrebafusp alfa can bind both targets at the same time, which is a necessary prerequisite for the envisioned mode of action of cinrebafusp alfa. Figure 6 below shows that a sigmoid binding curve results from this titration, proving that both targets can indeed be engaged at the same time, fulfilling the key requirement for simultaneous co-stimulatory engagement of T cells by HER2-positive target cells.

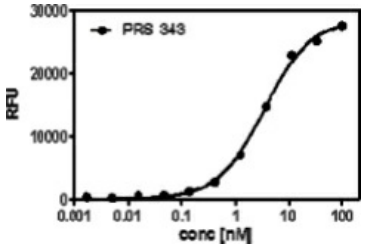


Figure 6 Cinrebafusp alfa simultaneous binding to targets HER2 and 4-1BB. Recombinant HER2 was coated on a microtiter plate, followed by titration of cinrebafusp alfa. Subsequently, a constant concentration of biotinylated human 4-1BB was added, which was detected via a peroxidase-conjugated avidin variant.

Mode of action – co-stimulatory T cell activation

We developed a novel T cell activation assay format to investigate whether cinrebafusp alfa is capable of co-stimulating T cells that have received a basic stimulus via the TCR. The assay, visualized in Figure 7 below, is based upon providing the TCR stimulus via an anti-CD3 antibody coated onto the plastic culture dish, while 4-1BB co-stimulation is achieved by tumor-target dependent clustering of 4-1BB on purified T cells.

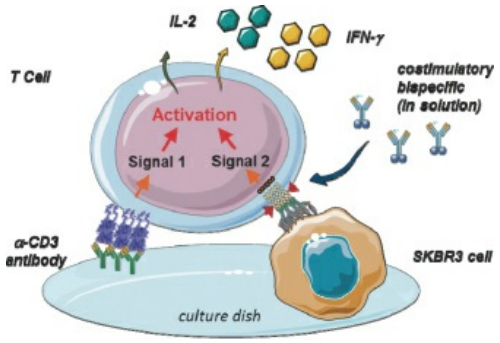


Figure 7 Visualization of co-stimulatory T cell activation assay. HER2-positive tumor cells are grown overnight on cell culture plates that have been precoated with low amounts of an anti-CD3 antibody to provide a limited primary activation of T cells via the T cell receptor. T cells are added to the wells together with the titrated 4-1BB/HER2 bispecific cinrebafusp alfa, leading to clustering of the co-stimulatory 4-1BB receptor, which in turn results in T cell co-stimulation. T cell co-stimulation is detected by increased supernatant IL-2 and IFN-γ levels in the culture supernatants after continued culture.

There is a clear induction of IL-2 (Figure 8A) and IFN-γ (Figure 8C) with increasing concentrations of cinrebafusp alfa. The fitted EC50 of this effect is similar for both proinflammatory cytokines, with 0.7 nM for IL-2 induction and 0.3 nM for IFN-α induction, respectively. That T cell co-stimulation is indeed, due to the bispecific engagement of T cells and SKBR3 cells, shown by two observations: firstly, the monospecific HER2-targeting antibody does not lead to enhanced T cell activation (average shown as dotted line in Figure A and Figure C), and secondly, disrupting the bispecific interaction with an excess of HER2-targeting antibody abolishes the effect of IL-2 and INF-γ induction almost completely, except at the highest concentrations of cinrebafusp alfa employed (Figure 8B and Figure 8D).

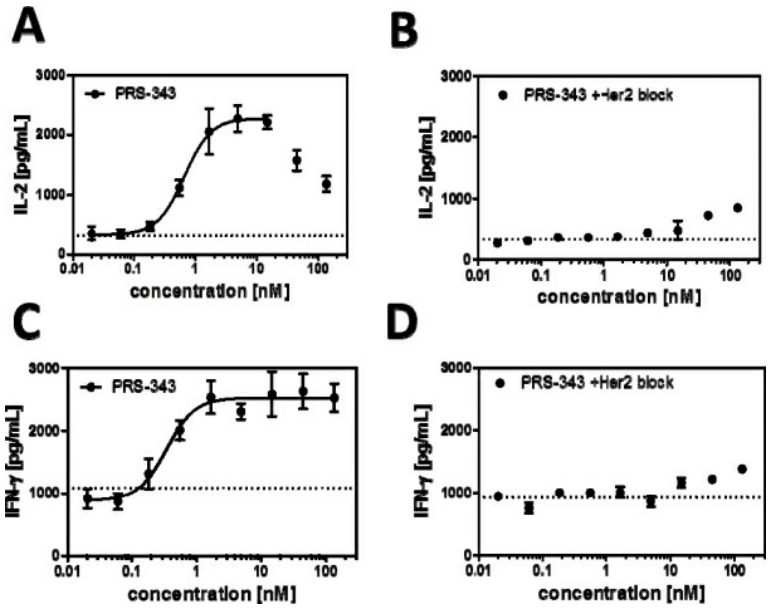
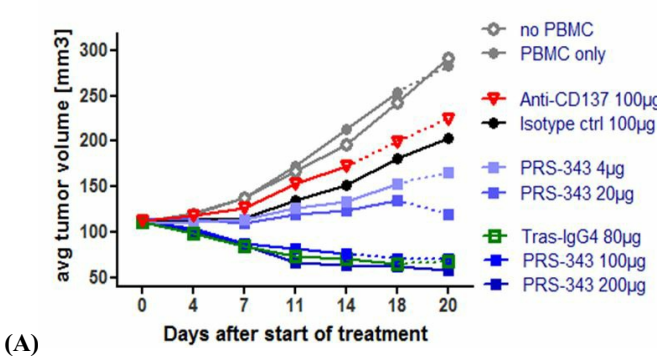
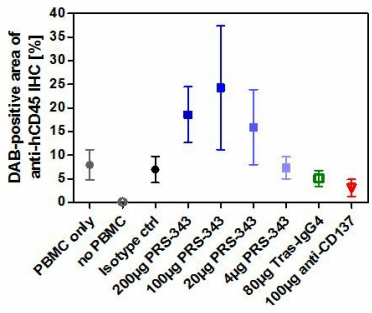


Figure 8 Experimental result of co-stimulatory T cell activation assay. HER2-positive tumor cells were grown overnight on 96-well plates that had been precoated with 0.25 µg/mL anti-CD3 antibody for 1 hour at 37°C. The next day, T cells purified from healthy donor peripheral blood mononuclear cells, or PBMC, were added to the wells together with the titrated 4-1BB/HER2 bispecific cinrebafusp alfa (filled circle) or trastuzumab as a control (dotted line). After three days in culture, IL-2 and IFN-γ, levels in the culture supernatants were measured by an electrochemoluminescence immunoassay. In parallel, the experiment was performed in the presence of an excess of trastuzumab (340 nM) to inhibit the binding of cinrebafusp alfa to the tumor cells, and IL-2 (C) and IFN-γ (D) levels were measured.

Proof of concept data utilizing a humanized SK-OV-3 mouse model demonstrated dose-dependent tumor growth inhibition compared to treatment with the isotype control (Figure 9). It is anticipated that the tumor growth inhibition, or TGI, in this model is predominantly caused by the anti-HER2 activity. The anti-tumor response observed with cinrebafusp alfa was accompanied by a significantly higher tumor infiltration with human lymphocytes (hCD45+). Interestingly, the anti-4-1BB benchmark neither displayed tumor growth inhibition nor enhanced lymphocyte infiltration into tumors compared to isotype. The tras-IgG4 control was also devoid of lymphocyte infiltration into the tumor but displayed a tumor growth inhibition comparable to cinrebafusp alfa. Taken together, these data show that cinrebafusp alfa provided dual activity by both increasing the frequency of TILs by bispecific targeting of CD137 and HER2 as well as mediating direct tumor growth inhibition by the direct, monospecific targeting of HER2.



(A)



(B)

Figure 9 Cinrebafusp alfa activity in mice engrafted with HER2-positive SK-OV-3 cell line and human PBMC. (A) Median of tumor growth. (B) Frequency of CD45+ cells determined by immunohistochemistry of tumors after study end.

Clinical data

We presented interim data from the phase 1 study of cinrebafusp alfa in a late-breaking presentation at the SITC annual meeting in November 2019. At SITC, we reported that cinrebafusp alfa was well-tolerated and had a favorable safety profile at all doses and schedules tested, demonstrated anti-tumor activity in a heavily pre-treated patient population across multiple tumor types and showed a potent increase in CD8+ T cell numbers in the tumor microenvironment in patients, indicative of 4-1BB agonism on T cells.

We also reported initial data from a phase 1 escalation study of cinrebafusp alfa in combination with atezolizumab at our R&D day on November 19, 2019. We reported that cinrebafusp alfa in combination with atezolizumab was well-tolerated and had a favorable safety profile at all doses tested, demonstrated anti-tumor activity in a heavily pre-treated patient population across multiple tumor types and showed a potent increase in CD8+ T cell numbers in the tumor microenvironment in patients demonstrating a clinical benefit, indicative of 4-1BB agonism on T cells and a mode of action distinct from atezolizumab alone.

We presented additional interim data from the phase 1 monotherapy study and atezolizumab combination study of cinrebafusp alfa in an oral presentation at the ESMO Virtual Congress in September 2020. As of the July 2020 cutoff date, 74 patients had been enrolled in the monotherapy study, including 21 additional patients enrolled in the active dose cohorts (≥2.5 mg/kg) since the data were presented at the SITC 2019 Annual Meeting, and 41 patients had been enrolled in the atezolizumab combination therapy study. In the monotherapy study, out of 33 response-evaluable patients at the time of the data cutoff of July 27, 2020, according to RECIST 1.1, one patient with stage 4 rectal adenocarcinoma achieved a confirmed complete response at the 18 mg/kg Q2W dose (cohort 13b), three patients achieved a partial response at the 8 mg/kg Q2W dose (cohort 11b), and stable disease was observed in 13 patients as best response out of 33 evaluable patients across the predicted active dose ranges (cohorts 9-13b), translating to an overall response rate, or ORR, of 12% and a disease control rate, or DCR, of 52%. Additionally, a significant expansion of CD8+ T cells in the tumor microenvironment of responders and a substantial increase of peripheral soluble 4-1BB were observed in the active dose cohorts, suggesting 4-1BB-mediated target engagement. Cinrebafusp alfa also showed an acceptable safety profile at all doses and schedules tested in each clinical study. In the atezolizumab combination trial, seven dose cohorts have been evaluated at a Q3W dosing schedule ranging from 0.05 mg/kg to 8 mg/kg in combination with a fixed 1200 mg dose of atezolizumab. In that trial, under RECIST 1.1, four patients achieved a confirmed partial response at active dose levels.

In January 2022, we dosed the first patient in the two-arm phase 2 study for cinrebafusp alfa in gastric cancer in the United States. Supported by additional data we presented from the phase 1 monotherapy study of cinrebafusp alfa in an oral presentation at the American Association for Cancer Research Virtual Congress, or AACR, in April 2021, the first arm of the phase 2 study will include the combination with ramucirumab and paclitaxel in HER2-high gastric cancer, while the second arm will be in combination with tucatinib in HER2-low gastric cancer. Collaboration partners Lilly and Seagen are supplying ramucirumab and tucatinib, respectively. The criteria for advancement of this program will evaluate a composite of measures, including a minimum target of 50% ORR in the HER2-high arm and a minimum target of 40% ORR in the HER2-low arm, duration of response, and safety. The Company plans to report initial data from the arm evaluating cinrebafusp alfa in combination with tucatinib in HER2-low gastric cancer in 2022. The Company expects to report data from the arm evaluating cinrebafusp alfa in combination with ramucirumab and paclitaxel in HER2-high gastric cancer in 2023. In June 2021, FDA granted orphan drug designation to cinrebafusp alfa for the treatment of HER2-high and HER2-low expressing gastric cancers.

The supporting data presented at AACR included an evaluation of 78 patients who had been enrolled in the monotherapy study as of the February 2021 cutoff date, including four additional patients enrolled in the active dose cohorts (≥2.5 mg/kg) since the

data were presented at the ESMO Virtual Congress in September 2020. Out of 42 response-evaluable patients at the time of the data cutoff of February 25, 2021, according to RECIST 1.1, one patient with stage 4 rectal adenocarcinoma achieved a confirmed complete response at the 18 mg/kg Q2W dose (cohort 13b), four patients achieved a partial response (three at the 8 mg/kg Q2W dose (cohort 11b) and one at the 18 mg/kg Q2W dose (cohort 13b)), and stable disease was observed in 17 patients as best response out of 42 evaluable patients across the predicted active dose ranges (cohorts 9-13b), translating to an ORR of 12% and a DCR of 52%. Consistent with the mechanism of action of cinrebafusp alfa, dose-dependent immune activation was demonstrated by showing an increase in CD8+, T cell, NK cells and cytotoxic activity in the tumor microenvironment and an increase of soluble 4-1BB in the blood, indicating target engagement of 4-1BB and activation of immune cells. Cinrebafusp alfa demonstrated durable anti-tumor activity in a heavily pre-treated patient population. Additionally, clinical benefit was observed in patients with "cold" tumors as well as those with low HER2 expression who were enrolled into the study on the basis of archived HER2-status and were later re-assessed on the basis of a pre-treatment biopsy. Cinrebafusp alfa also showed an acceptable safety profile at all doses and schedules tested in the clinical study with no dose-limiting toxicities. The totality of response data generated in cohorts 11b (8 mg/kg Q2W) and 13b support the recommended phase 2 dose of a two-cycle loading dose of 18 mg/kg (Q2W), following by an 8 mg/kg dose (Q2W) in subsequent cycles.

PRS-344/S095012

PRS-344/S095012 consists of a PD-L1-targeting antibody and 4-1BB-targeting Anticalin proteins genetically fused to each arm of the C-terminal heavy chain of the antibody.

4-1BB is a co-stimulatory receptor belonging to the TNFR super-family. Clustering of 4-1BB on the surface of T cells leads to T cell activation, proliferation and cytokine secretion. The mode of action of PRS-344/S095012 is to promote 4-1BB clustering by bridging 4-1BB-positive T cells with PD-L1-positive tumor cells, and to thereby provide a potent co-stimulatory signal to tumor antigen-specific T cells. PRS-344/S095012 is intended to localize 4-1BB activation in the tumor in a PD-L1 dependent manner. PD-L1 is a transmembrane protein belonging to the B7 family and is expressed on a variety of cells including T cells, B cells, epithelial cells and vascular endothelial cells. Most importantly, PD-L1 is found at high levels on tumor cells of several cancer types including but not limited to melanoma, lung, bladder, colon and breast cancer. Binding of PD-L1 to its receptor PD-1 leads to exhaustion of tumor-infiltrating T cells. PRS-344/S095012 blocks the PD-1/PD-L1 interaction and thus is capable of reversing T cell exhaustion in the tumor microenvironment. Preclinical data shows that the synergistic effect observed by targeting PD-L1 and 4-1BB simultaneously is stronger with PRS-344/S095012 than with the combination of anti-PD-L1 and anti-4-1BB antibodies.

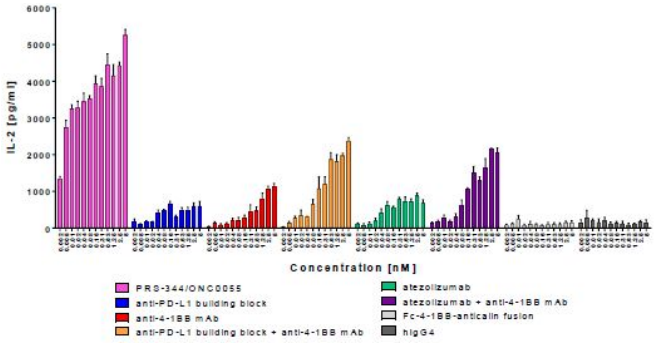


Figure 10 The combination of anti-PD-L1 benchmark and anti-4-1BB benchmark demonstrates the strong synergistic effect of T cell co-stimulation and checkpoint blockade in T cell activation. With PRS-344/S095012, this synergistic effect is massively increased.

Regulatory clearance for the phase 1/2 study of PRS-344/S095012, a 4-1BB/PD-L1 bispecific, has been granted in multiple countries and the first patient was dosed in November 2021. The first-in-human study will consist of evaluating the safety and tolerability profile of PRS-344/S095012 and determining its maximum tolerated dose, or MTD, and/or the recommended phase 2 dose, or RP2D, in patients with solid tumors. In addition, the PK profile as well as pharmacodynamic effects of the PRS-344/S095012 will be characterized in the study. Any initial signs of anti-tumoral activity will be correlated to safety and PK and further explored in expansion cohorts.

IO Market with respect to cinrebafusp alfa and PRS-344/S095012

In 2020, there were approximately 1.807 million estimated new cancer cases in the United States (NCI Surveillance, Epidemiology, and End Results Program) and approximately 19.3 million cancer cases worldwide (IARC GLOBOCAN 2020). The direct medical cost for cancer in the United States in 2015 was estimated to be approximately $80.2 billion by the Agency for Healthcare research and Quality, or the AHRQ.

Checkpoint inhibitors such as PD-1 and CTLA4-targeting antibodies have revolutionized the way certain cancers are treated and in 2018 the Noble Prize in Medicine was awarded to Dr. James Allison and Dr. Tasuku Honjo for their discovery of CTLA-4 and PD-1-targeting antibodies, respectively. By the end of 2021, a total of seven anti-PD-1 or PD-L1 monoclonal antibodies and one CTLA4 targeting antibody have been approved in the United States. In addition, other than the seven anti-PD-1 or PD-L1 monoclonal antibodies approved in the United States, eight other anti-PD-1 antibodies had been approved in China by the end of 2021. The majority of the global sales of checkpoint inhibitors comes from two anti-PD-1 monoclonal antibodies: pembrolizumab marketed by Merck & Co and nivolumab marketed by Bristol-Myers Squibb. In 2021, Merck & Co reported sales of $17.186 billion for pembrolizumab and Bristol-Myers Squibb reported sales of $7.5223 billion for nivolumab.

Other IO Programs

Current antibody-based therapies targeting tumor cell destruction or immune activation are hampered by, among other factors, low response rates and the induction of immune-related adverse events. Our IO pipeline beyond cinrebafusp alfa and PRS-344/S095012 is designed to target checkpoint proteins or, like cinrebafusp alfa, co-stimulatory proteins. These programs consist of a variety of multifunctional biotherapeutics that can encompass a fusion of antibodies with Anticalin proteins or two or more Anticalin proteins to each other. These combined molecules have the potential to build upon current therapies by modifying or regulating one or more immune functions on a single fusion protein, thereby having the potential to elevate immune responses within a tumor microenvironment. We believe that a tethered Anticalin protein directed at checkpoint or co-stimulatory targets can preferentially activate the immune system at the site of the tumor microenvironment thus providing efficacy with enhanced therapeutic index. We believe that these bispecific constructs represent a “platform within a product” opportunity in IO since it may be possible to apply a single combined Anticalin-antibody molecule in a number of different cancers. This belief is based on the shared underlying biology such as checkpoint and co-stimulatory biology found within tumors arising in different organs.

Servier Collaboration beyond PRS-344/S095012

In February 2020, we and Servier agreed to extend the research term of the three programs in development beyond PRS-344/S095012 for one year. This research extension includes reimbursement for Pieris’ internal efforts and an extension of the research license. As part of the expiration of the initial research term, the option to expand the collaboration beyond the initial five committed programs also expired. In March 2020, Servier notified us of its decision to discontinue co-development of two earlier preclinical stage programs for strategic reasons based upon an extensive portfolio review. The discontinuation of these two programs decreased the potential milestone payments we could receive in the future. In February 2021, the research term was extended again for another 12 months.

Given the discontinuation of the two preclinical stage programs in March 2020, and as further described below, our Servier Collaboration Agreement includes one additional program beyond PRS-344/S095012, PRS-352. We retain co-development and co-commercialization rights to PRS-344/S095012. PRS-352 is a preclinical-stage program within the Servier alliance addressing undisclosed targets in IO. We successfully completed non-GLP preclinical work in 2020 and handed over the program for further development at Servier. In 2021, we received a preclinical milestone with regard to PRS-352.

Seagen Collaboration

In addition, our collaboration with Seagen to discover and develop Anticalin-based tumor-targeted bispecific therapeutics in IO includes up to three programs.

We achieved a key development milestone for one of the programs in the Seagen collaboration in 2020, a bispecific tumor-targeted costimulatory agonist, triggering a $5 million payment. We have handed the program over to Seagen, which is responsible for further advancement and funding of the asset. The program is one of up to three potential programs in the Seagen alliance, and we believe the achieved milestone further validates our approach and leadership in immuno-oncology bispecifics, complementing the encouraging clinical data seen with cinrebafusp alfa.

In March 2021, Seagen made a $13.0 million equity investment in Pieris as part of an ongoing collaboration between the companies. Additionally, the companies have entered into a clinical trial and supply agreement to evaluate the safety and efficacy of combining Pieris' cinrebafusp alfa with Seagen's tucatinib, a small-molecule tyrosine kinase HER2 inhibitor, for the treatment of gastric cancer patients expressing lower HER2 levels (IHC2+/ISH- & IHC1+) as part of the upcoming phase 2

study to be conducted by Pieris. The companies have also amended their existing immuno-oncology collaboration whereby Pieris' option to co-develop and co-commercialize the second of three programs in the collaboration has been converted to a co-promotion option for one of the three programs in the United States. During the third quarter of 2021, we initiated the second program within the collaboration with Seagen.

Boston Pharmaceuticals Collaboration

In April 2021, we and Boston Pharmaceuticals, a subsidiary of Boston Pharma Holdings, LLC, entered into an exclusive product license agreement to develop PRS-342/BOS-342, a 4-1BB/GPC3 preclinical immuno-oncology Anticalin-antibody bispecific fusion protein. We completed the material and know-how transfer to BP and are currently supporting BP in manufacturing and IND-readiness activities for PRS-342/BOS-342.

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, scientific knowledge and strategies provide us with competitive advantages, we face and will continue to face intense competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies, and public and private research institutions, both in the United States and worldwide.

We compete, or will compete, with existing and new therapies that may become available in the future. Some of these competitors are pursuing the development of pharmaceuticals that target the same diseases and conditions that our drug candidates target. Any drug candidates that we are able to develop and commercialize will compete with existing and new drugs being developed by our competitors. Our competitors may develop or market products or other novel technologies that are more effective, safer, more convenient or less costly than any that may be commercialized by us or may obtain regulatory approval for their products more rapidly than we may obtain approval for ours.

The acquisition or licensing of pharmaceutical products is also very competitive, and a number of more established companies, some of which have acknowledged strategies to license or acquire products and many of which are bigger, have more institutional experience and have greater cash flows than us, may have competitive advantages over us, as may other emerging companies taking similar or different approaches to product licenses and/or acquisitions. In addition, a number of established research-based pharmaceutical and biotechnology companies may acquire products in late stages of development to augment their internal product lines, which may provide those companies with an even greater competitive advantage.

There are a number of other companies presently working to develop therapies for respiratory diseases and cancer, including divisions of large pharmaceutical companies and biotechnology companies of various sizes. There are also a variety of available drug therapies marketed for these diseases. Our drug candidates, if any are approved, may compete with these existing drug and other therapies, and to the extent they are ultimately used in combination with or as an adjunct to these therapies, our drug candidates may not be competitive with them. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well-established therapies and are widely accepted by physicians, patients and third-party payors. As a result, market acceptance of, and a significant share of the market for, any of our drug candidates that we successfully introduce to the market will pose challenges.

In addition to currently marketed therapies, there are also a number of drugs in clinical development to treat respiratory diseases and cancer. These medicines in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies and may not be provided by any of our current or future product candidates. As a result, they may provide significant competition for any of our product candidates.

Many of our competitors will have substantially greater financial, technical and human resources than we have. Additional mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated in some of our competitors. Competition may increase further as a result of advances made in the commercial applicability of technologies and greater availability of capital for investment in these fields. Our success will be based in part on our ability to build, obtain regulatory approval for and market acceptance of, and actively manage a portfolio of drugs that addresses unmet medical needs and creates value in patient therapy.

In addition, our competitors may have a variety of drugs in development or awaiting market approval that could reach the market and become established before we have a product to sell. Our competitors may also develop alternative therapies that could further limit the market for any drugs that we may develop. Many of our competitors are using technologies or methods different or similar to ours to identify and validate drug targets and to discover novel small molecule drugs. Many of our competitors and their collaborators have significantly greater experience than we do in the following:

- identifying and validating targets;

- screening compounds against targets;
- performing preclinical and clinical trials of potential pharmaceutical products; and
- obtaining regulatory approval.

In addition, many of our competitors and their collaborators have substantially greater advantages in the following areas:

- capital resources;
- research and development resources;
- manufacturing expertise and capabilities; and
- sales and marketing capabilities.

Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaborative arrangements with large pharmaceutical and established biotechnology companies. Many of our competitors have products that have been approved by the FDA, or its foreign counterparts, or are in advanced development. We face competition from other companies, academic institutions, governmental agencies and other public and private research organizations for collaborative arrangements with pharmaceutical and biotechnology companies, in recruiting and retaining highly-qualified scientific and management personnel and for licenses to additional technologies. Developments by others may render our product candidates or our technologies obsolete. Our failure to compete effectively could have a material adverse effect on our business.

PRS-060/AZD1402

Like PRS-060/AZD1402, new developments for the treatment of uncontrolled moderate to severe asthma patients mainly include drug candidates targeting the Th2 pathway by interfering with IL-4/IL-13, IL-5, TSLP or CRTH2. Such agents include mepolizumab (GSK, IL-5), reslizumab (Teva, IL-5), benralizumab (AstraZeneca, IL-5Rα), tezepelumab (Amgen/AstraZeneca, TSLP) and CBP201 (Connect Biopharma, IL-4Rα). These drugs are in later clinical development than PRS-060/AZD1402 or have been approved for severe eosinophilic asthma. Dupilumab (Sanofi/Regeneron, IL-4Rα) has been approved for moderate to severe asthma; the antibody omalizumab, directed against IgE, is also approved and marketed for the treatment of uncontrolled, moderate to severe asthma patients. However, in contrast to PRS-060/AZD1402, these antibodies are given to patients through injection and distribute systemically through the blood stream. CSJ117 (Novartis), an inhaled Fab fragment,and AZD8360 (AstraZeneca/Amgen), an inhaled antibody fragment, that both target TSLP, are currently in phase 2 and phase 1 clinical development, respectively. There are a number of other companies presently marketing or developing other therapies for asthmatic patients.

IO programs

The rationale behind the multispecific tumor-targeted co-stimulatory molecules is to activate the immune system in the tumor microenvironment. Other companies that also develop multispecific drug candidates designed to activate the immune system in a tumor dependent manner by targeting a co-stimulatory receptor, such as 4-1BB, include Roche, Molecular Partners, Merus, Inhibrx and Genmab, among others. Additionally, there are multiple drug candidates in preclinical or clinical trials targeting other co-stimulatory receptors, either in a tumor dependent or monospecific manner, including OX40, CD40, GITR, CD27 and ICOS.

The first checkpoint inhibitor targeting CTLA-4, ipilimumab, was approved for the treatment of melanoma patients in 2011 and is being marketed by Bristol-Myers Squibb. Nivolumab from Bristol-Myers Squibb was approved for the treatment of melanoma in 2014 as the first PD-1 inhibitor. Pembrolizumab from Merck & Co was the second PD-1 inhibitor to be approved and the first one in the United States. In addition to nivolumab and pembrolizumab, there are multiple approved checkpoint inhibitors targeting the PD-1/PD-L1 pathway, for example, those from Roche, AstraZeneca, Regeneron, Pfizer and Merck KGaA.

Additionally, a number of other companies, such as Amgen, Affimed, Macrogenics, F-star, Molecular Partners, Xencor, Immunocore and Zymeworks, also pursue other multispecific approaches in oncology, in which such therapies are in clinical or preclinical development.

Cinrebafusp alfa

Cinrebafusp alfa is bispecific Anticalin-antibody fusion protein targeting 4-1BB and HER2. Cinrebafusp alfa has a bifunctional proposed mode of action. It is designed to both promote 4-1BB clustering by bridging 4-1BB-positive T cells with HER2-positive tumor cells, and to thereby provide a co-stimulatory signal to tumor antigen-specific T cells and inhibit HER2 signaling. Other drug candidates targeting the co-stimulatory receptor 4-1BB include urelumab, which was being developed by

Bristol-Myers Squibb, and utomilumab, which is being developed by Pfizer, and is currently in clinical development (Trialtrove, December 10, 2020), among others. In the HER2-positive space, several companies are active with approved clinical and preclinical drugs candidates. The most prominent company is Roche, having three approved drugs on the market through its subsidiary Genentech. The first drug from Roche targeting HER2 is trastuzumab, which has been marketed for treatment of breast cancer patients since 1998 and for gastric cancer patients since 2010. The two other drugs are pertuzumab and ado-trastuzumab emtansine which both are marketed for breast cancer patients. In addition to cinrebafusp alfa, there are also other HER2 targeting drug candidates in clinical development designed to induce an immune response by bridging HER2-positive tumor cell with immune cells, for example, RG6194, a bispecific antibody targeting HER2 and CD3, from Roche, or NJH-395, an immune stimulating antibody conjugate targeting HER2 and TLR7/8, from Novartis (Pharmaprojects, December 10, 2020).

Phase 2 trials for cinrebafusp alfa in gastric cancer are currently ongoing. Trastuzumab in combination with cisplatin and 5-FU, or capecitabine, is currently recommended as standard of care for 1st line therapy for HER2+ metastatic gastric, or GEJ adenocarcinoma according to NCCN guidelines (NCCN Guidelines Version 5.2021 Gastric Cancer). Other drug candidates or novel combinations being developed in HER2+ gastric cancer include pembrolizumab in combination with trastuzumab and chemotherapy (Merck & Co, KEYNOTE-811), which received accelerated approval in the United States as 1st line therapy in May 2021, trastuzumab deruxtecan (Daiichi Sankyo/AstraZeneca, DESTINY-Gastric01, -Gastric02 and -Gastric03), an anti-HER2 ADC which was approved in the United States as 2L therapy in January 2021, margetuximab, an anti-HER2 antibody, in combination with a checkpoint inhibitor, with or without chemotherapy (MacroGenics, MAHOGANY), ALX148, an anti-CD47 antibody, in combination with trastuzumab, ramucirumab and paclitaxel (ALX Oncology, ASPEN-06), and Zanidatamab ZW25, a bispecific HER2/HER2 antibody (Zymeworks), among others. There are also other non-HER2 targeted drug candidates or combinations being developed more broadly, which may or may not overlap with drug candidates being developed in a HER2+ patient population.

At least two companies have publicly disclosed a competitor HER2 and 4-1BB bispecific program. MacroGenics presented data on a HER2 and 4-1BB bispecific during their R&D day on December 13th, 2016. In addition to MacroGenics, other companies have also disclosed 4-1BB-based bispecific drug candidates. Yuhan Corporation and ABL Bio presented a poster on a HER2 and 4-1BB bispecific (ABL105/ YH3236) at AACR 2020.

PRS-344/S095012

PRS-344/S095012 is bispecific Anticalin-antibody fusion protein targeting 4-1BB and PD-L1. Similar to cinrebafusp alfa, PRS-344/S095012 is designed to promote 4-1BB clustering by bridging 4-1BB-positive T cells with, in the case of PRS-344/S095012, PD-L1-positive tumor cells, and to thereby provide a co-stimulatory signal to tumor antigen-specific T cells. Furthermore, the direct PD-L1- targeting activity of PRS-344/S095012 may provide an additional therapeutic benefit by checkpoint blockade. Multiple companies have publicly disclosed competing 4-1BB and PD-L1 bispecific programs, including, for example, Genmab in collaboration with BioNTech (GEN1046), Incyte in collaboration with Merus (MCLA-145), Inhibrx in collaboration with Elpiscience (INBRX-105), F-star (FS-222), Numab in collaboration with CStone (NM21-1480), ABL Bio in collaboration with I-MAB (ABL503), Antengene (ATG-101), among others. GEN1046, MCLA-145, INBRX-105, NM21-1480, FS-222, ABL 503 and ATG-101 are currently in clinical development.

PRS-220

In addition to the currently approved drugs, Ofev (nintedanib) and Esbriet (pirfenidone), there are multiple other programs in development for the treatment of IPF. The majority of these programs are at an early stage and include a variety of targets. There is one competing program targeting CTGF in phase III clinical development, pamrevlumab (Fibrogen), an antibody administered by intravenous infusion. Besides pamrevlumab, there are further programs targeting CTGF at an early stage of development. Other late-stage competitors include tyvaso (United Therapeutics, inhaled formulation of treprostinil sodium) and PRM-151 (Roche, rhPTX-2), which are currently being tested in phase III clinical trials. Furthermore, a number of competing programs are in phase II clinical development, such as GB-0139 (Galecto, galectin-3), BMS-986278 (Bristol-Myers Squibb, LPA1), CC-539 (Bristol-Myers Squibb, JNK1), PLN-74809 (Pliant Therapeutics, avbeta1/avbeta 6) and setanaxib (GenKyoTex, NOX1/4). Whereby the first listed program is administered by inhalation and the subsequent programs are administered orally. Additionally, to the previously stated competitors, there are several other programs that are being developed for the treatment of IPF.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely and expect to continue to rely on third-party contract manufacturer organizations, or CMOs, for the manufacture of our drug candidates for

larger scale preclinical and clinical testing, as well as for commercial quantities of any drug candidates that may be approved for marketing.

We currently rely on multiple CMOs for all of our clinical supplies, including drug substances and finished drug products, and label and packaging for our preclinical research and clinical trials, including the phase 2a studies for PRS-060/AZD1402, the phase 2 studies for cinrebafusp alfa, the phase 1 study for PRS-344/S095012, and the planned phase 1 study for PRS-220.

We believe that we will be able to contract with other CMOs to obtain drug substances if our existing sources of drug substances were no longer available or sufficient, but there is no assurance that the drug substances would be available from other CMOs on acceptable terms, on the timeframe that our business would require or at all. We do not have supply commitments or other arrangements in place with our existing CMOs. We also do not currently have arrangements in place for redundant supply of bulk drug substance. We have also experienced reduced capacity offered by CMOs due to the COVID-19 pandemic.

We do not have any current contractual relationships for the manufacture of commercial supplies of any of our drug product candidates if they are approved. We intend to enter into agreements with a CMO and one or more back-up manufacturers for the commercial production of our product candidates as they near potential approval.

Any drug products to be used in clinical trials and any approved product that we may commercialize will need to be manufactured in facilities, and by processes, that comply with the FDA's cGMP requirements and comparable requirements of the regulatory agencies of other jurisdictions in which we are seeking approval. We currently employ internal resources to manage our CMOs.

We believe that PRS-060/AZD1402, cinrebafusp alfa, PRS-344/S095012, PRS-220 and our other Anticalin-branded drug candidates can be manufactured in reliable and reproducible biologic processes from readily available starting materials. PRS-060/AZD1402 is produced using a bacterial expression system similar to those that have been used in the past for the production of other proteins and which systems are widely used in the industry. Cinrebafusp alfa, PRS-344/S095012 and PRS-220 are produced using mammalian expression systems similar to those systems that are widely used in the industry for the production of antibodies. We believe that the manufacturing process is amenable to scale-up and will not require unusual or expensive equipment. We expect to continue to develop, on our own or with our collaborators, drug candidates that can be produced cost-effectively at contract manufacturing facilities.

Intellectual Property and Exclusivity

Our commercial success depends in part on our ability to obtain and maintain exclusivity of our proprietary Anticalin-based technologies through intellectual property protection for our drug candidates, libraries of different protein scaffolds and consensus sequences, the fundamental Anticalin platform technology, including novel therapeutic and diagnostic discoveries, as well as other proprietary know-how and trade secrets, and to operate without infringing on the intellectual property rights of others.

We seek to protect our exclusive position of Anticalin technologies by, among other means, prosecuting our own international, U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We have established intellectual property protection in relation to our Anticalin technologies in key global markets, including in North America, Europe and Asia. We also rely on trade secrets for confidential know-how, which we generally seek to protect through contractual (for example, confidentiality) agreements with employees and third parties.

We have protected the goodwill of our Company and our drug candidates, created through innovation and development, by putting in place trademark registrations of the Pieris and Anticalin marks as well as several defensive registrations.

We currently, and expect that we will continue to, file patent applications and maintain granted patents directed to our key drug candidates in an effort to establish intellectual property positions relating to new compositions of matter for these drug candidates, as well as novel medical applications of these compounds in the treatment, prevention or diagnosis of various indications. We also intend to seek patent protection, if available, with respect to biomarkers that may contribute to selecting the right patient population for the use of any of our drug candidates, or with respect to pharmaceutical formulations that may be useful to produce final medicinal products.

We own, or are the exclusive licensee of, a patent portfolio consisting of several issued U.S. patents, and their respective counterparts in a number of foreign jurisdictions, including pending patent applications under the Patent Cooperation Treaty, pending U.S. patent applications and corresponding pending patent applications in a number of foreign jurisdictions as well as pending provisional patent applications, as described in further detail below.

In applicable jurisdictions, such as the United States, we will seek patent term extensions for certain issued patents of ours. If we obtain marketing approval for our drug candidates in the United States or certain jurisdictions outside of the United States,

we may be eligible for regulatory protection, such as 4 years of data exclusivity and 12 years of market exclusivity for new biological entities in the United States and as mentioned below, up to five years of patent term extension potentially available in the United States, eight to 11 years of data and marketing exclusivity potentially available for new drugs in the European Union, up to five and a half years of patent extension in Europe (supplemental protection certificate) and eight years of exclusivity, similar to data exclusivity in the United States, potentially available in Japan under its re-examination system. There can be no assurance that we will qualify for any such regulatory exclusivity or that any such exclusivity will prevent competitors from seeking approval solely on the basis of their own studies. See "Government Regulation."

We hold issued patents and pending patent applications in the United States and other foreign jurisdictions, which patents are related to libraries of different scaffolds and consensus sequences such as human apolipoprotein D, human NGAL and human tear lipocalin, and are expiring or expected to expire between 2022 and 2030, subject to any patent term adjustments and terminal disclaimers in the United States. We also own a number of patents and patent applications at various stages of prosecution directed towards compositions of matter and in some cases, formulations or methods of use, of our preclinical and clinical drug candidates. Where possible, we will pursue patent term adjustments in the United States and any applicable foreign jurisdictions.

As a result of our research and licensing agreement, or the TUM License, with Technische Universität München, or TUM, we hold a worldwide exclusive license to multiple issued patents and pending patent applications. These patents and patent applications relate to Anticalin proteins derived from hNGAL lipocalin muteins and/or a library of an hNGAL scaffold of a certain consensus sequence, which patent is expected to expire in 2029, subject to any patent term adjustments or terminal disclaimers in the United States. We also hold an exclusive license to issued patents or pending patent applications related to bacterial lipocalin muteins and a1m lipocalin muteins.

We hold a number of issued patents and pending patent applications in the United States and foreign jurisdictions directed to newly-discovered or improved scaffold libraries of lipocalin muteins, compounds derived therefrom (i.e., specific drug candidates) or the uses of such compounds to treat, prevent and mitigate certain diseases and conditions whose pathological development involve the targets of interest as well as to diagnose, prognose and select treatments for the diseases and conditions. We would expect that these patents and any patents that may issue from pending applications would likely expire between 2029 and 2042 without taking into account possible patent term adjustments or other extensions. However, any and all of these pending patent applications may not result in issued patents, and not all issued patents may be maintained in force for their entire term. We are actively pursuing intellectual property protection for our IO drug candidates in key global markets that, if granted, could expire as late as 2042 or later depending on the date of the filing of such patent applications.

In addition to issued patents, we hold trademarks in the United States for the Pieris and Anticalin marks. Similarly, we hold their respective counterparts, either as registered trademarks or as pending applications, in a number of foreign jurisdictions. We expect that we will continue to look for trademark protection for the goodwill associated with our Company and our drug candidates in the countries or regions where we will have investment, research and development, sales or other activities.

We also rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive advantage. We strive to protect our proprietary information, in part, by using confidentiality agreements and/or invention assignment agreements with our collaborators, scientific advisors, employees and consultants. The confidentiality agreements are designed to protect our proprietary information and, in the case of agreements requiring invention assignment, to grant us ownership of technologies that are developed through a relationship with a third party. We also actively manage our publication and patent applications in that we only disclose information necessary to stir scientific interest or demonstrate patentability without materially compromising the secrecy of our valuable trade secrets and know-how. While we consider trade secrets and know-how to be a critical component of our intellectual property, trade secrets and know-how can be difficult to protect. In particular, with respect to our technology platform, we anticipate that these trade secrets and know-how will, over the course of time, be disseminated within the industry through independent development, the publication of journal articles describing the methodology and the movement of personnel skilled in the technology from academic to industry positions and vice versa. As a result, those proprietary trade secrets and know-how may lose their value to us over a period of time, and we may lose any competitive advantage afforded by them, as they become public knowledge.

Strategic Partnerships and Other License Agreements

Since inception, we have entered into several strategic partnerships and other license or option agreements to complement our drug discovery and development. Specifically, we have entered into strategic partnerships with Servier, AstraZeneca, Seagen and Genentech, or collectively, the Strategic Partnerships, and other non-strategic license agreements or collectively, the License Agreements. Under the Strategic Partnerships and License Agreements, we have developed and conducted or will develop and conduct selection and screening of drug candidates, as well as *in vitro* potency and efficacy testing, using our Anticalin-brand drug discovery platform, our Anticalin libraries and other proprietary methods to generate, identify and characterize drug candidates against certain biological targets associated with several diseases. The current Strategic

Partnerships have provided us with approximately $172.2 million in cash from upfront and milestone payments through December 31, 2021. With respect to discontinued agreements, we have no ongoing performance obligations and do not expect to receive any significant additional consideration pursuant to those agreements.

Under our ongoing Strategic Partnerships and License Agreements, our partners are obligated to use commercially reasonable efforts to develop and commercialize drug candidates identified in the course of the collaboration. We are entitled to receive from our partners' research, development and regulatory milestone payments and, in some cases, including in the Servier, AstraZeneca, Seagen and Genentech collaborations, royalties on net sales for products developed and commercialized under these collaborations. With respect to most of our Strategic Partnerships, we have commercial rights, including the option to co-develop, co-commercialize or co-promote one or more therapeutic programs with the applicable partners. We plan to continue to actively seek out additional collaboration partners that fit within our corporate development strategy.

The Strategic Partnerships represent our cornerstone collaborations in our key therapeutic areas of respiratory diseases and IO and include co-development and co-commercialization options. Certain terms and conditions of these Strategic Partnerships are summarized below.

Our collaboration with AstraZeneca

On May 2, 2017, we entered into the AstraZeneca Collaboration Agreement and a Non-exclusive Anticalin Platform Technology License Agreement with AstraZeneca, or the AstraZeneca Platform License, collectively referred to as the AstraZeneca Agreements, which became effective on June 10, 2017, following expiration of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976. Under the AstraZeneca Agreements the parties will advance several novel inhaled Anticalin proteins. On March 29, 2021, we entered into the first amendment to the Non-exclusive Anticalin Platform License Agreement dated May 2, 2017 and the second amendment to the License and Collaboration Agreement dated May 2, 2017. Under the amendments, the parties agreed to restructure certain commercial economics for the PRS-060/AZD1402 program by adjusting various milestones and royalty provisions, while fundamentally maintaining the overall value split between AstraZeneca and the Company. In connection with the amendments, we entered into a Subscription Agreement pursuant to which we have agreed to issue to AstraZeneca 3,584,230 shares of our common stock for a total purchase price of $10.0 million in a private placement transaction.

Under the AstraZeneca Agreements, we received an upfront, non-refundable payment of $45.0 million. In addition, we initiated a phase 1 study for PRS-060/AZD1402, or the AstraZeneca Lead Product, in December 2017 for which we received a $12.5 million milestone payment. In March 2021, we achieved a $13.0 million milestone in connection with the initiation of the phase 2a study for this program. We are also eligible to receive research, development, commercial and sales milestone payments and royalty payments. The total potential milestones, as of December 31, 2021, are categorized as follows: research, development and commercial milestones up to $1.1 billion and sales milestones up to $4.3 billion. We may receive tiered royalties on sales of potential products commercialized by AstraZeneca and for co-developed products and gross margin share of worldwide sales, depending on our level of committed investment.

The term of each of the AstraZeneca Agreements ends upon the expiration of all of AstraZeneca's payment obligations under such AstraZeneca Agreement. The AstraZeneca Collaboration Agreement may be terminated by AstraZeneca in its entirety for convenience beginning 12 months after its effective date upon 90 days' notice or, if we have obtained marketing approval for the marketing and sale of a product, upon 180 days' notice. Each program may be terminated at AstraZeneca's option; if any program is terminated by AstraZeneca, we will have full rights to such program. The AstraZeneca Collaboration Agreement may also be terminated by AstraZeneca or us for material breach upon 180 days' notice of a material breach (or 30 days with respect to payment breach), provided that the applicable party has not cured such breach by the permitted cure period (including an additional 180 days if the breach is not susceptible to cure during the initial 180-day period) and dispute resolution procedures specified in the AstraZeneca Collaboration Agreement have been followed. Each party may also terminate an AstraZeneca Agreement if the other party challenges the validity of patents related to certain intellectual property licensed under such AstraZeneca Agreement, subject to certain exceptions for infringement suits, acquisitions and newly-acquired licenses. The AstraZeneca Collaboration Agreement may also be terminated due to the other party's insolvency and may in certain instances be terminated on a product-by-product and/or country-by-country basis. The AstraZeneca Platform License will terminate upon termination of the AstraZeneca Collaboration Agreement, on a product-by-product and/or country-by-country basis.

Our collaboration with Servier

On January 4, 2017, we entered into the Servier Collaboration Agreement and a non-exclusive Anticalin platform license agreement with Servier, or the Servier Platform License, collectively referred to as the Servier Agreements. Pursuant to the terms of the Servier Agreements, we, along with Servier, initially pursued five bispecific therapeutic programs. In September 2019, Servier notified the Company of its decision to discontinue co-development of PRS-332, a PD-1-LAG-3 bispecific that

served as the initial development program under the Pieris-Servier alliance, for strategic reasons. After having conducted an extensive portfolio review, Servier decided in March 2020 to focus on continued and accelerated development of the two most advanced programs, PRS-344/S095012 and PRS-352, and to discontinue development of two earlier-stage programs in the collaboration.

Under the Servier Agreements, we received an upfront payment of €30.0 million (approximately $32.0 million) and have achieved two preclinical milestones related to PRS-344/S095012 as well as one clinical milestone related to PRS-344/S095012 and one preclinical milestone related to PRS-352. We may also receive additional development-dependent and commercial milestone payments for each program. The total development, regulatory and sales-based milestone payments to us, as of December 31, 2021, could exceed €210.0 million during the life of the collaboration and are dependent on the final number of projects pursued and the number of co-development options exercised by us. We will share preclinical and clinical development costs for each co-developed program with Servier. In addition, we will be entitled to receive tiered royalties up to low double digits on the sales of commercialized products in the Servier territories.

The term of each of the Servier Agreements ends upon the expiration of all of Servier's payment obligations under such Servier Agreement. The Servier Agreements may be terminated by either of us for material breach upon 90 days' or 120 days' notice of a material breach, with respect to the Servier Collaboration Agreement and the Servier Platform License, respectively, provided that the applicable party has not cured such breach by the applicable 90-day or 120-day permitted cure period, and dispute resolution procedures specified in the applicable Servier Agreement have been followed. The Servier Agreements may also be terminated due to the other party's insolvency or for a safety issue, and may in certain instances be terminated on a product-by-product and/or country-by-country basis. The Servier Platform License will terminate upon termination of the Servier Collaboration Agreement, on a product-by-product and/or country-by-country basis.

Our collaboration with Seagen

On February 8, 2018, we entered into the Seagen Collaboration Agreement and a non-exclusive Anticalin platform technology license agreement with Seagen, or the Seagen Platform License, collectively referred to as the Seagen Agreements, pursuant to which the parties will develop multiple targeted bispecific IO treatments for solid tumors and blood cancers.

Under the terms of the Seagen Agreements, Seagen paid us a $30 million upfront fee and will pay tiered royalties on net sales up to the low double-digits. Additionally, Seagen will pay us up to $1.2 billion in total success-based payments, as of December 31, 2021, across three product candidates. The companies will pursue multiple Anticalin-antibody fusion proteins during a research phase, and Seagen has the option to select up to three therapeutic programs for further development. On March 25, 2021 we announced an amendment to the Seagen Collaboration Agreement whereby our option to co-develop and co-commercialize the second of three programs in the collaboration was converted to a co-promotion option for one of the three programs in the United States, with Seagen solely responsible for the development and overall commercialization of that program. We will be entitled to increased royalties in the event that we choose to exercise the co-promotion option for that program. As a result of this amendment, Seagen will solely develop, fund and commercialize all three programs. Seagen may also decide to select additional candidates from the initial research phase for further development in return for the payment to us of additional fees, milestone payments and royalties.

The term of each of the Seagen Agreements ends upon the expiration of all of Seagen's payment obligations under such Seagen Agreement. The Seagen Collaboration Agreement may be terminated by Seagen on a product-by-product basis for convenience beginning 12 months after its effective date upon 90 days' notice or, for any program where a pivotal study has been initiated, upon 180 days' notice. Any program may be terminated at Seagen's option. If any program is terminated by Seagen after a pre-defined pre-clinical stage, we will have full rights to continue such program. If any program is terminated by Seagen prior to such pre-defined pre-clinical stage, we will have the right to continue to develop such program but will be obligated to offer a co-development option to Seagen for such program. The Seagen Collaboration Agreement may also be terminated by Seagen or us for an uncured material breach by the other party upon 90 days' notice, subject to extension for an additional 90 days if the material breach relates to diligence obligations and subject, in all cases, to dispute resolution procedures. The Seagen Collaboration Agreement may also be terminated due to the other party's insolvency and may in certain instances, including for reasons of safety, be terminated on a product-by-product basis. Each party may also terminate the Seagen Agreements if the other party challenges the validity of any patents licensed under the Seagen Agreements, subject to certain exceptions. The Seagen Platform License will terminate upon termination of the Seagen Collaboration Agreement, whether in its entirety or on a product-by-product basis.

In June 2020, we and Seagen entered into amendments to the Seagen Agreements, or together, the Amendment. The Amendment extended the deadline for Seagen to nominate a second and third antibody target and triggered a $5.0 million milestone payment due from Seagen as Seagen made a go decision on the first collaboration product.

In addition to the March 2021 second amendment to the Seagen Collaboration Agreement, we entered into a clinical trial and supply agreement with Seagen to evaluate the safety and efficacy of combining our cinrebafusp alfa with Seagen's TUKYSA®

(tucatinib), a small-molecule tyrosine kinase HER2 inhibitor, for the treatment of gastric cancer patients expressing lower HER2 levels (IHC2+/ISH- & IHC1+) as part of the phase 2 study. Finally, as part of this transaction, we entered into a subscription agreement pursuant to which we agreed to issue to Seagen 3,706,174 shares of our common stock for a total purchase price of $13.0 million, or $3.51 per share, in a private placement transaction.

Our License Agreements are older than our Strategic Partnerships and relate to non-strategic therapeutic areas, or do not provide us with co-development and co-commercialization rights. A brief summary of certain terms of selected License Agreements are provided below.

Our collaboration with Lilly

On August 10, 2020, we entered into a Clinical Trial Collaboration and Supply Agreement, or the Lilly Agreement, with Eli Lilly and Company, or Lilly, pursuant to which we and Lilly will collaborate on a phase 2 clinical study, or the Study, to determine the safety and efficacy of our cinrebafusp alfa in combination with the standard of care regimen for the second-line treatment of advanced or metastatic gastric cancer, ramucirumab (CYRAMZA®) and paclitaxel for the second-line treatment of HER2+ gastric cancer.

Under the terms of the non-exclusive Lilly Agreement, we will sponsor the Study and Lilly will supply us with ramucirumab as well as provide input on certain clinical and regulatory aspects of the Study in exchange for jointly owning clinical data and inventions relating to the combination regimen that may arise from the Study. Any material changes to the protocol for the Study, and any changes relating to ramucirumab, will require Lilly's prior written consent, which shall not be unreasonably withheld, conditioned or delayed.

The Lilly Agreement will expire upon completion of the parties' contractual obligations. The Lilly Agreement may also be terminated (a) by either party for an uncured material breach by the other party upon 60 days' notice, subject to a reasonable extension if such material breach requires more than 60 days to cure; (b) by either party in the event that the Study unreasonably affects patient safety, provided that the terminating party promptly notifies the other party and the other party is given the opportunity to propose modifications to the Study to address the safety issues; (c) by either party, following 15 days' written notice, if regulatory action is taken preventing the terminating party from providing its compound or if the terminating party decides to discontinue development of its compound; (d) by either party, immediately upon written notice to the other party for breach by the other party of its material obligations under certain sections of the Lilly Agreement, or breach of certain of the other party's representations and warranties; and (e) by Lilly in the event of certain safety concerns related to the use of ramucirumab in the Study.

Our collaboration with Boston Pharmaceuticals

On April 24, 2021, we and BP Asset XII, Inc., or Boston Pharmaceuticals, a subsidiary of Boston Pharma Holdings, LLC, entered into an exclusive product license agreement, or the BP Agreement, to develop PRS-342, a 4-1BB/GPC3 preclinical immuno-oncology Anticalin-antibody bispecific fusion protein.

Under the terms of the BP Agreement, Boston Pharmaceuticals exclusively licensed worldwide rights to PRS-342. We received an upfront payment of $10.0 million and are further entitled to receive up to $352.5 million in development, regulatory and sales-based milestone payments, tiered royalties up to low double-digits on sales of PRS-342 and a percentage of consideration received by Boston Pharmaceuticals in the event of a sublicense of a program licensed under the BP Agreement or a change of control of Boston Pharmaceuticals. We will also contribute up to $4.0 million toward manufacturing activities.

The term of the BP Agreement ends upon the expiration of all of Boston Pharmaceuticals' payment obligations thereunder. The BP Agreement may be terminated by Boston Pharmaceuticals in its entirety for convenience beginning nine months after its effective date upon 60 days' notice or, for any program under the BP Agreement which has received marketing approval, upon 120 days' notice. If any program is terminated by Boston Pharmaceuticals, we will have full rights to continue such program. The BP Agreement may also be terminated by Boston Pharmaceuticals or us for an uncured material breach by the other party upon 180 days' notice (60 days in the case of non-payment of undisputed amounts due and payable), subject to extension for an additional 180 days in certain cases and subject, in all cases, to dispute resolution procedures. The Agreement may also be terminated due to the other party's insolvency. We may also terminate the BP Agreement if Boston Pharmaceuticals challenges the validity of any patents licensed under the BP Agreement, subject to certain exceptions.

We do not have any obligations to assist in the research and development efforts of Boston Pharmaceuticals under the BP Agreement. However, we have an obligation to fund up to $4.0 million in costs, including out-of-pocket costs incurred by Boston Pharmaceuticals, in connection with the manufacture of products under the BP Agreement. The arrangement with Boston Pharmaceuticals provides for the transfer of the following: (i) exclusive license of PRS-342, (ii) non-exclusive Pieris platform license, (iii) initial know-how, (iv) product cell line license, and (v) materials (as each such term is defined under the BP Agreement).

Our collaboration with Genentech

On May 19, 2021, we and Genentech, Inc., or Genentech, entered into a Research Collaboration and License Agreement, or the Genentech Agreement, to discover, develop and commercialize locally delivered respiratory and ophthalmology therapies that leverage the Company's proprietary Anticalin technology. Upon signing the Genentech Agreement, Genentech paid the Company a $20 million upfront fee. In addition, we may be eligible to receive up to approximately $1.4 billion in additional milestone payments across multiple programs, as well as tiered royalty payments on net sales at percentages ranging from the mid-single to low double-digits, subject to certain standard reductions and offsets.

Under the terms of the Genentech Agreement, we will be responsible for discovery and preclinical development of two initial programs. We will be responsible for research activities following target nomination through the late-stage research go decision. We and Genentech will then collaborate on drug candidate characterization until the development go decision. After the development go decision, Genentech will be responsible for pursuing the preclinical and clinical development of each program, and thereafter, the commercialization efforts. Each party will be responsible for the costs incurred to perform their respective responsibilities. Genentech has an option to expand the collaboration to encompass two additional programs with the payment of a $10 million fee per additional program. If Genentech exercises its option to start additional programs, payment to us of additional fees, milestone payments and royalties would result.

Unless earlier terminated, the term of the Genentech Agreement continues until no royalty or other payment obligations are or will become due under the Genentech Agreement. The Genentech Agreement may be terminated (i) by either party based on insolvency or breach by the other party and such insolvency proceeding is not dismissed or such breach is not cured within 90 days; or (ii) after nine months from the effective date of the Genentech Agreement, by Genentech as a whole or on a product-by-product and/or country-by-country basis upon 90 days' prior written notice before the first commercial sale of a product or upon 180 days' prior written notice after the first commercial sale of a product.

While the Genentech Agreement allows for up to four research programs, only two research programs are initially identified and committed in the Genentech Agreement. To reach a total of up to four research programs, we have granted Genentech options to nominate an additional two collaboration targets of their choosing, subject to the legal availability of the target to be researched. Genentech will have three years after the effective date to nominate the subsequent targets. We have also granted Genentech options to replace any of the collaboration targets identified with another target. However, at no point will there be more than four identified collaboration targets for which there are ongoing research programs.

The arrangement with Genentech provides for the transfer of the following goods or services: (i) exclusive research and commercial license for the collaboration programs, (ii) a non-exclusive platform improvement license, (iii) research and development services, (iv) participation in a governance committee, and (v) replacement target options on the first two programs upon a screening failure, which were assessed as material rights.

In-License Agreements

In addition to the Strategic Licenses and Other License Agreements, we have in-licensed a number of technologies and therapeutics, hereinafter referred to as the In-License Agreements, to advance our pipeline and programs, some of which are described below.

TUM License

On July 4, 2003, we entered into our TUM License which was subsequently renewed and amended on July 26, 2007. The TUM License established a joint research effort led by Professor Arne Skerra, Chair of Biological Chemistry of TUM, to optimize Anticalin technologies for use in therapeutic, prophylactic and diagnostic applications and as research reagents, and to gain fundamental insights in lipocalin scaffolds. We provided certain funding for TUM research efforts performed under the agreement. The research phase of this collaboration ended on February 28, 2013.

Under the terms of the TUM License, TUM assigned to us certain materials and records resulting from the research. We retained rights to inventions made by our employees, and TUM assigned to us all inventions made under the agreement jointly by our employees and TUM personnel, provided that our employees made certain inventive contributions. With respect to all other inventions made in the course of the research, TUM granted to us worldwide exclusive license rights under patents and patent applications claiming such inventions. TUM retained rights to practice these inventions for research and teaching purposes.

As a result of research efforts to date under the TUM License, we hold a worldwide exclusive license under our agreement with TUM to multiple patents and patent applications related to certain Anticalin proteins and libraries. We bear the costs of filing, prosecution and maintenance of patents assigned or licensed to us under the agreement.

As consideration for the assignments and licenses, we are obliged to pay to TUM license payments on development of our proprietary products claimed by patents assigned or licensed to us by TUM. For each of such proprietary products developed by us, we could be required to pay up to an aggregate of approximately €0.2 million ($0.2 million) in license payments to TUM under the agreement.

We also are obliged to pay low single-digit royalties, including annual minimum royalties, on sales of such products. Should we grant licenses or sublicenses to those patents to third parties, we are obliged to share a percentage of resulting revenue with TUM, which percentage of resulting revenue is creditable against our annual license payments to TUM. Our payment obligations are reduced by our proportionate contribution to a joint invention. Payment obligations terminate on expiration or annulment of the last patent covered by the agreement.

We can terminate the licenses to any or all licensed patents upon specified advance notice to TUM. TUM may terminate the license provisions of the agreement only for cause. Termination of the agreement does not terminate our rights in patents assigned to us.

Pieris and TUM initiated discussions in the second quarter of 2018 to clarify, expand and restructure the TUM License, including the parties' obligations under such license agreement. The parties' discussions relate to revised commercial terms and to re-initiating additional collaborations between faculty at TUM and Pieris. While an amended and restated license agreement has not yet been completed, we intend to enter into such an amendment. These discussions may also lead to an increase in our collaborative research activities with TUM.

Enumeral License Agreements

In the second quarter of 2016, we entered into two license agreements, collectively the PD-1 In-License, with Enumeral Biomedical Holdings, Inc., or Enumeral, pursuant to which we in-licensed certain intellectual property related to an Enumeral-generated antibody against PD-1 and an option to in-license up to two additional antibodies against undisclosed targets. Under the PD-1 In-License, we acquired a non-exclusive worldwide license (except in the exclusive field of licensed antibodies fused to Anticalin proteins in the oncology area) under the applicable Enumeral patents and know-how to research, develop and commercialize fusion proteins incorporating Enumeral's PD-1 antibody and one or more Anticalin proteins for use in the oncology area. On January 29, 2018, Enumeral filed a voluntary petition for relief under Chapter 11 of the United States Bankruptcy Code in the Bankruptcy Court for the District of Massachusetts, or the Bankruptcy Court. In connection with those proceedings, Enumeral transferred the intellectual property related to the PD-1 In-License to PD-1 Acquisition Group, LLC, or Acquisition Group, who have assumed the rights and obligations of Enumeral with respect to the PD-1 In-License.

Under the terms of the PD-1 In-License, we are obliged to pay to Acquisition Group development and sales milestones on development of products incorporating the Enumeral antibody, as well as low to lower-middle single-digit royalties as a percentage of net sales depending on the amount of net sales in the applicable years. In the event that we are required to pay a license fee or royalty to any third party related to the licensed products, our royalty payment obligations to Acquisition Group will be reduced by the amount of such third-party fees or payments, up to 50% of the royalty payment for each calendar year due to Acquisition Group. Payment obligations terminate on a product-by-product and country-by-country basis on the later of 10 years from the first commercial sale of a product incorporating the Enumeral antibody or the last to expire, lapse or be abandoned of a claim from the licensed Enumeral patents filed as of the effective date of the PD-1 In-License that cover the manufacture, use, offer for sale, sale or import of a product incorporating the Enumeral antibody.

The term of the PD-1 In-License ends upon the expiration of the last to expire patent covered under the license unless earlier terminated by us or Acquisition Group in accordance with the terms of the PD-1 In-License.

Kelun License Agreement

In connection with our efforts to develop multispecific Anticalin-based proteins designed to engage immunomodulatory targets, during the second quarter of 2017, we entered into a license and transfer agreement, or the Kelun Agreement, with Sichuan Kelun-Biotech Biopharmaceutical Co. Ltd., or Kelun. Under the Kelun Agreement, Kelun has granted to us a non-exclusive worldwide license (with the right to sublicense) under certain intellectual property owned or controlled by Kelun to research, develop, manufacture and commercialize bi- and multi- specific fusion proteins that include an antibody developed by Kelun specific for an undisclosed target and one or more Anticalin proteins.

Government Regulation

The research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing, sales, among other things, of drug products are extensively regulated by governmental authorities in the United States and other countries. 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 requirements, require the expenditure of substantial time and financial resources.

U.S. Government regulation of drug and biological products

In the United States, the FDA regulates human drugs under the Federal Food, Drug, and Cosmetic Act, or the FDCA, and in the case of biologics, also under the Public Health Service Act, or the PHSA, and their implementing regulations. Failure to comply with the applicable U.S. requirements may subject an applicant to administrative or judicial sanctions, such as FDA refusal to approve pending new drug applications, or NDAs, or biologics license applications, or BLAs, or the agency's issuance of warning letters, or the imposition of fines, civil penalties, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or criminal prosecution brought by the FDA and the U.S. Department of Justice or other governmental entities.

The process required by the FDA before a drug or biologic may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices regulations or other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, current good clinical practices, or cGCPs, and other clinical-trial related regulations to evaluate the safety and efficacy of the investigational product for each proposed indication;
- submission to the FDA of an NDA or BLA for marketing approval, including payment of application user fees;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug or biologic is produced to assess compliance with cGMP to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- potential FDA audit of the clinical trial sites to assure compliance with cGCPs and the integrity of the clinical data submitted in support of the NDA or BLA; and
- FDA review and approval of the NDA or BLA, including satisfactory completion of an FDA advisory committee review of the product candidate, where appropriate or if applicable, prior to any commercial marketing or sale of the product in the United States.

Preclinical studies

Before testing any drug or biological product candidate in humans, the product candidate must undergo rigorous preclinical testing. The preclinical developmental stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. The sponsor must submit the results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before human clinical trials may begin.

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as*in vitro* and animal studies, to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including good laboratory practices, or GLP, regulations for safety and toxicology studies. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after an IND for an investigational drug candidate is submitted to the FDA and human clinical trials have been initiated.

Human clinical trials in support of an NDA or BLA

All clinical trials must be conducted under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing the objectives of the study, the parameters to be used in monitoring the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND. Study subjects must sign an informed consent form before participating in a clinical trial. There are also requirements governing the reporting of on-going clinical trials and clinical trial results to public registries. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can

begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence. Clinical holds may also be imposed by the FDA at any time before or during studies due to safety concerns or non-compliance.

In addition, an IRB representing each institution that is participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must thereafter conduct a continuing review and re-approve the trial at least annually. The IRB must review and approve, among other things, the trial protocol and informed consent information to be provided to clinical trial subjects. An IRB must operate in compliance with FDA regulations.
Information about certain clinical trials, including details of the protocol and eventually study results, also must be submitted within specific time frames to the National Institutes of Health, or NIH, for public dissemination on the ClinicalTrials.gov data registry. Information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in some cases for up to two years after the date of completion of the trial. Failure to timely register a covered clinical study or to submit study results as provided for in the law can give rise to civil monetary penalties and also prevent the non-compliant party from receiving future grant funds from the federal government. The NIH's Final Rule on ClinicalTrials.gov registration and reporting requirements became effective in 2017, and the government has recently begun enforcing those requirements against non-compliant clinical trial sponsors.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- ***Phase 1:*** The product candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- ***Phase 2:*** This phase involves studies in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- ***Phase 3:*** Clinical trials are undertaken with an expanded patient population to further evaluate dosage, clinical efficacy and safety in an expanded patient population, often at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product candidate and provide, if appropriate, an adequate basis for product labeling. These trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA or BLA.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events, or SAEs, occur. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the clinical protocol, cGCP, or other IRB requirements or if the drug has been associated with unexpected serious harm to patients.

During the development of a new drug or biological product, sponsors have the opportunity to meet with the FDA at certain points, including prior to submission of an IND, at the end of phase 2, and before submission of an NDA or BLA. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the end of phase 2 meeting to discuss their phase 2 clinical results with the agency and to present their plans for the pivotal phase 3 studies that they believe will support approval of the new drug or biological product.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the physical characteristics of the drug or biological product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality, potency and purity of the final drug or biological product. For biological products in particular, the PHSA emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined in order to help reduce the risk of the introduction of adventitious agents. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Marketing application submission and FDA review

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, along with information relating to the product's chemistry, manufacturing, and controls and proposed labeling, are submitted to the FDA as part of an NDA or BLA requesting approval to market the product for one or more indications. Our Anticalin-based product candidates are proteins that will be regulated as biological products subject to the BLA marketing pathway. BLA in particular must contain proof of the biological product candidate's safety, purity, potency and efficacy for its proposed indication or indications. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of the FDA. Under federal law, the fee for the submission of an NDA or BLA is substantial (for example, for FY2022 this application fee exceeds $3.1 million), and the sponsor of an approved NDA or BLA is also subject to an annual program fee, currently more than $369,000 per program. These fees are typically adjusted annually, but exemptions and waivers may be available under certain circumstances.

The FDA conducts a preliminary review of all NDAs and BLAs within 60 days of receipt and informs the sponsor by the 74th day after the FDA's receipt of the submission whether an application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA or BLA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing.

After the submission is accepted for filing, the FDA begins an in-depth substantive review. As noted above, the FDA has agreed to specified performance goals in the review process of NDAs and BLAs. Applications are meant to be reviewed within ten months from the date it is accepted for submission or filing, and the applications for "priority review" products are meant to be reviewed within six months from the date the application is accepted for submission or filing, as discussed in more detail below. The review process may be extended by the FDA for three additional months to consider new information or in the case of a clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, for original BLAs, the FDA has ten months from the filing date in which to complete its initial review of a standard application and respond to the applicant, and six months from the filing date for an application with "priority review." For all BLAs and new molecular entity, or NME, NDAs, the ten and six-month time periods run from the filing date; for all other original applications, the ten and six-month time periods run from the submission date. Despite these review goals, it is not uncommon for FDA review of an NDA or BLA to extend beyond the goal date.

Before approving a BLA, the FDA will typically conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether the manufacturing processes and facilities comply with cGMPs. The FDA will not approve the 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. The FDA also may inspect the sponsor and one or more clinical trial sites to assure compliance with cGCP requirements and the integrity of the clinical data submitted to the FDA.

Additionally, the FDA may refer any NDA or BLA, including applications for novel biologic candidates which present difficult questions of safety or efficacy, to an advisory committee. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations when making final decisions on approval. The FDA likely will re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, if it determines that a REMS is necessary to ensure that the benefits of the drug outweigh its risks and to assure the safe use of the drug or biological product. The REMS could include medication guides, physician communication plans, assessment plans and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS is needed, the sponsor of the NDA or BLA must submit a proposed REMS. The FDA will not approve a BLA without a REMS, if required.

Under the Pediatric Research Equity Act, or PREA, as amended, a BLA or supplement to a BLA must contain data that are adequate to assess the safety and efficacy of the product candidate for the claimed indications in all relevant pediatric populations and to support dosing and administration for each pediatric population for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. The Food and Drug Administration Safety and Innovation Act, or the FDASIA, enacted in 2012, made permanent the PREA to require a sponsor who is planning to

submit a marketing application for a product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration to submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the phase 3 or phase 2/3 clinical trial. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including trial objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from pre-clinical studies, early phase clinical trials or other clinical development programs.

The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. The FDA reviews a BLA to determine, among other things whether the product is safe, pure and potent and that the facility (or facilities) in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. The approval process is lengthy and often difficult, and the FDA may refuse to approve an NDA or BLA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. On the basis of the FDA's evaluation of the NDA or BLA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue either an approval letter or a Complete Response Letter, or CRL. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL indicates that the review cycle of the application is complete and the application will not be approved in its present form. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. The CRL may require additional clinical or other data, additional pivotal phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the applicant may choose to either resubmit the NDA or BLA addressing all of the deficiencies identified in the letter or withdraw the application. If and 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. The FDA has committed to reviewing such resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If a product receives regulatory approval from the FDA, the approval is limited to the conditions of use (e.g., patient population, indication) described in the application. Further, depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, require that post-approval trials, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing trials or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Fast Track, Breakthrough Therapy and Priority Review Designations

The FDA is authorized to designate certain products for expedited development or review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs include fast track designation, breakthrough therapy designation and priority review designation.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need by providing a therapy where none exists or a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast track designation provides opportunities for more frequent interactions with the FDA review team to expedite development and review of the product. The FDA may also review sections of the NDA or BLA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor and the FDA agree on a schedule for the submission of the application sections and the sponsor pays any required user fees upon submission of the first section of the NDA or BLA. In addition, fast track designation may be withdrawn by the sponsor or rescinded by the FDA if the designation is no longer supported by data emerging from the clinical trial process.

In addition, with the enactment of FDASIA in 2012, Congress created a new regulatory program for product candidates designated by FDA as "breakthrough therapies" upon a request made by the IND sponsors. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment

effects observed early in clinical development. Drugs or biologics designated as breakthrough therapies are also eligible for accelerated approval of their respective marketing applications. The FDA must take certain actions with respect to breakthrough therapies, such as holding timely meetings with and providing advice to the product sponsor, which are intended to expedite the development and review of an application for approval of a breakthrough therapy.

Finally, the FDA may designate a product for priority review if it is a drug or biologic that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines at the time that the marketing application is submitted, on a case- by-case basis, whether the proposed drug represents a significant improvement in treatment, prevention or diagnosis of disease when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months for an original BLA or for an NME NDA from the date of filing.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Furthermore, fast track designation, breakthrough therapy designation and priority review do not change the standards for approval and may not ultimately expedite the development or approval process.

Accelerated approval pathway

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval from the FDA and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a drug or biologic when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform post-marketing clinical trials to verify and describe the predicted effect on IMM or other clinical endpoint, and the product may be subject to expedited withdrawal procedures. Drugs and biologics granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval when the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate long-term clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. For example, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large clinical trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm the predicted clinical benefit of the product during post-marketing studies, would allow the FDA to withdraw approval of the drug. All promotional materials for product candidates being considered and approved under the accelerated approval program are subject to prior review by the FDA.

Patent term restoration

Depending upon the timing, duration and specifics of FDA approval of our drugs, some of our U.S. patents may be eligible for limited patent term extension. These patent term extensions permit a patent restoration term of up to five years as compensation for any patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND, and the submission date of an NDA or BLA, plus the time between the submission date of an NDA or BLA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension, and the extension must be applied for prior to expiration of the patent. The United States Patent and Trademark Office, or the USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Pediatric exclusivity

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

Reference product exclusivity for biological products

In March 2010, the Patient Protection and Affordable Care Act was enacted in the United States and included the Biologics Price Competition and Innovation Act of 2009, or the BPCIA. The BPCIA amended the PHSA to create an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. To date, the FDA has approved a number of biosimilars, including the first interchangeable monoclonal antibody biosimilar in 2021, and numerous biosimilars have been approved in Europe. The FDA has also issued several guidance documents outlining its approach to reviewing and approving biosimilars and interchangeable biosimilars.

A biosimilar product is defined as one that is highly similar to a reference product notwithstanding minor differences in clinically inactive components and for which there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity and potency of the product. An interchangeable product is a biosimilar product that can be expected to produce the same clinical results as the reference product in any given patient and, for products administered multiple times to an individual, that the product and the reference product may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biological product without such alternation or switch. Upon licensure by the FDA, an interchangeable biosimilar may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product, although to date no such products have been approved for marketing in the United States.

The biosimilar applicant must demonstrate that the product is biosimilar based on data from (1) analytical studies showing that the biosimilar product is highly similar to the reference product; (2) animal studies (including toxicity); and (3) one or more clinical studies to demonstrate safety, purity and potency in one or more appropriate conditions of use for which the reference product is approved. In addition, the applicant must show that the biosimilar and reference products have the same mechanism of action for the conditions of use on the label, route of administration, dosage and strength, and the production facility must meet standards designed to assure product safety, purity and potency.

A reference biological product is granted 12 years of market exclusivity from the time of first licensure of the product, and the first approved interchangeable biologic product will be granted an exclusivity period of up to one year after it is first commercially marketed. If pediatric studies are performed and accepted by the FDA as responsive to a Written Request, the 12-year exclusivity period will be extended for an additional six months. In addition, the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a supplement for the reference product for a subsequent application filed by the same sponsor or manufacturer of the reference product (or licensor, predecessor in interest or other related entity) for a change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength or for a modification to the structure of the biological product that does not result in a change in safety, purity or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of

exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the "first licensure" of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

The BPCIA is complex and is still being interpreted and implemented by the FDA and by federal judges. In addition, recent government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation and meaning of the BPCIA is subject to significant uncertainty.

Orphan drug designation and exclusivity

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug as defined by the FDA for treatment of the same indication or disease.

Post-approval requirements

Following approval of a new product, the manufacturer and the approved product are subject to pervasive and continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting of adverse experiences with the product, product sampling and distribution restrictions, complying with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations (i.e., "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. If there are any modifications to the product, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA/BLA or an NDA/BLA supplement, which may require the applicant to develop additional data or conduct additional pre-clinical studies and clinical trials. The FDA may also place other conditions on approvals including the requirement for a REMS to assure the safe use of the product. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. The manufacturing facilities for our product candidates must meet cGMP requirements and satisfy the FDA or comparable foreign regulatory authorities' satisfaction before any product is approved and our commercial products can be manufactured. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. These manufacturers must comply with cGMP regulations that require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved drugs or biologics are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. Future inspections by the FDA and other regulatory agencies may identify compliance issues at the facilities of our CMOs that may disrupt production or distribution or require substantial resources to correct. In addition, the discovery of conditions that violate these rules, including failure to conform to cGMPs, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA or BLA, including voluntary recall and regulatory sanctions as described below.

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or other enforcement-related letters or clinical holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs/BLAs or supplements to approved NDAs/BLAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- consent decrees, corporate integrity agreements, debarment or exclusion from federal health care programs; or mandated modification of promotional materials and labeling and the issuance of corrective information.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. Most recently, the Drug Supply Chain Security Act, or DSCSA, was enacted with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States, including most biological products. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors and dispensers over a 10-year period that is expected to culminate in November 2023. From time to time, new legislation and regulations may be implemented that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. It is impossible to predict whether further legislative or regulatory changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Regulation outside of the United States

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products outside of the United States. Whether or not we obtain FDA approval for a product candidate, we must obtain approval by the comparable regulatory authorities of foreign countries or economic areas, such as the 28-member European Union, before we may commence clinical trials or market products in those countries or areas. With the United Kingdom withdrawal from the European Union on January 31, 2020, UK licensing decisions will be transferred from EMA to The Medicines and Healthcare Products Regulatory Agency, or MHRA, the UK Regulatory Body. For a period of two years following January 1, 2021, the UK will continue to adopt decisions taken by the European Commission on the approval of new marketing authorizations. However, companies will be required to submit an identical application to the MHRA upon the Medicinal Products for Human Use, or CHMP, positive opinion of the application. The MHRA will then wait for the European Commission decision on approval. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly between countries and jurisdictions and can involve additional testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

European Union drug development, review and approval

In the European Union, our product candidates also may be subject to extensive regulatory requirements. As in the United States, medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained. Similar to the United States, the various phases of pre-clinical and clinical research in the European Union are subject to significant regulatory controls.

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on GCP, and the related national implementing provisions of the individual EU Member States govern the system for the approval of clinical trials in the European Union. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other

documents, an IMPD (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, and where relevant the implementing national provisions of the individual EU Member States and further detailed in applicable guidance documents. All suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the competent national authority and the Ethics Committee of the Member State where they occurred.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) was adopted and it became effective on January 31, 2022. The Clinical Trials Regulation will be directly applicable in all of the EU Member States, repealing the current Clinical Trials Directive 2001/20/EC. The extent to which ongoing clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable, the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

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

To obtain a marketing authorization of a drug in the European Union, we may submit marketing authorization applications, or MAA, either under the so-called centralized or national authorization procedures.

Centralized procedure

The centralized procedure provides for the grant of a single marketing authorization following a favorable opinion by the European Medicines Agency, or EMA, that is valid in all EU member states, as well as Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for medicines produced by specified biotechnological processes, products designated as orphan medicinal products, advanced-therapy medicines (such as gene-therapy, somatic cell-therapy or tissue-engineered medicines) and products with a new active substance indicated for the treatment of specified diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions and viral diseases. The centralized procedure is optional for products that represent a significant therapeutic, scientific or technical innovation, or whose authorization would be in the interest of public health. Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee for Medicinal Products for Human Use, or the CHMP. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is of 150 days, excluding stop-clocks.

National authorization procedures

There are also two other possible routes to authorize medicinal products in several EU countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:

- Decentralized procedure. Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one EU country of medicinal products that have not yet been authorized in any EU country and that do not fall within the mandatory scope of the centralized procedure.
- Mutual recognition procedure. In the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other EU countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

Under the above described procedures, before granting the marketing authorization, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Conditional approval

In specific circumstances, E.U. legislation (Article 14(7) Regulation (EC) No 726/2004 and Regulation (EC) No 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use) enables applicants to obtain a conditional marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products) if (1) the risk-benefit balance of the product candidate is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) the product fulfills unmet medical needs and (4) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

Pediatric studies

Prior to obtaining a marketing authorization in the European Union, applicants have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are set forth in Regulation (EC) No 1901/2006, which is referred to as the Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine in children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine in children is not needed or is not appropriate, such as for diseases that only affect the elderly population.

Before a marketing authorization application can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.

European Union regulatory exclusivity

In the European Union, new products authorized for marketing (i.e., reference products) qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the European Union during a period of eight years from the date on which the reference product was first authorized in the European Union. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until ten years have elapsed from the initial authorization of the reference product in the EU. The ten-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

European Union orphan designation and exclusivity

The criteria for designating an orphan medicinal product in the European Union, are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The ten-year market exclusivity in the European Union may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- the applicant consents to a second orphan medicinal product application; or
- the applicant cannot supply enough orphan medicinal product.

PRIME designation

The EMA grants access to the Priority Medicines, or PRIME, program to investigational medicines for which it determines there to be preliminary data available showing the potential to address an unmet medical need and bring a major therapeutic advantage to patients. As part of the program, the EMA provides early and enhanced dialogue and support to optimize the development of eligible medicines and speed up their evaluation, aiming to bring promising treatments to patients sooner.

Periods of authorization and renewals

A marketing authorization is valid for five years in principle and the marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the E.U. market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid (the so-called sunset clause).

Rest of the world regulation

For other countries outside of the European Union and the United States, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from jurisdiction to jurisdiction. Additionally, the clinical trials must be conducted in accordance with cGCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Coverage, pricing and reimbursement

Sales of pharmaceutical products approved by the FDA will depend in significant part on the availability of third-party coverage and reimbursement for the products. Third-party payors include government healthcare programs in the United States such as Medicare and Medicaid, managed care providers, private health insurers and other organizations. These third-party payors are increasingly challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the reimbursement status of newly approved healthcare products. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. We may need to conduct expensive pharmacoeconomic studies to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development. Our product candidates may not be considered cost-effective. It is time consuming and expensive to seek reimbursement from third-party payors. Reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. Some countries provide that drug products may

be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of our product candidate to currently available therapies (so called health technology assessment, or HTA) in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Other member states allow companies to fix their own prices for drug products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally tend to by significantly lower.

The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states and parallel distribution (arbitrage between low-priced and high-priced member states) can further reduce prices. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Other U.S. health care laws and regulations

If our product candidates are approved in the United States, we will have to comply with various U.S. federal and state laws, rules and regulations pertaining to health care fraud and abuse, including anti-kickback laws and physician self-referral laws, rules and regulations. Violations of the fraud and abuse laws are punishable by criminal and civil sanctions, including, in some instances, exclusion from participation in federal and state health care programs, including Medicare and Medicaid. These laws include:

- the federal anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal health care program such as Medicare and Medicaid;
- the federal False Claims Act imposes civil penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any health care benefit program or making false statements relating to health care matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH Act, and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal transparency requirements under the Physician Payments Sunshine Act require manufacturers of FDA-approved drugs, devices, biologics and medical supplies covered by Medicare, Medicaid or the Children's Health Insurance Program to report, on an annual basis, to the Department of Health and Human Services, or DHHS, information related to payments and other transfers of value to physicians, teaching hospitals, and certain advanced non-physician health care practitioners and physician ownership and investment interests; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving health care items or services reimbursed by nongovernmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines, or the relevant compliance guidance promulgated by the federal government, in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures to the extent that those laws impose requirements that are more stringent than the Physician Payments Sunshine Act. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Notably, in November 2020, the DHHS finalized significant changes to the regulations implementing the Anti-Kickback Statute, as well as the civil monetary penalty rules regarding beneficiary inducements, with the goal of offering the health care

industry more flexibility and reducing the regulatory burden associated with those fraud and abuse laws, particularly with respect to value-based arrangements among industry participants.

Health care reform in the United States and potential changes to health care laws

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and devices and to spur innovation, but its ultimate implementation is uncertain. In addition, in August 2017, the FDA Reauthorization Act was signed into law, which reauthorized the FDA's user fee programs and included additional drug and device provisions that build on the Cures Act. Furthermore, the next FDA reauthorization package is currently being negotiated and is due to be finalized by Congress in 2022, while several other FDA-related changes are also being proposed in Congress, including within a "Cures 2.0" bill that is likely to have bipartisan support. If we are not able to maintain regulatory compliance, we may lose any marketing approval that we otherwise may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

As previously mentioned, a primary trend in the U.S. health care industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products and services, implementing reductions in Medicare and other health care funding and applying new payment methodologies. For example, in March 2010, the Affordable Care Act was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced 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; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans; imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers' outpatient drugs coverage under Medicare Part D; and established a Center for Medicare Innovation at the U.S. Centers for Medicare and Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, andas a result certain sections of the Affordable Care Act have not been fully implemented or effectively repealed. However, following several years of litigation in the federal courts, in June 2021, the U.S. Supreme Court upheld the Affordable Care Act when it dismissed a legal challenge to the law's constitutionality. Further legislative and regulatory changes under the Affordable Care Act remain possible, although the new federal administration under President Biden has signaled that it plans to build on the Affordable Care Act and expand the number of people who are eligible for health insurance subsidies under it. It is unknown what form any such changes or any law would take, and how or whether it may affect the pharmaceutical industry as a whole or our business in the future. We expect that changes or additions to the Affordable Care Act, the Medicare and Medicaid programs, such as changes allowing the federal government to directly negotiate drug prices, and changes stemming from other health care reform measures, especially with regard to health care access, financing or other legislation in individual states, could have a material adverse effect on the health care industry in the United States.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act that affect health care expenditures. There also has been heightened governmental scrutiny in recent years over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for pharmaceutical and biologic products. For example, the 2021 Consolidated Appropriations Act signed into law on December 27, 2020 incorporated extensive health care provisions and amendments to existing laws, including a requirement that all manufacturers of drug products covered under Medicare Part B report the product's average sales price to DHHS beginning on January 1, 2022, subject to enforcement via civil money penalties.

As another example, on December 20, 2019, former President Trump signed the Further Consolidated Appropriations Act for 2020 into law (P.L. 116-94) that includes a piece of bipartisan legislation called the Creating and Restoring Equal Access to Equivalent Samples Act of 2019 or the "CREATES Act." The CREATES Act aims to address the concern articulated by both the FDA and others in the industry that some brand manufacturers have improperly restricted the distribution of their products, including by invoking the existence of a REMS for certain products, to deny generic and biosimilar product developers access to samples of brand products. Because generic and biosimilar product developers need samples to conduct certain comparative testing required by the FDA, some have attributed the inability to timely obtain samples as a cause of delay in the entry of generic and biosimilar products. To remedy this concern, the CREATES Act establishes a private cause of action that permits a generic or biosimilar product developer to sue the brand manufacturer to compel it to furnish the necessary samples on "commercially reasonable, market-based terms." Whether and how generic and biosimilar product developments will use this new pathway, as well as the likely outcome of any legal challenges to provisions of the CREATES Act, remain highly uncertain and its potential effects on our future commercial products are unknown.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on

certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate PBMs and other members of the health care and pharmaceutical supply chain, an important decision that may lead to further and more aggressive efforts by states in this area.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. We expect that additional state and federal health care reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for health care products and services.

Corporate Information

On December 17, 2014, Pieris, Pieris GmbH and the former stockholders of Pieris GmbH entered into an acquisition agreement, or the Acquisition Agreement. Pursuant to the Acquisition Agreement, the stockholders of Pieris GmbH contributed all of their equity interests in Pieris GmbH to Pieris in exchange for shares of Pieris common stock, which resulted in Pieris GmbH becoming a wholly-owned subsidiary of Pieris, which we refer to as the Acquisition.

Upon the closing of the Acquisition on December 17, 2014, Pieris ceased to be a "shell company" under applicable rules of the Securities and Exchange Commission, or the SEC. As of December 31, 2019, we no longer qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act. As such, we are no longer eligible to take advantage of certain reduced disclosure and other requirements that are otherwise applicable to public companies, including without limitation, (i) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, and (ii) complying with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis.

Rule 12b-2 of the Exchange Act establishes a class of company called a "smaller reporting company," which effective September 10, 2018, was amended to include companies with a public float of less than $250 million as of the last business day of their most recently completed second fiscal quarter or, if such public float is less than $700 million, had annual revenues of less than $100 million during the most recently completed fiscal year for which audited financial statements are available. For the year ended December 31, 2021, we qualify as a smaller reporting company.

As a smaller reporting company, we are eligible to and have taken advantage of certain extended accounting standards and exemptions from various reporting requirements that are not available to public reporting companies that do not qualify for those classifications. These exemptions include, but are not limited to, reduced disclosure obligations regarding executive compensation in our periodic and annual reports, exemption from the requirement to provide a compensation discussion and analysis describing compensation practices and procedures, and reduced financial statement disclosure in our registration statements, which must include two years of audited financial statements rather than the three years of audited financial statements that are required for other public reporting companies. Smaller reporting companies are also eligible to provide such reduced financial statement disclosure in annual reports on Form 10-K.

For as long as we continue to be a smaller reporting company, we expect that we will take advantage of the reduced disclosure obligations available to us as a result of this classification. We will remain a smaller reporting company until we have a public float of $250 million or more as of the last business day of our most recently completed second fiscal quarter, and we could retain our smaller reporting company status indefinitely depending on the size of our public float.

Employees

We consider our relationship with our employees to be good. In order to successfully develop our drug candidates, we must be able to attract and retain highly skilled personnel. We anticipate hiring additional employees for research and development, clinical and regulatory affairs, and general and administrative activities over the next few years.

Headcount Data

As of December 31, 2021, we had 124 full-time employees and 17 permanent part-time employees. None of our employees are represented by a labor union or covered by a collective bargaining agreement. Our corporate headquarters is located in Boston, MA and our R&D facility is located in Hallbergmoos, Germany. As such, 25, or 17.7%, of our employees were located in the United States and 116, or 82.3%, of our employees were located in Germany. We also utilize the services of consultants, clinical research organizations and other third parties on a regular basis from locations across the world.

Corporate Values and Ethics

We strongly believe that our success depends on all of our employees identifying with our company's purpose and understanding how their work contributes to the Company's overall strategy. To this end, we engaged in an inclusive all-company process to develop our company purpose, vision, mission and values.

"Improving Lives" has been defined as the purpose of Pieris

Our corporate culture and values, along with our employees are the most valuable assets of the Company. These values, which are the foundation of our Company culture, are:

- Passion,
- Integrity,
- Excellence,
- Responsibility,
- Innovation, and
- Spirit of Collaboration.

These values form part of our goal setting and review process to ensure accountability to these values at all levels. Annual anonymous engagement surveys ensure that we can assess our company culture against expectations and intentions. In order to further ensure we live our values and our culture stays unique and strong, our Board of Directors and executive management team put significant focus on our human capital resources.

We utilize a variety of channels to facilitate open and direct communication, including: (i) monthly all-hands staff meetings, (ii) regular open learning forums to promote peer learning or town hall meetings with executives; (iii) regular ongoing update communications; and (iv) employee surveys beyond the annual engagement survey referenced above on an as-needed basis.

Employee Compensation and Benefits

Our compensation programs are designed to align the compensation of our employees with the Company's performance and to provide the proper incentives to attract, retain and motivate employees to achieve superior results. The structure of our compensation programs balances incentive earnings for both short-term and long-term performance. Specifically:

- We provide employee base salaries that are competitive and consistent with employee positions, skill levels, experience, knowledge and geographic location.
- To foster a stronger sense of ownership and align the interests of employees with those of our shareholders, we offer both a stock option program and employee stock purchase program to eligible employees under our broad-based equity incentive plans.
- We engage nationally and internationally recognized outside compensation and benefits consulting firms to independently evaluate the effectiveness of our executive compensation and benefit programs and to provide benchmarking against our peers within the industry.
- Annual increases and incentive compensation are based on merit, which is communicated to employees at the time of hiring and documented through our talent management process as part of our annual review procedures and upon internal transfer and/or promotion.
- All employees are eligible for health insurance, paid and unpaid leaves, retirement benefits and life and disability/accident coverage. We also offer a variety of voluntary benefits that allow employees to select the options that meet their needs, including flexible time-off, flexible working arrangements, paid parental leave, health programs and onsite food and drink. We aim to provide location-specific attractive benefits packages in all of our locations. We pursue a shared compensation and benefits philosophy and have implemented size and phase-appropriate solutions for each country.

Diversity and Inclusion

Ingrained in our culture is the philosophy that each individual offers diverse perspectives, backgrounds and experiences that create great outcomes when we are united as a team. We respect our people and embrace our differences. We welcome everyone and value the ideas generated by our collective uniqueness. We aspire that all of our teammates reach their full potential and we encourage them to be confident in their differences. As of December 31, 2021, approximately 60% of our global workforce was female and 43% of our employees in managerial or supervisory roles were female.

Employee Development and Training

We invest significant resources in developing and retaining the talent needed to achieve our business goals. To support our employees in reaching their full potential, we offer internal and promote external learning and development opportunities. Education assistance is offered to financially support employees who seek to expand their knowledge and skill base.

Response to COVID-19

Beginning in March 2020 and continuing through all of 2021, we have supported our employees and government efforts to curb the COVID-19 pandemic through a multifaceted communication, infrastructure and behavior modification and enforcement effort, with the main objective to keep our laboratories in operation while protecting our employees' health and safety:

- Establishing clear and regular COVID-19 policies, safety protocols and weekly updates to all employees;
- Increasing physical distancing in workspaces for employees working onsite by scheduling adjustments and adding work from home flexibility;
- Adjusting attendance policies to encourage those who are sick or are able to perform their work from home to stay home;
- Increasing cleaning protocols across all locations;
- Providing additional personal protective equipment and cleaning supplies;
- Implementing site-specific protocols to address actual and suspected COVID-19 cases and potential exposure;
- Prohibiting all domestic and international non-essential travel for all employees; and
- Requiring masks to be worn in all locations.

Additionally, we have provided our employees with a stipend to ensure a safe and efficient workspace at home.

Available Information

Our Internet address is www.pieris.com. Copies of our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports, are available to you free of charge through the Investors section of our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the SEC. The information contained on, or that can be accessed through, our website is not part of this Annual Report on Form 10-K. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference.

Item 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, together with the other information contained in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes, before making any decision to invest in shares of our common stock. This Annual Report on Form 10-K contains forward-looking statements. If any of the events discussed in the risk factors below occurs, our business, prospects, results of operations, financial condition and cash flows could be materially harmed. If that were to happen, the trading price of our common stock could decline, and you could lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks not currently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations.

Following is a summary of our Risk Factors:

- We have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future. We currently have no product revenues and no approved products and will need to raise additional capital to operate our business.
- We are highly dependent on the success of PRS-060/AZD1402, our lead candidate in our respiratory pipeline, and cinrebafusp alfa, the lead candidate in our IO pipeline. We are executing a broad development program for each of PRS-060/AZD1402 and cinrebafusp alfa and clinical and regulatory outcomes for each of PRS-060/AZD1402 and cinrebafusp alfa, if not successful, will significantly harm our business.
- Our limited operating history as a clinical-stage company may hinder our ability to successfully meet our objectives.
- Our global operations subject us to various risks, and our failure to manage these risks could adversely affect our results of operations.
- If we fail to comply with environmental, health and safety laws and regulations that apply to us, we could become subject to fines or penalties or incur costs that could harm our business.

- Our current operations are largely concentrated in two locations and any adverse events affecting these locations may have material adverse consequences on our business.
- Our failure to comply with data protection laws and regulations could lead to government enforcement actions, private litigation and/or adverse publicity and could negatively affect our operating results and business.
- Significant disruptions of information technology systems or security breaches could adversely affect our business.
- We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.
- We could be subject to product liability lawsuits based on the use of our drug candidates in clinical testing or, if obtained, following our products' marketing approval and commercialization. If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to cease clinical testing or limit commercialization of our drug candidates.
- Our business has been and may continue to be adversely affected by the ongoing coronavirus pandemic.
- We are heavily dependent on the successful development of our drug candidates and programs and we cannot be certain that we will receive regulatory approvals or be able to successfully commercialize our products even if we receive regulatory approvals.
- Preclinical and clinical testing of our drug candidates that has been conducted to date or will be conducted in the future may not have been or may not be performed in compliance with applicable regulatory requirements, which could lead to increased costs or material delays for their further development.
- Our research and development efforts are focused on a rapidly evolving area of science, and our approach to drug discovery and development is novel and may never lead to marketable products.
- Clinical drug development involves a lengthy and expensive process with uncertain outcomes, clinical trials are difficult to design and implement, and any of our clinical trials could produce unsuccessful results or fail at any stage in the process.
- If we experience delays or difficulties in the enrollment of research subjects in clinical trials, those clinical trials could take longer than expected to complete and our receipt of necessary regulatory approvals could be delayed or prevented.
- The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA or comparable foreign regulatory authorities.
- The review processes of regulatory authorities are lengthy, time consuming, expensive and inherently unpredictable. If we are unable to obtain approval for our drug candidates from applicable regulatory authorities, we will not be able to market and sell those drug candidates in those countries or regions and our business could be substantially harmed.
- Our failure to obtain marketing approval in jurisdictions other than the United States and Europe would prevent our product candidates from being marketed in these other jurisdictions. Any approval that we are granted for our product candidates in the United States or Europe would not assure approval of product candidates in the other or in any other jurisdiction.
- Our product candidates may cause undesirable side effects that could delay or prevent their marketing approval, limit their commercial potential, or result in significant negative consequences following marketing approval, if marketing approval is obtained.
- We may expend our limited resources to pursue a particular drug candidate or indication that does not produce any commercially viable products and may fail to capitalize on drug candidates or indications that may be more profitable or for which there is a greater likelihood of success.
- We rely on third parties to conduct our clinical trials and preclinical studies. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or otherwise conduct the trials as required or comply with regulatory requirements, we may not be able to obtain regulatory approval for our drug candidates, commercialize our product candidates when expected or at all, and our business could be substantially harmed.
- We rely and expect to continue to rely completely on third parties to formulate, manufacture, and transport our preclinical, clinical trial and commercial drug supplies. The development and commercialization of any of our drug candidates could be stopped, delayed or made less profitable if those third parties fail to provide us with sufficient

quantities of such drug supplies or fail to do so at acceptable quality levels, including in accordance with applicable regulatory requirements or contractual obligations, and our operations could be harmed as a result.

- Disagreements with respect to the commercial terms of our sales, licensing, purchase or manufacturing agreements may limit our commercial success.
- We depend on third parties and intend to continue to license or collaborate with third parties, and events involving these strategic partners or any future collaboration could delay or prevent us from developing or commercializing products.
- Our success depends in part on the efforts of our current and possible future collaborators, who will likely have substantial control and discretion over the continued development and commercialization of drug candidates that are the subject of our collaborations.
- We may not receive any further milestone, royalty or license payments under our current collaborations.
- Our commercial success depends upon attaining significant market acceptance of our drug candidates, if approved, among physicians, patients, third-party payors and other members of the medical community.
- Biologics carry unique risks and uncertainties, which could have a negative impact on future results of operations.
- Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.
- If we breach any of the agreements under which we license from third parties the intellectual property rights or commercialization rights to our drug candidates, particularly our license agreements with TUM and Kelun, we could lose license rights that are important to our business and our operations could be materially harmed.
- If our efforts to protect the proprietary nature of the intellectual property related to our technologies are not adequate, we may not be able to compete effectively and our business could be harmed.
- Claims that we infringe the intellectual property rights of others may prevent or delay our drug discovery and development efforts.
- We may desire to, or be forced to, seek additional licenses to use intellectual property owned by third parties, and such licenses may not be available on commercially reasonable terms, or at all.
- Certain technologies and patents have been developed with partners and we may face restrictions on this jointly developed intellectual property.
- If we are not able to attract and retain highly qualified personnel, we may not be able to successfully implement our business strategy.
- We have broad discretion in how we use our cash, cash equivalents and investments, including the net proceeds from our collaborations, public and private securities offerings, and may not use these financial resources effectively, which could affect our results of operations and cause our stock price to decline.
- We have had and have previously reported material weaknesses in our internal controls over financial reporting. If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, our ability to operate our business and investors' views of us.
- Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans or otherwise, could result in dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

A detailed discussion of the above Risk Factors follows below.

Risks Related to Our Business, Financial Position, Capital Requirements, Managing our Growth and Other Legal Compliance Matters

We have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future. We currently have no product revenues and no approved products and will need to raise additional capital to operate our business.

We are a clinical-stage biopharmaceutical company. To date, we have not generated any commercial sales revenue, are not profitable, and have incurred losses since our inception in 2001. For the years ended December 31, 2021 and 2020, we reported net loss of $45.7 million and $37.2 million, respectively. As of December 31, 2021, we had an accumulated deficit of $257.1

million. We expect to continue to incur losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for, our drug candidates and the commercialization of approved products, if any.

We are currently focused primarily on the development of our respiratory and IO programs.We have collaborations with major multi-national pharmaceutical companies. In particular, we have alliances with AstraZeneca and Genentech to treat respiratory diseases, with Genentech also in ophthalmology and with Servier, Seagen, and Boston Pharmaceuticals in IO. Our partner AstraZeneca is currently in phase 2a studies of PRS-060/AZD1402, our lead respiratory drug candidate, in multiple countries. Our IO program includes our lead IO drug candidate, cinrebafusp alfa, which is currently in phase 2 studies, as well as PRS-344/S095012 in partnership with Servier, which is currently in phase 1 studies. Together these programs will result in our continued incurrence of significant research, development and other expenses and resources. If our research and development efforts, including preclinical studies or clinical trials for any of our drug candidates fail or produce unsuccessful results and those drug candidates do not gain regulatory approval, or if any of our drug candidates, if approved, fail to achieve market acceptance, we may never become profitable. In addition, the failure of one drug candidate or program may have an adverse impact on other drug candidates and programs within our class of Anticalin-based therapies. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. 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.

We are highly dependent on the success of PRS-060/AZD1402, our lead candidate in our respiratory pipeline, and cinrebafusp alfa, the lead candidate in our IO pipeline. We are executing a broad development program for each of PRS-060/AZD1402 and cinrebafusp alfa and clinical and regulatory outcomes for each of PRS-060/AZD1402 and cinrebafusp alfa, if not successful, will significantly harm our business.

Our future success is highly dependent on our ability to successfully develop, obtain regulatory approval for and commercialize PRS-060/AZD1402 and cinrebafusp alfa. In general, most early-stage investigatory drugs, including inhaled drug candidates such as PRS-060/AZD1402 and oncology drug candidates such as cinrebafusp alfa, do not become approved drugs. Accordingly, there is a very meaningful risk that either or both of PRS-060/AZD1402 and cinrebafusp alfa will not succeed in one or more clinical trials sufficient to support one or more regulatory approvals. To date, clinical and preclinical outcomes from PRS-060/AZD1402 and cinrebafusp alfa have had a significant impact on our market valuation, financial position and business prospects, and we expect this to continue in future periods. If one or more clinical trials of PRS-060/AZD1402 or cinrebafusp alfa is not successful, it would materially harm our market valuation, prospects, financial condition and results of operations.

We will need substantial additional funding to continue our operations, which could result in significant dilution or restrictions on our business activities. We may not be able to raise capital when needed, if at all, or on terms acceptable to us, which would force us to delay, reduce or eliminate some or all of our product development programs or commercialization efforts and could cause our business to fail.

Our operations have consumed substantial amounts of cash since our inception. We expect to need substantial additional funding to continue the preclinical and clinical development of our drug candidates, as well as to launch and commercialize any drug candidates for which we receive regulatory approval.

We will require additional capital for the further development and commercialization of our drug candidates and programs, and may need to raise additional funds sooner than we currently anticipate if we choose to and are able to expand more rapidly than we currently anticipate. Further, we expect our expenses to increase in connection with our ongoing activities, particularly as we continue to advance, expand and monitor the performance of our preclinical and clinical programs, such as PRS-060/AZD1402, cinrebafusp alfa, PRS-220 and PRS-344/S095012, as well as additional programs that we advance through preclinical development and into the clinic and whose performance we monitor. In addition, if we obtain regulatory approval for any of our drug candidates, we expect to incur significant commercialization expenses related to regulatory requirements, product manufacturing, marketing, sales and distribution.

Furthermore, we expect to continue to incur additional costs associated with operating as a public company. We may also encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may increase our capital needs and/or cause us to spend our cash resources faster than we expect.

To date, we have financed our operations through a mix of equity investments from private and public investors, the incurrence of debt, grant funding and the receipt of up-front and milestone payments due under our various collaboration agreements, and we expect to continue to finance our operations in part through equity investments from public investors for the foreseeable future. Additional funding from those or other sources may not be available when or in the amounts needed, on acceptable terms, or at all. Our ability to secure additional funding from those or other sources could be significantly impacted by a

multitude of events that are beyond our control, including, but not limited to, changes in the macroeconomic environment and other events affecting the stock market, including the availability of research and other information, favorable or unfavorable, published by securities or industry analysts and news agencies.

Raising capital through the sale of equity or securities convertible into equity would result in dilution to our then-existing stockholders, which could be significant depending on the price at which we may be able to sell our securities. If we raise additional capital through the incurrence of indebtedness, we would likely become subject to covenants restricting our business activities, and holders of debt instruments may have rights and privileges senior to those of our equity investors. In addition, servicing the interest and principal repayment obligations under debt facilities could divert funds that would otherwise be available to support research and development, clinical or commercialization activities.

If we obtain capital through collaborative or licensing arrangements, these arrangements could require us to relinquish rights to our Anticalin-based technology or drug candidates and could result in receipt of only a portion of the revenues associated with the potential commercialization of our partnered drug candidates.

If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development activities for our drug candidates or any future commercialization efforts. Any of these events could significantly harm our business, financial condition, and prospects.

Our limited operating history as a clinical-stage company may hinder our ability to successfully meet our objectives.

We were formed in 2001, and since that time our focus has been on discovery of Anticalin-brand drug candidates. We are currently conducting clinical development of PRS-060/AZD1402, in partnership with AstraZeneca, cinrebafusp alfa, and PRS-344/S095012, in partnership with Servier, and we are also advancing other drug candidates through preclinical development with the intention of initiating additional clinical-stage programs. In addition to our focus on respiratory diseases and IO, we are also exploring additional indications that may be suitable for Anticalin-based therapies. Our drug candidates are in the early stages of development, have not obtained marketing approval, have never generated any revenue from sales and will require extensive testing before commercialization. We have limited experience with clinical-stage operations, including manufacturing required to support clinical activities and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. In addition, the early-stage nature of our drug discovery and development operations can only provide limited operating results upon which investors can evaluate our business and prospects.

Our limited operating history may adversely affect our ability to implement our business strategy and achieve our business goals, which include, among others, the following activities:

- developing our drug candidates using unproven technologies;
- undertaking preclinical development and clinical trials as well as formulating and manufacturing products;
- obtaining the human, financial and other resources necessary to develop, test, manufacture, commercialize and market our drug candidates;
- engaging corporate partners to assist in developing, testing, manufacturing and marketing our drug candidates;
- continuing to build and maintain an intellectual property portfolio covering our technology and drug candidates;
- satisfying the requirements of clinical trial protocols, including patient enrollment, establishing and demonstrating the clinical safety and efficacy of our drug candidates and obtaining necessary regulatory approvals;
- achieving acceptance and use by the medical community of our Anticalin platform and drug candidates after they receive regulatory approvals;
- maintaining, growing and managing our internal teams as and to the extent we increase our operations and develop new segments of our business;
- developing and maintaining successful collaboration, strategic and other relationships for the development and commercialization of our drug candidates that receive regulatory approvals with existing and new partners; and
- managing our cash flows and any growth we may experience in an environment where costs and expenses relating to clinical trials, regulatory approvals and commercialization continue to increase.

If we are unsuccessful in accomplishing any or all of these objectives, we may not be able to raise capital, expand our business, develop our drug candidates or continue our operations.

Our global operations subject us to various risks, and our failure to manage these risks could adversely affect our results of operations.

Our business is subject to certain risks associated with doing business globally. One of our growth strategies is to pursue opportunities for our business in several areas of the world, including the United States, Europe (including Germany), Asia and Australia, any or all of which could be adversely affected by the risks set forth below. Accordingly, we face significant operational risks as a result of doing business internationally, such as:

- fluctuations in foreign currency exchange rates;
- potentially adverse tax consequences and changes in tax laws;
- challenges in providing solutions across a significant distance, in different languages, different time zones and among different cultures (particularly, for as long as travel is limited due to the COVID-19 pandemic);
- different, complex and changing laws governing intellectual property rights, sometimes affording reduced protection of intellectual property rights in certain countries;
- difficulties in staffing and managing foreign operations, particularly in new geographic locations, and related compliance with employment, immigration and labor laws for employees or other staff living abroad;
- restrictions imposed by local labor practices and laws on our business and operations;
- economic weakness, including inflation, or rapid changes in government, economic and political policies and conditions, political or civil unrest or instability, economic or trade sanctions, closure of markets to imports, terrorism or epidemics and other similar outbreaks or events;
- compliance with a wide variety of complex foreign laws, treaties and regulations;
- compliance with the U.S. Foreign Corrupt Practices Act, or the FCPA, and other anti-corruption and anti-bribery laws;
- unexpected changes in tariffs, trade barriers and other regulatory or contractual limitations on our ability to develop or sell our products in certain foreign markets; and
- becoming subject to the laws, regulations and court systems of multiple jurisdictions.

Our failure to manage the market and operational risks associated with our international operations could limit the future growth of our business and adversely affect our results of operations.

Our international operations pose currency risks, which may adversely affect our operating results and net income.

Due to our operations outside of the United States, we are exposed to market risk related to changes in foreign currency exchange rates. Changes in the relative values of currencies occur regularly and, in some instances, could materially adversely affect our business, our financial condition, the results of our operations or our cash flows. Our operating results may be affected by volatility in currency exchange rates and our ability to effectively manage our currency transaction risks. Our reporting currency is the U.S. dollar, however, 79% of our operating expenses and all of our revenues are recorded in non-U.S. entities. As such, our financial statements are translated for reporting purposes as follows: (1) asset and liability accounts at year-end rates, (2) income statement accounts at weighted average exchange rates for the year and (3) stockholders' equity accounts at historical rates. Corresponding translation gains or losses are recorded in stockholders' equity.

We incur currency transaction risks whenever we enter into either a purchase or a sale transaction using a currency other than the euro, our functional currency, particularly in our arrangements for the purchase of supplies or licensing and collaboration agreements with partners outside of the United States. In such cases, we may suffer an exchange loss because we do not currently engage in currency swaps or other currency hedging strategies to address this risk.

As we continue to operate and enter into agreements and arrangements in the United States, Germany, Australia and elsewhere internationally, our exposure to currency risks will increase. We do not manage our foreign currency exposure in a manner that would eliminate the effects of changes in foreign exchange rates. Therefore, changes in exchange rates between these foreign currencies and the U.S. dollar will affect our revenues and expenses and could result in exchange losses in any given reporting period.

Given the volatility of exchange rates, especially as a result of ongoing developments of the COVID-19 pandemic, we can give no assurance that we will be able to effectively manage our currency transaction risks or that any volatility in currency exchange rates will not have an adverse effect on our results of operations.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other

remedial measures and legal expenses, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the FCPA, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The FCPA and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential FCPA violations and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

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

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA, or other legal requirements, including Trade Control laws. If we are not in compliance with the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the FCPA, other anti-corruption laws or Trade Control laws by U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of any hazardous materials and wastes. The use of these materials in our business could result in contamination or injury, which could cause damage for which we may be responsible but may not have sufficient resources to pay. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with these laws and regulations, which we may not be able to afford.

Although we maintain workers' compensation insurance for our operations in Germany 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 applicable to us. These current or future laws and regulations may impair our research, development or production efforts or impact the research activities we pursue, particularly with respect to research involving human subjects or animal testing. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions, which could cause our financial condition to suffer.

Health and safety regulations in the United States, Germany, and Australia and in the countries where our technology and potential products are or may be developed, licensed or sold may prevent the sale or use of our technology or products in the future.

We are subject to a variety of regulations regarding worker health and safety in the United States, the European Union (Germany), Australia and in the countries where our technology and potential products are licensed or may be sold. These regulations may continue to change due to the ongoing developments of the COVID-19 pandemic. Because our technology and potential products may frequently involve the manufacture or use of certain chemical or biological compounds, we are required to certify their safety for industrial use and development in a variety of countries and contexts. As there has not been sufficient testing to determine the long-term health and environmental risks of our Anticalin-based drug candidates and the materials used in the production of such drug candidates and any future products, future regulations may ban the use of our products due to the potential risk they pose to workers or may limit the use of our drug candidates in research and commercial settings. Any such regulations may have a substantial negative impact on our business and revenues and may cause our business to fail. Because we cannot guarantee the long-term safety of use or exposure to materials used during development or manufacture of our products, we may face liability for health risks or harms caused as a result of developing, manufacturing or other processes that use such materials. Any such claims may have a negative impact on our revenues and may prove substantially disruptive to our business in the future.

We may be limited in our use of our net operating loss carryforwards.

As of December 31, 2021, we had net operating loss carryforwards for United States federal income tax purposes of $33.1 million and net operating loss carryforwards for state income tax purposes of $37.4 million. Tax loss carryforwards that were generated prior to December 31, 2017 expire through 2037; U.S. federal tax loss carryforwards generated after that date do not expire. State loss carryforwards expire starting in 2035. In the United States, utilization of the net operating loss carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, and similar state provisions due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of net operating loss carryforwards that can be utilized annually to offset future taxable income and tax, respectively. If we were to lose the benefits of these loss carryforwards, our future earnings and cash resources would be materially and adversely affected. We completed a Section 382 study through December 31, 2020. Based on the study, we underwent an ownership change for Section 382 purposes which occurred in February 2018. As a result of the ownership change, our net operating loss and tax credit carryforwards as of the ownership change dates are subject to limitation under Section 382; however, these limitations are not expected to result in any of the impacted net operating loss and tax credit carryforwards to expire unutilized. Any net operating losses or tax credits generated after the February 2018 change are not subject to this annual limitation. However, subsequent ownership changes, as defined by Section 382, may potentially further limit the amount of net operating loss and tax credit carryforwards that could be utilized to offset future taxable income and tax.

As of December 31, 2021, we had German corporate income tax and trade tax net operating loss carryforwards of approximately $154.8 million and $153.9 million, respectively, which may be used to reduce our future taxable income in Germany. Under current German laws, tax loss carryforwards may only be used to offset any relevant later assessment period (calendar year) by $1.2 million plus 60% of the exceeding taxable income and trade profit of such period and do not expire. In addition, certain transactions, including transfers of shares or interest in the loss holding entity, may result in the partial or total forfeiture of tax losses existing at that date. Partial or total forfeiture of tax losses may further occur in corporate reorganizations of the loss holding entity.

Our business and operations would suffer in the event of system failures, and our operations are vulnerable to interruption by natural disasters, terrorist activity, power loss, adverse public health events and other events beyond our control, the occurrence of which could materially harm our business and drug development efforts.

Despite the implementation of security measures, our internal computer systems and those of our contractors and consultants are vulnerable to damage from computer viruses, hacking, ransomware, cyber-attacks, unauthorized access as well as telecommunication and electrical failures. Our information technology and other internal infrastructure systems, including corporate firewalls, servers, leased lines and connection to the Internet, face the risk of systemic failure that could disrupt our operations. Although we have invested significant resources to enhance the security of our computer systems, there can be no assurances we will not experience unauthorized intrusions into our computer systems, or those of our CROs, vendors, contractors and consultants, that we will successfully detect future unauthorized intrusions in a timely manner or that future unauthorized intrusions will not result in material adverse effects on our financial condition, reputation or business prospects.

While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs and operations. For example, the loss of clinical trial data from completed, ongoing, or planned clinical trials could result in delays in our regulatory approval efforts and we may incur substantial costs to attempt to recover or reproduce such data. Likewise, we currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates and any future product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. Certain data security breaches must be reported to affected individuals and the government, and in some cases to the media, under provisions of HIPAA, other U.S. federal and state law and requirements of non-U.S. jurisdictions, and financial penalties may also apply. If any disruption or security breach resulted in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and/or the further development of our drug candidates could be delayed.

We are also vulnerable to accidents, electrical blackouts, labor strikes, terrorist activities, war, natural disasters, adverse public health events and other events beyond our control, and we have not undertaken a systematic analysis of the potential consequences to our business as a result of all of such events and do not have an applicable recovery plan in place. Any disruption to our operations or the operations of our collaborators or suppliers from these kinds of events would likely impact our drug development efforts, operating results and our financial condition. With respect to potential impacts of the ongoing novel coronavirus pandemic, see "*The COVID-19 pandemic and its emerging variants, or any future pandemic, could adversely affect our business, including research, clinical trials, supply chain interruptions and financial condition.*"

As another example, certain clinical development activities related to our partnered phase 2a study of PRS-060/AZD1402 are located in Ukraine, which is currently being invaded by Russia. This invasion and military conflict could materially disrupt clinical development efforts and may disrupt future planned clinical development activities in the country. Although the length and impact of this military action is highly unpredictable, clinical trial sites in Ukraine could suspend or terminate trials, and patients could be forced to evacuate or voluntarily choose to relocate far from clinical trial sites, making them unavailable for further dosing or necessary follow-up. Our partner may be unable, in a timely manner, to identify and secure alternative sites to fulfill the clinical trial activities we had planned to undertake in Ukraine. If our clinical trials are interrupted or delayed, there may be insufficient data to support regulatory approvals of PRS-060/AZD1402, and data-read outs for the program as well as any commercialization may be delayed, which could reduce our potential revenue and hurt the competitive position of our product candidate. Any such disruptions to the development of PRS-060/AZD1402, one of our core clinical-stage programs, could have a material adverse impact on our ability to raise additional capital.

In addition, certain of our development efforts, particularly those related to the phase 2 study of PRS-060/AZD1402, which is being conducted in Australia, in addition to multiple other countries, are located in geographical areas that are known to be prone to certain natural disasters and weather events, including wildfires. In 2019 and 2020, dozens of wildfires erupted in New South Wales, Australia, prompting the government of Australia to declare a state of emergency. Should such a natural disaster that causes disruption to our development efforts occur again in Australia or elsewhere, thereby impeding our ability or the ability of our collaborators to timely conduct our clinical trials, our ability to conduct our business could be severely restricted and our business, clinical development efforts, prospects, and results of operations could be adversely affected as a result. The extent to which any natural disaster may impact our results will depend on future developments, which are highly uncertain and cannot be predicted.

Although we carry insurance to protect us against some losses or damages resulting from certain types of disasters, the extent of that insurance is limited in scope and amount, and we cannot assure you that our insurance coverage will be sufficient to satisfy any damages and losses. If our facilities are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption may have a material adverse effect on our business, financial position, results of operations, and prospects.

Our current operations are largely concentrated in two locations, and any adverse events affecting these locations may have material adverse consequences on our business.

Our current operations are carried out primarily in our facilities located in Hallbergmoos, Germany and Boston, Massachusetts. Any unplanned event, such as a flood, fire, explosion, earthquake, extreme weather condition, medical epidemic or pandemic, power shortage, telecommunication failure, or other natural or man-made accident, or an incident that prevents us from fully utilizing our facilities in these two locations, may have a material adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates, or interruption of our business operations. In the event of an accident or incident at these facilities, we cannot assure you that our insurance coverage will be sufficient to satisfy any damages and losses. If our facilities are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption may have a material adverse effect on our business, financial position, results of operations and prospects.

Our failure to comply with data protection laws and regulations could lead to government enforcement actions, private litigation and/or adverse publicity and could negatively affect our operating results and business.

We are subject to data protection laws and regulations that address privacy and data security. The legislative and regulatory landscape for data protection continues to evolve, and in recent years there has been an increasing focus on privacy and data security issues. In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws and federal and state consumer protection laws govern the collection, use, disclosure and protection of health-related and other personal information. Failure to comply with 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. For example, in January of 2020, the California Consumer Privacy Act, or CCPA, went into effect, which marked the first U.S. state to adopt comprehensive privacy legislation. The CCPA establishes a new privacy framework for covered businesses by creating an expanded definition of personal information, establishing new data privacy rights for California residents, and creating a new and potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. Additionally, a new privacy law, the California Privacy Rights Act, or CPRA, was approved by California voters in November of 2020, and certain provisions are effective as of January 1, 2022, with

full effectiveness as of 2023. The CPRA significantly modifies the CCPA, potentially resulting in further uncertainty, additional costs and expenses in an effort to comply and additional potential for harm and liability for failure to comply. Among other things, the CPRA established a new regulatory authority, the California Privacy Protection Agency, which is tasked with enacting new regulations under the CPRA and will have expensed enforcement authority. Virginia and Colorado enacted similar data protection laws in 2021, which will take effect in 2023, and other U.S. states have proposals under consideration, increasing the regulatory compliance risk.

Numerous other countries have, or are developing, laws governing the collection, use and transmission of personal information as well. EU member states and other jurisdictions have adopted data protection laws and regulations, which impose significant compliance obligations.

On May 25, 2018, the GDPR went into effect, implementing a broad data protection framework that expanded the scope of EU data protection law, including to non-EU entities that process, or control the processing of, personal data relating to individuals located in the EU, including clinical trial data. The GDPR sets out a number of requirements that must be complied with when handling the personal data of EU based data subjects, including: providing expanded disclosures about how their personal data will be used; higher standards for organizations to demonstrate that they have obtained valid consent or have another legal basis in place to justify their data processing activities; the obligation to appoint data protection officers in certain circumstances; new rights for individuals to be "forgotten" and rights to data portability, as well as enhanced current rights (e.g., access requests); the principal of accountability and demonstrating compliance through policies, procedures, training and audit; and a new mandatory data breach regime. In particular, medical or health data, genetic data and biometric data are all classified as "special category" data under the GDPR and afford greater protection and require additional compliance obligations. Further, EU member states have a broad right to impose additional conditions—including restrictions—on these data categories. This is because the GDPR allows EU member states to derogate from the requirements of the GDPR mainly in regard to specific processing situations (including special category data and processing for scientific or statistical purposes). For example, we are subject to the GDPR and the German federal data privacy law, the Bundesdatenschutzgesetz, and we are subject to the regulatory authority of the Bavarian data protection authority, the BayLDA. As the EU states continue to reframe their national legislation to harmonize with the GDPR, we will need to monitor compliance with all relevant EU member states' laws and regulations, including where permitted derogation from the GDPR are introduced.

We are also subject to evolving EU laws on data export, because we transfer data outside of the EU to ourselves or third parties. The GDPR only permits exports of data outside of the EU where there is a suitable data transfer solution in place to safeguard personal data (e.g., the EU Commission approved Standard Contractual Clauses). On July 16, 2020, the Court of Justice of the EU, or the CJEU, issued a landmark opinion in the case Maximilian Schrems vs. Facebook (Case C-311/18) (Schrems II). This decision calls into question certain data transfer mechanisms as between the EU member states and the US. The CJEU is the highest court in Europe and the Schrems II decision heightens the burden on data importers to assess U.S. national security laws on their business future actions of EU data protection authorities are difficult to predict at the early date. Consequently, there is some risk of any data transfers from the EU being halted. If we have to rely on third parties to carry out services for us, including processing personal data on our behalf, we are required under GDPR to enter into contractual arrangements to help ensure that these third parties only process such data according to our instructions and have sufficient security measures in place. Any security breach or non-compliance with our contractual terms or breach of applicable law by such third parties could result in enforcement actions, litigation, fines and penalties or adverse publicity and could cause customers to lose trust in us, which would have an adverse impact on our reputation and business. Any contractual arrangements requiring the processing of personal data from the EU to us in the United States will require greater scrutiny and assessments as required under Schrems II and may have an adverse impact on cross-border transfers of personal data, or increase costs of compliance. The GDPR provides an enforcement authority to impose large penalties for noncompliance, including the potential for fines of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater.

Applicable data privacy and data protection laws may conflict with each other, and by complying with the laws or regulations of one jurisdiction, we may find that we are violating the laws or regulations of another jurisdiction. Despite our efforts, we may not have fully complied in the past and may not in the future.If we become liable under laws or regulations applicable to us, we may be required to pay significant fines and penalties, our reputation may be harmed, and we may be forced to change the way we operate. That could require us to incur significant expenses, which could significantly affect our business.

Significant disruptions of information technology systems or security breaches could 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 large amounts of confidential information (including, among other things, trade secrets or other intellectual property, proprietary business information and personal information). It is critical that

we do so in a secure manner to maintain the confidentiality and integrity 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 vendors who may or could have access to our confidential information. The size and complexity of our information technology systems, and those of third-party vendors with whom we contract, and the large amounts of confidential information stored on those systems, make such systems vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or to cyber-attacks by malicious third parties. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include 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.

Significant disruptions of our information technology systems, or those of our third-party vendors or business partners, or security breaches could adversely affect our business operations and/or result in the loss, misappropriation and/or unauthorized access, use or disclosure of, or the prevention of access to, confidential information, including, among other things, trade secrets or other intellectual property, proprietary business information and personal information, and could result in financial, legal, business and reputational harm to us. For example, any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, could harm our reputation, require us to comply with federal and/or state breach notification laws and foreign law equivalents, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, including the imposition of significant fines, penalties, or other liability for any noncompliance with certain privacy and data security laws. Security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures to protect our information technology systems and infrastructure, there can be no assurance that such measures will prevent service interruptions or security breaches that could adversely affect our business. In addition, our liability insurance may not be sufficient in type or amount to cover us against costs of or claims related to security breaches, cyber-attacks and other related breaches. A cybersecurity breach could adversely affect our reputation and could result in other negative consequences, including disruption of our internal operations, increased cybersecurity protection costs, lost revenue, or litigation.

U.S. tax legislation and future changes to applicable U.S. or foreign tax laws and regulations may have a material adverse effect on our business, financial condition and results of operations.

We are subject to income and other taxes in the United States and foreign jurisdictions. Changes in laws and policy relating to taxes or trade may have an adverse effect on our business, financial condition and results of operations. This Annual Report on Form 10-K does not discuss any such tax legislation or changes to tax laws and regulations, or the manner in which it might affect us or purchasers of our securities. We urge our investors to consult with their legal and tax advisors with respect to such legislation and the potential tax consequences of investing in our securities.

We are also subject to different tax regulations in each of the jurisdictions where we conduct our business or where our management is located. We expect the scope and extent of regulation in the jurisdictions in which we conduct our business, or where our management is located, as well as regulatory oversight and supervision, to generally continue to increase. Generally, future changes in applicable U.S. or foreign tax laws and regulations, or their interpretation and application could have an adverse effect on our business, financial conditions and results of operations.

Inadequate funding for or other adverse actions taken by the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent our product candidates from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business rely, which could negatively impact our business.

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

During the global response to the COVID-19 pandemic, moreover, there have been strategic redeployments of government resources to priority projects, including FDA and EMA resources and staff, which have affected routine and for-cause manufacturing inspections and could have an impact on the timeline for review and approval of new marketing applications.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown or

slowdown occurs, it could significantly affect the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns or slowdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological advances. In addition, the competition in the asthma and cancer markets is intense. We have competitors in the United States and internationally, including major multinational pharmaceutical companies, fully integrated pharmaceutical and biotechnology companies, smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, and other public and private research organizations.

There are several third-party drug candidates that could compete with drug candidates in our pipeline.

Drug candidates interfering with the function of type 2 helper T cells, or Th2, the biological pathway for PRS-060/AZD1402, and thus anticipated to compete with PRS-060/AZD1402, include those that are being developed or commercialized by Sanofi/Regeneron (dupilumab), GSK (mepolizumab), Teva (reslizumab), AstraZeneca (benralizumab, IL-5Rα), Connect Biopharma (CBP-201) and Amgen/AstraZeneca (tezepelumab). Drugs targeting immunomodulatory targets and thus anticipated to compete with our IO programs include those that are currently marketed by Bristol-Myers Squibb (ipilimumab and nivolumab), Merck & Co (pembrolizumab), Roche (atezolizumab), Merck Serono/Pfizer (avelumab) and AstraZeneca (durvalumab), among others and drug candidates being developed by Bristol-Myers Squibb (for example, urelumab), Pfizer (for example, utomilumab) and other clinical stage drug candidates also compete with our proprietary and partnered IO programs. Additionally, a number of other companies, such as Amgen, Affimed, Macrogenics, Daiichi Sankyo, F-star, Inhibrx, Molecular Partners, Xencor, Immunocore and Zymeworks, also are pursuing multispecific or targeted approaches in oncology, and have therapies in development or already commercialized. In addition, with respect to cinrebafusp alfa, HER2-targeted therapies, or therapies targeting HER2+ patients, in development or already commercialized could compete with us, including drugs developed by Daiichi Sankyo (trastuzumab deruxtecan), Macrogenics (Margetuximab) and Zymeworks (zanidatamab), Seagen (tucatinib), and ALX Oncology (ALX-148). For additional information about third-party drug candidates that could compete with the drug candidates in our pipeline, see “Business--Competition.”

These existing or future competing products may provide therapeutic convenience or clinical or other benefits for a specific indication greater than our products or may offer comparable performance at a lower cost. If any of our products for which we receive regulatory approval fail to capture and maintain market share, we may not achieve sufficient product revenue and our business will suffer.

Many of our competitors have substantially greater financial, technical and other resources than we do, such as larger research and development staff and experienced marketing and manufacturing organizations, as well as significantly greater experience in:

- developing drugs;
- undertaking preclinical testing and clinical trials;
- obtaining FDA and other regulatory approvals of drugs;
- prosecuting and enforcing intellectual property rights;
- formulating and manufacturing drugs; and
- launching, marketing and selling drugs.

Established pharmaceutical companies may invest heavily to accelerate discovery and development of or in-license novel compounds that could make our drug candidates less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA, EMA, MHRA or other regulatory approval, or discovering, developing and commercializing medicines before we do, which would have a material adverse effect on our business and ability to achieve profitability from future sales of our approved drug candidates, if any. For additional information about our competitors, please see "Business--Competition."

We could be subject to product liability lawsuits based on the use of our drug candidates in clinical testing or, if obtained, following our products’ marketing approval and commercialization. If product liability lawsuits are brought against us, we

may incur substantial liabilities and may be required to cease clinical testing or limit commercialization of our drug candidates.

We could be subject to product liability lawsuits if any drug candidate we develop allegedly causes injury or is found to be otherwise unsuitable for human use during product testing, manufacturing, marketing or sale. Any such product liability claim may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against these claims, we will incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources.

Regardless of merit or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for any products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants or sites;
- significant costs to defend the related litigation;
- substantial monetary awards to clinical trial participants or patients;
- loss of revenue;
- increased insurance costs; and
- the inability to commercialize any products that we may develop.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the clinical testing and commercialization of products we develop on our own or with collaborators. While we currently carry insurance in an amount and on terms and conditions that are customary for similarly situated companies and that are satisfactory to our board of directors, our insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer.

In the future, we will seek to obtain appropriate insurance coverage with respect to any future clinical trials of our other drug candidates, but we may not be able to obtain the levels of coverage desired on acceptable terms, or at all. If we do secure product liability insurance, we may subsequently determine that additional amounts of coverage would be desirable at later stages of clinical development of our drug candidates or upon commencing commercialization of any drug candidate that obtains required approvals, but we may not be able to obtain such additional coverage amounts when needed on acceptable terms, or at all. Unless and until we obtain such insurance, we would be solely responsible for any product liability claims relating to our preclinical and clinical development activities. Further, even after any such insurance coverage is obtained, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by any insurance policies we may then have or that is in excess of the limits of our insurance coverage. We would be required to pay any amounts awarded by a court or negotiated in a settlement that exceed the coverage limitations or that are not covered by any product liability insurance we may obtain, and we may not have, or be able to obtain, sufficient capital to pay such amounts. A successful product liability claim or series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business, operations, and prospects.

We will need to grow the size of our organization, and we may not successfully manage any growth we may achieve.

Our success will depend upon the expansion of our operations and our ability to successfully manage our growth. Our future growth, if any, may place a significant strain on our management and on our administrative, operational, and financial resources, requiring us to implement and improve our operational, financial, and management systems.

In addition, our ability to manage our growth effectively will hinge upon our ability to expand, train, manage, and motivate our employees. As of December 31, 2021, we have 124 full-time employees and 17 permanent part-time employees. As our development and commercialization plans and strategies develop, these demands may also require the hiring of additional research, development, managerial, operational, sales, marketing, financial, accounting, legal, and other personnel.

Moreover, future growth could require the development of additional expertise by management and impose significant added responsibilities on members of management, including:

- effectively managing our clinical trials and submissions to regulatory authorities for marketing approvals;

- effectively managing our internal research and development efforts such as discovery research and preclinical development;
- identifying, recruiting, maintaining, motivating and integrating additional employees;
- effectively managing our internal and external business development efforts with current or future partners, such as entering into additional collaboration arrangements and increasing out-licensing revenues;
- establishing relationships with third parties essential to our business and ensuring compliance with our contractual obligations to such third parties;
- developing and managing new divisions of our internal business, including any sales and marketing segment we elect to establish;
- maintaining our compliance with public company reporting and other obligations, including establishing and maintaining effective internal control over financial reporting and disclosure controls and procedures; and
- improving our managerial, development, operational and finance systems.

We may not be able to accomplish any of those tasks, and our failure to do so could prevent us from effectively managing future growth, if any, and successfully growing our company.

Any increase in resources devoted to research and product development without a corresponding increase in our operational, financial, and management systems could have a material adverse effect on our business, financial condition and results of operations.

We may make future acquisitions that could disrupt our business, cause dilution to our stockholders and harm our financial condition and operating results.

We may, in the future, make acquisitions of, or investments in, companies that we believe have products or capabilities that are a strategic or commercial fit with our current business or otherwise offer opportunities for our company. In connection with these acquisitions or investments, we may:

- issue common stock or other forms of equity that would dilute our existing stockholders' percentage of ownership;
- incur debt and assume liabilities; and
- incur amortization expenses related to intangible assets or incur large and immediate write-offs.

We may not be able to complete acquisitions on favorable terms, if at all. If we do complete an acquisition, we cannot assure you that it will ultimately strengthen our competitive position or that it will be viewed positively by financial markets or investors. Furthermore, future acquisitions could pose numerous additional risks to our operations, including:

- problems integrating the purchased business, products or technologies;
- challenges in achieving strategic objectives, cost savings and other anticipated benefits;
- increases to our expenses;
- the assumption of significant liabilities that exceed the limitations of any applicable indemnification provisions or the financial resources of any indemnifying party;
- inability to maintain relationships with key business partners of the acquired businesses;
- diversion of management's attention from their day-to-day responsibilities;
- difficulty in maintaining controls, procedures and policies during the transition and integration;
- entrance into marketplaces where we have no or limited prior experience and where competitors have stronger marketplace positions;
- potential loss of key employees, particularly those of the acquired entity; and
- that historical financial information may not be representative or indicative of our results as a combined company.

The United Kingdom's withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business, including our ability to obtain regulatory approvals in the United Kingdom or the European Union.

The United Kingdom officially withdrew from the European Union on January 31, 2020 in a decision commonly referred to as "Brexit," and the consequent transitionary period came to an end on December 31, 2020. A substantial amount of uncertainty remains regarding the implementation of Brexit and changes to the relationship between the United Kingdom and the European Union. Depending on the ongoing implementation of Brexit, the full extent to which Brexit may impact the business and

regulatory environment in the United Kingdom, the European Union or other countries, remains unknown. In addition, Brexit could also result in similar referendums or votes in other European countries in which we do business.

In connection with Brexit, the United Kingdom and the European Union entered into a trade agreement known as the Trade and Cooperation Agreement, which was provisionally applicable as of January 1, 2021 and was ratified by the European Parliament on May 1, 2021. This agreement is intended to govern the legal relationship between the European Union and the United Kingdom post-Brexit. Any breakdowns in implementation of the Trade and Cooperation Agreement or other Brexit-related arrangements negotiated by the United Kingdom and the European Union could, among other outcomes, disrupt the free movement of goods, services and people between the United Kingdom and the European Union, and result in increased legal and regulatory complexities as well as potential higher costs of conducting business in Europe. Given the lack of comparable precedent, it remains unclear what financial, trade and legal implications Brexit will have and how it will affect us.

In line with the Trade and Cooperation Agreement, the United Kingdom has established its own regulatory framework for product candidates, which is not identical to the European Union regulatory framework. Industry experience with navigating the two regulatory frameworks is limited at this point in time. Further regulatory divergences could arise. Any failure of the European Union and the United Kingdom to implement and maintain the Trade and Cooperation Agreement could result in the United Kingdom or the European Union significantly altering regulations affecting the clearance or approval of our product candidates that are developed in the United Kingdom or the European Union. Any delay in obtaining, or inability to obtain, any marketing approvals in the United Kingdom as a result of Brexit or failures in the implementation of the Trade and Cooperation Agreement or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and reduce our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

In addition, the announcement, negotiation and implementation of Brexit and the withdrawal of the United Kingdom from the European Union have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and they may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Any of these effects of Brexit, among others, could adversely affect our business, our results of operations, liquidity and financial condition.

The COVID-19 pandemic and its emerging variants, or any future pandemic, could adversely affect our business, including research, clinical trials, supply chain interruptions and financial condition.

Our business has been and could continue to be be adversely affected by health epidemics in regions where we have our research and development operations, ongoing preclinical or clinical studies, contract research or manufacturing activities, collaboration partner activities or other business activities and could cause significant disruption in the operations of third-party manufacturers and contract research organizations upon which we rely. For example, the outbreak in late 2019 of the novel strain of virus named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), or coronavirus, which causes coronavirus disease 2019, or COVID-19, evolved into a global pandemic that spread to most regions of the world and is still ongoing.

The coronavirus pandemic, and its emerging variants have spread to most countries, including the United States and European and Asia-Pacific countries, and this includes countries in which we have planned or currently have active clinical trial sites. As a result we have and may continue to experience disruptions that could severely impact our business, clinical trials and pre-clinical studies, including:

- An impact on various aspects of our planned or ongoing clinical trials. Actual and potentially continuing impacts of the coronavirus pandemic on our various clinical trials include patient dosing and study monitoring, which have been and may continue to be paused or delayed due to changes in policies at various clinical sites, federal, state, local or foreign laws, rules and regulations, including quarantines or other travel restrictions, prioritization of healthcare resources toward pandemic efforts, including diminished attention of physicians serving as our clinical trial investigators and reduced availability of site staff supporting the conduct of our clinical trials, interruption or delays in the operations of the FDA, or other reasons related to the coronavirus pandemic. As the coronavirus pandemic continues, other aspects of our clinical trials have and may continue to be adversely affected, delayed or interrupted, including, site initiation, patient recruitment and enrollment, availability of clinical trial materials and data analysis. For example, due to pandemic lockdowns across the United States, monitoring of the clinical trial sites by our CROs was delayed for the phase 1 cinrebafusp alfa monotherapy and atezolizumab combination studies in 2021. Remote monitoring was eventually implemented by various sites which permitted our CROs to continue site monitoring. In addition, our CROs experienced staffing shortages because of the pandemic, which similarly delayed data monitoring, verification, and entry in the studies. Though it is unclear what impact these delays had, we estimate that the studies were delayed by a

few months. Patient dosing was not impacted and was completed in 2021 in both studies. Similarly, in 2021, site initiation for PRS-344/S095012 was delayed several weeks at a trial site in Australia due to the travel restrictions between Australian states, as well as site lockdown, which prevented on-site visits. In addition, some patients and clinical investigators may not be able to comply with clinical trial protocols and patients may choose to withdraw from our studies or we may have to pause enrollment or we may choose to or be required to pause enrollment and/or patient dosing in our ongoing clinical trials in order to preserve healthcare resources and protect trial participants. It is unknown how long these pauses or disruptions could continue.

- Our reliance on third parties to, among other things, manufacture and transport drug substance and drug product for our clinical trials, ship investigational drugs and clinical trial samples, perform quality testing and supply other goods and services to run our business. Third parties in our international supply chain for materials have and may continue to be adversely impacted by restrictions resulting from the coronavirus pandemic, or other infectious diseases, including staffing shortages, production slowdowns or halts, and disruptions in delivery systems, which has and may continue to disrupt our supply chain, limiting our ability to manufacture our product candidates for our clinical trials and conduct our research and development operations. For example, we currently rely on multiple CMOs for all of our clinical supplies, including APIs, drug substances and finished drug products, and label and packaging for our preclinical research and clinical trials, including the phase 2a study for PRS-060/AZD1402 and the phase 2 studies for cinrebafusp alfa, and any tariffs, differing regulatory requirements and other restrictions on the free movement of goods between the United Kingdom and the European Union, or between other countries, as a result of the pandemic may have an adverse impact on this part of our supply chain. This could therefore negatively impact our clinical operations and, in particular, the advancement of our lead respiratory program, PRS-060/AZD1402, and lead oncology programs, including cinrebafusp alfa, which would adversely affect our business, our results of operations and financial condition.
- Our request that most of our personnel in the United States, and some in Germany, work remotely, including all of our administrative employees, restricted on-site staff to only those who must perform essential activities that must be completed on-site, limited the number of staff in any given research and development laboratory and implemented policies to protect the health of those staff. Our increased reliance on personnel working from home may negatively impact productivity, affect our ability to retain employees or disrupt, delay or otherwise adversely impact our business. In addition, this could increase our cybersecurity risk, create data accessibility concerns and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with local and federal regulators, ethics committees, manufacturing sites, research or clinical trial sites and other important agencies and contractors.
- Our employees and contractors conducting research and development activities who may not be able to access our laboratory for an extended period of time if they get sick and need to quarantine, or if we or governmental authorities potentially modify current restrictions. For example, our lab operations had experienced some impact due to our employees and contractors becoming sick and needing to quarantine at home. Although this only minimally affected our productivity, further restrictions limiting access to our laboratory for an extended period could delay timely completion of preclinical activities and initiation of additional clinical trials for our programs.
- Health regulatory agencies globally may continue to experience disruptions in their operations as a result of the coronavirus pandemic. The FDA and comparable foreign regulatory agencies may continue to have slower response times or be under-resourced to continue to monitor our clinical trials and, as a result, review, inspection and other timelines may be materially delayed. It is unknown how long these disruptions could continue. Any elongation or de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially affect the development and study of our product candidates. For example, regulatory authorities may require that we not distribute a product candidate lot until the relevant agency authorizes its release. Such release authorization may be delayed as a result of the coronavirus pandemic and could result in delays to our clinical trials.
- The trading prices for our common stock and other biopharmaceutical companies have been highly volatile due to the coronavirus pandemic. As a result, we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the spread of the coronavirus could materially and adversely affect our business and the value of our common stock.

The coronavirus pandemic continues to evolve. The ultimate impact of the coronavirus pandemic and its emerging variants on our business operations is highly uncertain and subject to change and will depend on future developments, which cannot be accurately predicted, including the duration of the pandemic, the geographic spread of the disease, additional or modified government actions, new information that will emerge concerning the severity and impact of COVID-19 and its emerging variants and the actions taken to contain coronavirus or address its impact in the short and long term, among others. We do not know the full extent of potential delays or impacts on our business, our clinical trials, our research programs, healthcare systems or the global economy. We will continue to monitor the situation closely.

Risks Related to the Discovery and Development of Our Drug Candidates

We are heavily dependent on the successful development of our drug candidates and programs and we cannot be certain that we will receive regulatory approvals or be able to successfully commercialize our products even if we receive regulatory approvals.

We currently have no products that are approved for commercial sale. We expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to our respiratory programs, including PRS-060/AZD1402; our other partnered programs with AstraZeneca; our proprietary respiratory programs; our proprietary IO programs, particularly cinrebafusp alfa; our partnered programs with Servier including PRS-344/S095012; our partnered programs with Seagen, Boston Pharmaceuticals and Genentech; as well as our other programs. In partnership with AstraZeneca, PRS-060/AZD1402 is in clinical development with a completed phase 1 SAD study for which data was reported in November 2018, a completed phase 1 MAD study for which interim data was reported in October 2019. The phase 2a asthma study is ongoing in multiple sites globally. For cinrebafusp alfa, a phase 1 study was initiated in the second quarter of 2017 and a phase 1 study of the drug candidate in combination with atezolizumab was initiated in the third quarter of 2018. We presented data from the phase 1 monotherapy study and atezolizumab combination study of cinrebafusp alfa in an oral presentation at the ESMO Virtual Congress in September 2020, and we presented additional data from the phase 1 monotherapy study of cinrebafusp alfa in an oral presentation at the American Association for Cancer Research Virtual Congress in April 2021. In June 2021, FDA granted orphan drug designation to cinrebafusp alfa for the treatment of HER2-high and HER2-low expressing gastric cancers. In January 2022, we dosed the first patient in our two-arm phase 2 study for cinrebafusp alfa in gastric cancer in the United States. In partnership with Servier, the first patient was dosed in November 2021 for the phase 1/2 study of PRS-344/S095012/S095012. We are engaged in research and development activities with respect to a number of additional drug candidates and programs. All of our other drug candidates are in the discovery or early preclinical to IND-enabling stage. Accordingly, our business is currently substantially dependent on the successful development, clinical testing, regulatory approval and commercialization of PRS-060/AZD1402, cinrebafusp alfa, PRS 344 and our other IO and respiratory programs, which may never occur.

Before we can generate any revenues from sales of our lead drug candidates, we must complete the following activities for each of them, any one of which we may not be able to successfully complete:

- conduct additional preclinical and clinical development with successful outcomes;
- manage preclinical, manufacturing and clinical activities;
- obtain regulatory approval from the FDA and other comparable foreign regulatory authorities;
- establish manufacturing relationships for the clinical and post-approval supply of the applicable drug candidate in compliance with all regulatory requirements;
- build a commercial sales and marketing team, either internally or by contract with third parties;
- establish and maintain patent and trade secret protection or regulatory exclusivity for our product candidates;
- develop and implement marketing strategies for successful commercial launch of our product candidates, if and when approved;
- secure acceptance of our products, if and when approved, by patients, from the relevant medical communities and from third-party payors;
- compete effectively with other therapies;
- establish and maintain adequate health care coverage and reimbursement;
- ensure continued compliance with any post-marketing requirements imposed by regulatory authorities, including any required post-marketing clinical trials or the elements of any post-marketing REMS that may be required by the FDA or comparable requirements in other jurisdictions to ensure the benefits of the product outweigh its risks;
- maintain continued acceptable safety profile of the product candidates following approval; and
- invest significant additional cash in each of the above activities.

If we are unable to address one or more of these factors in a timely manner or at all, we could experience significant delays in the successful commercialization of, or an inability to successfully commercialize, our product candidates, which would materially harm our business. If we do not receive regulatory approvals for one or more of our product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approvals to manufacture and market our product candidates, our revenues will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights, competitors products in the same markets, market acceptance, and other factors. If the markets for patient subsets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of such products, if approved.

Clinical testing of PRS-060/AZD1402, cinrebafusp alfa and PRS-344/S095012 is ongoing, while clinical testing for other programs, including our other IO and respiratory programs, has not yet commenced, and the results of any future clinical trials or preclinical studies of these programs, if unsuccessful, could lead to our abandonment of the development of those drug candidates. If studies of these drug candidates produce unsuccessful results and we are forced or elect to cease their development, our business and prospects would be substantially harmed.

Preclinical and clinical testing of our drug candidates that has been conducted to date or will be conducted in the future may not have been or may not be performed in compliance with applicable regulatory requirements, which could lead to increased costs or material delays for their further development.

Given the complexity as well as the uncertainty inherent in preclinical and other nonclinical studies and clinical trials, and because of our limited operating experience, we may discover that our own development activities are not in compliance with applicable regulatory requirements or are otherwise deficient, and therefore, determine that the development of our drug candidates on the basis of those trials and studies is not warranted or will be delayed.

We have also entered into license, partnership and option arrangements, such as with Servier, AstraZeneca, Seagen, Boston Pharmaceuticals and Genentech, relating to certain drug candidates and we may continue to do so in the future. Under some of these arrangements, the development of some of those drug candidates has been, or in the future may be, conducted wholly by such partners or third parties with which the partners contract. As a result, we have not been or may not be closely involved with or have any control over those development activities. Although some of our partners have provided information regarding those drug candidates and the related studies conducted to date, including data that is included in this Annual Report on Form 10-K, we have not received and may not receive in the future, comprehensive information regarding all of those development activities, including the raw data from certain studies that have been conducted, information regarding the design, procedural implementation and structure and information regarding the manufacture of the drug candidates used in the studies. Because we may have limited or no input on the development of these drug candidates, we may discover that all or certain elements of the trials and studies our partners have performed have not been, or may not in the future be, in compliance with applicable regulatory standards or have otherwise been or may be deficient, and that advancement of the development of these drug candidates on the basis of those trials and studies is not warranted.

Further, the majority of our development activities for each of our drug candidates, including our completed phase 1 study with PRS-060/AZD1402 in Australia, phase 2a study with PRS-060/AZD1402 at multiple sites globally, our phase 1 and 2 studies with cinrebafusp alfa in the United States, as well as our phase 1/2 study for PRS-344/S095012, and our anticipated future clinical trials, have been, are being or may in the future be conducted in whole or in part outside of the United States, including in Europe, Australia or Asia. We may also conduct some of our future development activities in other countries or regions. As a result, although those studies may meet the standards of applicable foreign regulatory bodies, the structure and design of those clinical trials and preclinical studies may not meet applicable FDA requirements and also may not meet the requirements of the applicable regulatory authorities in other foreign countries in which we desire to pursue marketing approval.

If the studies conducted by us or our partners or collaborators do not comply with applicable regulatory requirements or are otherwise not eligible for continued development in the United States or abroad, then we or our partners may be forced to conduct new studies in order to progress the development of our drug candidates. We, or our partners, may not have the funding or other resources to conduct or complete these additional studies, which would severely delay or prevent the development plans for these drug candidates and their commercialization. Any such deficiency and delay in the development of these drug candidates would significantly harm our business plans, product revenues and prospects.

Our research and development efforts are focused on a rapidly evolving area of science, and our approach to drug discovery and development is novel and may never lead to marketable products.

Biopharmaceutical product development is generally a highly speculative undertaking and by its nature involves a substantial degree of risk. Our specific line of business, the discovery of Anticalin-brand drug therapeutics for patients with a variety of diseases and conditions, such as asthma and cancer, is an emerging field, and the scientific discoveries that form the basis for our efforts to develop drug candidates are relatively new. Further, the scientific evidence to support the feasibility of developing drug candidates based on those discoveries is both preliminary and limited. In contrast to companies that focus on more traditional drug classes, such as antibodies and small molecules, we believe that we are the first, if not the only, company to work with Anticalin-brand drug therapeutics and work to advance these to a clinical stage of development. We are not aware of any company that has successfully developed and obtained approval for a drug based on Anticalin proteins. As a result, identifying drug targets based in part on their suitability with Anticalin-brand drug therapeutics, which is a fundamental aspect of our business approach, may not lead to the discovery or development of any drugs that successfully treat patients with the diseases and conditions we intend to target. Moreover, the lack of successful precedents in the development of Anticalin

proteins could result in added complexities or delays in our development efforts. The failure of the scientific underpinnings of our business model to produce viable drug candidates would substantially harm our operations and prospects.

We may not be successful in our efforts to build a pipeline of drug candidates.

A key element of our strategy is to use and expand our Anticalin-based drug platform to build a pipeline of drug candidates to address different targets and advance those drug candidates through clinical development for the treatment of a variety of different types of diseases. Although our research efforts to date have resulted in identification of a series of targets, we may not be able to develop drug candidates that have good drug-like properties (including characteristics such as target affinity, stability and half-life) and are safe and effective inhibitors or promoters of all or any of these targets. Even if we are successful in building a product pipeline, the potential drug candidates that we identify may not be suitable for clinical development for a number of reasons, including that they may cause harmful side effects or demonstrate other characteristics that indicate a low likelihood of receiving marketing approval or achieving market acceptance. If our methods of identifying potential drug candidates fail to produce a pipeline of potentially viable drug candidates, then our success as a business will be dependent on the success of fewer potential drug candidates, which introduces risks to our business model and potential limitations to any success we may achieve.

Clinical drug development involves a lengthy and expensive process with uncertain outcomes, clinical trials are difficult to design and implement, and any of our clinical trials could produce unsuccessful results or fail at any stage in the process.

Clinical trials conducted on humans are expensive and can take many years to complete, and outcomes are inherently uncertain. Failure can occur at any time during the process. Additionally, any positive results of preclinical studies and early clinical trials of a drug candidate may not be predictive of the results of later-stage clinical trials, such that drug candidates may reach later stages of clinical trials and fail to show the desired safety and efficacy traits despite having shown indications of those traits in preclinical studies and early-stage clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier phases of the trials. Therefore, the results of any ongoing or future clinical trials we conduct may not be successful.

In 2021, we initiated a phase 1 study for PRS-344/S095012 in collaboration with Servier and we also initiated a two-arm phase 2 study for cinrebafusp alfa in combination with tucatinib and in combination with ramucirumab and paclitaxel. A phase 2a study for PRS-060/AZD1402 was also initiated in 2021. We or our partners may, however, experience delays in pursuing those or any other clinical trials, and any planned clinical trials may not begin on time, may require redesign, may not enroll sufficient healthy volunteers or patients in a timely manner and may not be completed on schedule, if at all.

Additional clinical trials may be delayed, suspended or prematurely terminated because costs are greater than we anticipate or for a variety of reasons (which may be heightened as a result of the ongoing COVID-19 pandemic), such as:

- delay or failure in reaching agreement with the FDA or a comparable foreign regulatory authority on a trial design that we are able to execute;
- delay or failure in obtaining authorization to commence a trial, including approval from the appropriate IRB to conduct testing of a candidate on human subjects, or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical trial;
- delay in reaching, or failure to reach, agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- inability, delay or failure in identifying and maintaining a sufficient number of trial sites, many of which may already be engaged in other clinical programs;
- delay or failure in recruiting and enrolling suitable volunteers or patients to participate in a trial;
- delay or failure in developing and validating companion diagnostics, if they are deemed necessary, on a timely basis;
- failure of patients to complete a trial or return for post-treatment follow-up;
- inability to monitor patients adequately during or after treatment;
- clinical sites and investigators deviating from trial protocols, failing to conduct the trial in accordance with regulatory requirements or dropping out of a trial;
- failure to initiate or delay of or inability to complete a clinical trial as a result of a clinical hold imposed by the FDA or comparable foreign regulatory authority due to observed safety findings or other reasons;

- negative or inconclusive results in our clinical trials, and our decision to or regulators' requirement that we conduct additional non-clinical studies, clinical trials or that we abandon one or more of our product development programs; or
- inability to manufacture sufficient quantities of a drug candidate of acceptable quality for use in clinical trials.

We rely and plan to continue to rely on CROs, CMOs and clinical trial sites to ensure the proper and timely conduct of our clinical trials. Although we have and expect that we will continue to have agreements in place with CROs and CMOs governing their contracted activities and conduct, we will have limited influence over their actual performance. As a result, we ultimately do not and will not have control over a CRO's or CMO's compliance with the terms of any agreement it may have with us, its compliance with applicable regulatory requirements or its adherence to agreed-upon time schedules and deadlines, and a future CRO's or CMO's failure to perform those obligations could subject any of our clinical trials to delays or failure.

Further, we may also encounter delays if a clinical trial is suspended or terminated by us, by any IRB or ethics committee, by a Data Safety Monitoring Board, or DSMB, or by the FDA or EMA, or other regulatory authority. A suspension or termination
may occur due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements, inspection of the clinical trial operations or trial site by the FDA, EMA, MHRA or other regulatory authorities, exposing participants to health risks caused by unforeseen safety issues or adverse side effects, development of previously unseen safety issues, failure to demonstrate a benefit from using a drug candidate or changes in governmental regulations or administrative actions. We cannot predict with any certainty the schedule for commencement or completion of any currently ongoing, planned or future clinical trials.

Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of marketing approval for our product candidates.

If we experience delays in the commencement or completion of, or suspension or termination of, any clinical trial for our drug candidates, the commercial prospects of the drug candidate could be harmed, and our ability to generate product revenues from the drug candidate may be delayed or eliminated. In addition, any delays in completing our clinical trials will increase our costs, slow down our drug candidate development and approval process and jeopardize regulatory approval of our drug candidates and our ability to commence sales and generate revenues. The occurrence of any of these events could harm our business, financial condition, results of operations and prospects significantly.

If we experience delays or difficulties in the enrollment of research subjects in clinical trials, those clinical trials could take longer than expected to complete and our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our drug candidates if we are unable to locate and enroll a sufficient number of research subjects to participate in these trials, including as a result of challenges posed by the ongoing COVID-19 pandemic.. In particular, for some diseases and conditions we are or will be focusing on, our pool of suitable patients may be smaller and more selective and our ability to enroll a sufficient number of suitable patients may be limited or take longer than anticipated. In addition, some of our competitors have ongoing clinical trials for drug candidates that treat the same indications as our drug candidates, and volunteers or patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' drug candidates.

Patient enrollment for any of our clinical trials may also be affected by other factors, including without limitation:

- the size and nature of the target patient population;
- the severity of the disease under investigation;
- the frequency of the molecular alteration we are seeking to target in the applicable trial (e.g., HER2 positivity and expression levels in our clinical studies of cinrebafusp alfa);
- the patient eligibility criteria for the clinical trial in question;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the perceived risks and benefits of the drug candidate under study in the clinical trial;
- the approval and availability of other therapies to treat the disease or disorder that is being investigated in the clinical trial;
- the extent of the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor volunteers or patients adequately during and after treatment;
- the presence of other drug candidates in clinical development for the same indication or against the same target; and
- the proximity and availability of clinical trial sites for prospective participants.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our drug candidates, and we may not have or be able to obtain sufficient cash to fund such increased costs when needed, which could result in the further delay or termination of clinical trials.

The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA or comparable foreign regulatory authorities.

We currently have no products approved for sale and we cannot guarantee that we will ever have marketable products. Clinical failure can occur at any stage of clinical development. Clinical trials may produce negative or inconclusive results, and we or any future collaborators may decide, or regulators may require us, to conduct additional clinical trials or nonclinical studies. We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective for use in a diverse population before we can seek marketing approvals for their commercial sale. Success in preclinical studies and early-stage clinical trials does not mean that future larger registration clinical trials will be successful. This is because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and comparable foreign regulatory authorities despite having progressed through preclinical studies and early-stage clinical trials. In particular, no Anticalin-based drug products have been approved or commercialized in any jurisdiction, and the outcome of our preclinical studies and early-stage clinical trials may not be predictive of the success of later-stage clinical trials.

From time to time, we may publish or report interim or preliminary data from our clinical trials. Interim or preliminary data from clinical trials that we may conduct may not be indicative of the final results of the trial and are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Interim or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the interim or preliminary data. As a result, interim or preliminary data should be viewed with caution until the final data are available.

The review processes of regulatory authorities are lengthy, time consuming, expensive and inherently unpredictable. If we are unable to obtain approval for our drug candidates from applicable regulatory authorities, we will not be able to market and sell those drug candidates in those countries or regions and our business could be substantially harmed.

The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of drug products are, and will remain, subject to extensive regulation by the FDA in the United States and by the respective regulatory authorities in other countries where regulations differ. We are not permitted to market our biological product candidates in the United States until we receive the respective approval of a BLA from the FDA, or in any foreign countries until we receive the requisite approval from the respective regulatory authorities in such countries. The time required to obtain approval, if any, by the FDA, EMA, MHRA and comparable foreign authorities is unpredictable, but typically takes many years following the commencement of clinical trials, if approval is obtained at all, and depends upon numerous factors, including the substantial discretion of the regulatory authorities and the type, complexity and novelty of the product candidates involved. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional nonclinical studies or clinical trials. We have not submitted a marketing application such as a BLA to the FDA, an MAA to the EMA or any similar application to any other jurisdiction. We have limited experience in planning and conducting the clinical trials required for marketing approvals, and we have and expect to continue to rely on third-party CROs to assist us in this process. Obtaining marketing approval requires the submission of extensive nonclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process, and in many cases the inspection of manufacturing, processing and packaging facilities by the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use, or there may be deficiencies in cGMP compliance by us or by our CMOs that could result in the candidate not being approved. Moreover, we have not obtained regulatory approval for any drug candidate in any jurisdiction and it is possible that none of our existing drug candidates or any drug candidates we may seek to develop in the future will ever obtain regulatory approval.

Our drug candidates could fail to receive, or could be delayed in receiving, regulatory approval for many reasons, including any one or more of the following:

- the FDA, EMA, MHRA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;

- we may be unable to demonstrate to the satisfaction of the FDA, EMA, MHRA or comparable foreign regulatory authorities that a drug candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA, EMA, MHRA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a drug candidate's clinical and other benefits outweigh its safety risks;
- the FDA, EMA, MHRA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of a BLA or other submission or to obtain regulatory approval in the United States or elsewhere;
- upon review of our clinical trial sites and data, the FDA or comparable foreign regulatory authorities may find our record keeping or the record keeping of our clinical trial sites to be inadequate;
- the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies may fail to meet the requirements of the FDA, EMA, MHRA or comparable foreign regulatory authorities;
- the FDA, EMA, MHRA or comparable foreign regulatory authorities may fail to approve the companion diagnostics we contemplate developing internally or with partners; and
- the change of the medical standard of care or the approval policies or regulations of the FDA, EMA, MHRA or comparable foreign regulatory authorities may significantly change in a manner that renders our clinical data insufficient for approval.

The time and expense of the approval process, as well as the unpredictability of future clinical trial results and other contributing factors, may result in our failure to obtain regulatory approval to market, in one or more jurisdictions, PRS-060/AZD1402, cinrebafusp alfa, PRS-344/S095012, our other respiratory and IO programs, our discovery stage programs or any other drug candidates we are developing or may seek to develop in the future, which would significantly harm our business, results of operations and prospects. In such case, we may also not have the resources to conduct new clinical trials and/or we may determine that further clinical development of any such drug candidate is not justified and may discontinue any such programs.

In addition, even if we were to obtain regulatory approval in one or more jurisdictions, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may not approve prices we may propose to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials (referred to as "conditional" or "accelerated" approval depending on the jurisdiction), or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Any of the foregoing circumstances could materially harm the commercial prospects for our drug candidates.

Our failure to obtain marketing approval in jurisdictions other than the United States and Europe would prevent our product candidates from being marketed in these other jurisdictions. Any approval that we are granted for our product candidates in the United States or Europe would not assure approval of product candidates in the other or in any other jurisdiction.

In order to market and sell our future products in jurisdictions other than the United States or Europe, we or our third-party collaborators must obtain separate marketing approvals in that jurisdiction and comply with numerous and varying regulatory requirements. The review and approval procedures can vary drastically among jurisdictions, and each jurisdiction may impose different testing and other requirements to obtain and maintain marketing approval. Further, the time required to obtain those approvals, if any, may differ substantially among jurisdictions. In addition, some countries or regions outside the United States and Europe require approval of the sales price of a drug before it can be marketed in that country or region. In many countries, separate procedures must be followed to obtain reimbursement. Moreover, approval by the FDA, EMA, MHRA or an equivalent foreign authority does not ensure approval by regulatory authorities in any other countries or regions. As a result, the ability to market and sell a drug candidate in more than one jurisdiction can involve significant additional time, expense and effort, and would subject us and our collaborators to the numerous and varying post-approval requirements of each jurisdiction governing commercial sales, manufacturing, pricing and distribution of our drug candidates. We or any third parties with whom we may collaborate may not have the resources to pursue those approvals, and we or they may not be able to obtain any approvals that are pursued. The failure to obtain marketing approval for our drug candidates in foreign jurisdictions could severely limit their potential market and ability to generate revenue.

Our product candidates may cause undesirable side effects that could delay or prevent their marketing approval, limit their commercial potential, or result in significant negative consequences following marketing approval, if marketing approval is obtained.

Undesirable side effects caused by our product candidates could cause us or the FDA or other regulatory authorities to interrupt, delay or halt our clinical trials and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or other regulatory authorities of our product candidates. In the event that our clinical trials produce undesirable side effects, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. In addition to this, the product-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims.

Clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. If our product candidates receive marketing approval and we or others identify undesirable side effects caused by such product candidates (or any other similar products) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such product candidates;
- regulatory authorities may require the addition of labeling statements, specific warnings or a contraindication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients, or we may be required to implement a REMS to ensure that the benefits of the product outweigh the risks;
- we may be required to change the way such product candidates are distributed or administered, or change the labeling of the product candidates;
- we may be subject to regulatory investigations and government enforcement actions;
- the FDA or a comparable foreign regulatory authority may require us to conduct additional clinical trials or costly post-marketing testing and surveillance to monitor the safety and efficacy of the product;
- we may decide to recall such product candidates from the marketplace after they are approved;
- we could be sued and held liable for injury caused to individuals exposed to or taking our product candidates; and
- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidates and could substantially increase the costs of commercializing our product candidates, if approved, and significantly impact our ability to successfully commercialize our product candidates and generate revenues.

We may expend our limited resources to pursue a particular drug candidate or indication that does not produce any commercially viable products and may fail to capitalize on drug candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we must focus our efforts on particular research programs and drug candidates for specific indications. As a result, we may forgo or delay pursuit of opportunities with other drug candidates or for other indications that later prove to have greater commercial potential. Further, our resource allocation decisions may result in our use of funds for research and development programs and drug candidates for specific indications that may not yield any commercially viable products.

If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, or if market conditions change, we may relinquish valuable rights to that drug candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate. Any such failure to properly assess potential drug candidates could result in missed opportunities and/or our focus on drug candidates with low market potential, which would harm our business and financial condition.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our clinical trials and preclinical studies. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or otherwise conduct the trials as required or comply with regulatory requirements, we may not be able to obtain regulatory approval for our drug candidates, commercialize our product candidates when expected or at all, and our business could be substantially harmed.

We depend upon independent investigators and contractors, such as CROs, universities and medical institutions, to conduct our clinical trials and preclinical studies. We rely upon, and plan to continue to rely upon, such third-party entities to execute our clinical trials and preclinical studies and to monitor and manage data produced by and relating to those studies and trials. However, in the future, we may not be able to establish arrangements with CROs when needed or on terms that are acceptable to us, or at all, which could negatively affect our development efforts with respect to our drug candidates and materially harm our business, operations and prospects. As a result of the use of third-party contractors, we will have only limited control over certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies, including each of our clinical trials, is conducted in accordance with the applicable protocol, legal and regulatory requirements as well as scientific standards, and our reliance on any third-party entity will not relieve us of our regulatory responsibilities.

Based on our present expectations, we and our third-party contractors will be required to comply with cGCP for all of our drug candidates in clinical development. Regulatory authorities enforce cGCP through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of our contractors fail to comply with applicable cGCP, the clinical data generated in the applicable trial may be deemed unreliable and the FDA, EMA, MHRA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving a drug candidate for marketing, which we may not have sufficient cash or other resources to support and which would delay our ability to generate revenue from future sales of such drug candidate. Any agreements governing our relationships with CROs or other contractors with whom we currently engage or may engage in the future may provide those outside contractors with certain rights to terminate a clinical trial under specified circumstances. If such an outside contractor terminates its relationship with us during the performance of a clinical trial, we would be forced to seek an engagement with a substitute contractor, which we may not be able to do on a timely basis or on commercially reasonable terms, if at all, and the applicable clinical trial would experience delays or may not be completed.

If our contractors do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the data they obtain is compromised due to a failure to adhere to our clinical protocols, legal and regulatory requirements or for other reasons, such as the COVID-19 pandemic, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for, or successfully commercialize, the affected drug candidates. In addition, we will be unable to control whether or not they devote sufficient time and resources to our preclinical and clinical programs. These outside contractors may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves. As a result, our operations and the commercial prospects for the affected drug candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed. These contractors may also have relationships with other commercial entities, some of whom may compete with us. If our contractors assist our competitors to our detriment, our competitive position would be harmed.

If our relationships with any third parties conducting our studies are terminated, we may be unable to enter into arrangements with alternative third parties on commercially reasonable terms, or at all. Switching or adding third parties to conduct our studies involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. These difficulties may be exacerbated as a result of the COVID-19 pandemic. Although we carefully manage our relationships with third parties conducting our studies, we cannot assure you that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material and adverse effect on our business, financial condition and results of operations.

We rely and expect to continue to rely completely on third parties to formulate and manufacture our preclinical, clinical trial and commercial drug supplies. The development and commercialization of any of our drug candidates could be stopped, delayed or made less profitable if those third parties fail to provide us with sufficient quantities of such drug supplies or fail to do so at acceptable quality levels, including in accordance with applicable regulatory requirements or contractual obligations, and our operations could be harmed as a result.

We have no experience in drug formulation or manufacturing. We do not currently have, nor do we plan to acquire, the infrastructure or capability internally, such as our own manufacturing facilities, to manufacture our preclinical and clinical drug supplies for our clinical trials and preclinical studies or commercial quantities of any drug candidates that may obtain regulatory approval. Therefore, we lack the resources and expertise to formulate or manufacture our own drug candidates. We have entered into agreements with CMOs for the clinical-stage manufacturing of certain drug candidates, including PRS-060/AZD1402, cinrebafusp alfa, and PRS-344/S095012 as well as other drugs involved in our clinical trials and preclinical studies. We plan to enter into agreements with one or more manufacturers to manufacture, supply, store and distribute drug supplies for our current and future clinical trials and/or commercial sales, if any. We intend to establish or continue those relationships for the supply of our drug candidates; however, there can be no assurance that we will be able to retain those relationships on commercially reasonable terms, if at all. If we are unable to maintain those relationships, we could experience delays in our development efforts as we locate and qualify new CMOs. If any of our current drug candidates or any drug candidates we may

develop or acquire in the future receives regulatory approval, we will rely on one or more CMOs to manufacture the commercial supply of such drugs.

Our reliance on a limited number of CMOs exposes us to the following risks:

- We may be unable to identify manufacturers on acceptable terms, or at all, because the number of qualified potential manufacturers is limited. Following BLA approval, if successful, a change in the manufacturing site could require additional approval from the FDA. This approval would require new testing and compliance inspections.
- Our third-party manufacturers might be unable to formulate and manufacture our drugs in the volume and of the quality and cost required to meet our clinical and commercial needs, if any.
- Our future CMOs may not perform as contractually agreed or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store and distribute our products.
- Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA and some state agencies to ensure strict compliance with cGMP regulations and other U.S. and corresponding foreign requirements. We do not have control over third-party manufacturers' compliance with these regulations and standards.
- If any third-party manufacturer makes improvements in the manufacturing process for our products, we may not own, or may have to share, the intellectual property rights to the innovation.

Each of these risks could delay our clinical trials, the marketing approval, if any, of our drug candidates or the commercialization of our drug candidates, which could result in higher costs or could deprive us of potential product revenues.

Although our agreements with our CMOs require them to perform according to certain cGMP requirements such as those relating to quality control, quality assurance and qualified personnel, we cannot control the conduct of our CMOs to implement and maintain these standards. If any of our CMOs cannot successfully manufacture material that conforms to our specifications and the regulatory requirements of the FDA, EMA, MHRA or other comparable foreign authorities, we would be prevented from obtaining regulatory approval for our drug candidates unless and until we engage a substitute CMO that can comply with such requirements, which we may not be able to do. Any such failure by any of our CMOs would significantly impact our ability to develop, obtain regulatory approval for or market our drug candidates, if approved.

Further, we plan to rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our drug candidates for our clinical trials. We do not have, nor do we expect to enter into, any agreements for the commercial production of these raw materials, and we do not expect to have any control over the process or timing of our CMOs' acquisition of raw materials needed to produce our drug candidates. Any significant delay in the supply of a drug candidate or the raw material components of an ongoing clinical trial due to a manufacturer's need to replace a third-party supplier of raw materials could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our drug candidates. Additionally, if our future manufacturers or we are unable to purchase these raw materials to commercially produce any of our drug candidates that gains regulatory approvals, the commercial launch of our drug candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenues from the sale of our drug candidates.

Disagreements with respect to the commercial terms of our sales, licensing, purchase or manufacturing agreements may limit our commercial success.

The rights and obligations of the partners to which we may license our Anticalin-based technology are governed by the licensing and collaboration agreements we enter into with those partners. In addition, our relationships with CMOs are governed by the service agreements between us and each of the manufacturers. Although we attempt to address the full range of possible events that may occur during the development or the manufacturing of Anticalin-based drug candidates and products, unanticipated or extraordinary events may occur beyond those contemplated by such agreements. Furthermore, our business relationships with our product manufacturers and our collaborators may include assumptions, understandings or agreements that are not included in our agreements with them, or that are inaccurately or incompletely represented by their terms. In addition, key terms in such agreements may be misunderstood or contested, even when we and the other party previously believed that we both had a mutual understanding of such terms.

Any differences in interpretation or misunderstandings between us and other parties may result in substantial costs and delays with respect to the development, manufacturing or sale of Anticalin-based drugs, and may negatively impact our revenues and operating results. Product manufacturers may fail to produce the products and partners may fail to develop the drug candidates with the diligence or under the timeline or in the manner we anticipated, and results may differ from the terms upon which we had agreed. As a result, we may be unable to supply drugs of the quality or in the quantity demanded or required. We may suffer harm to our reputation in the market from missed development goals or deadlines and may be unable to capitalize upon

market opportunities as a result. Resolution of these problems may entail costly and lengthy litigation or dispute resolution procedures. In addition, there is no guarantee that we will prevail in any such dispute or, if we do prevail, that any remedy we receive, whether legal or otherwise, will adequately redress the harm we have suffered. The delays and costs associated with such disputes may themselves harm our business and reputation and limit our ability to successfully compete in the market.

We depend on third parties and intend to continue to license or collaborate with third parties, and events involving these strategic partners or any future collaboration could delay or prevent us from developing or commercializing products.

Our business strategy, along with our short- and long-term operating results, depend in part on our ability to execute on existing strategic collaborations and to license or partner with new strategic partners. We have entered into and expect in the future to enter into collaborative arrangements with both U.S.-based and foreign pharmaceutical and drug development companies, which will lead, finance or otherwise collaborate with us or assist us in the development, manufacturing and marketing of our drug products. We believe collaborations allow us to leverage our resources and technologies and we anticipate deriving some revenues from research and development fees, license fees, milestone payments, and royalties from our collaborative partners.

Our prospects, therefore, may depend to some extent upon our ability to attract and retain collaborative partners and to develop technologies and products that meet the requirements of current or prospective collaborative partners. We have limited control over the amount and timing of resources that our current collaborators or any future collaborators devote to our collaborations or potential products, in particular with respect to our collaborations with AstraZeneca for the development of PRS-060/AZD1402, with Servier for the development of PRS-344/S095012, with Boston Pharmaceuticals for the development of PRS-342, and our other collaborations with Genentech and Seagen. These collaborators may breach or terminate their agreements with us or otherwise fail to conduct their collaborative activities successfully and in a timely manner. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new, amended or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology. Further, our collaborators may not develop or commercialize products that arise out of our collaborative arrangements or devote sufficient resources to the development, manufacturing, marketing or sale of these products. In addition, our collaborative partners may have the right to guide strategy regarding prosecution of relevant patent applications, abandon research projects and/or terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed-upon research terms. By entering into such collaborations, we may forego opportunities to collaborate with other third parties who do not wish to be associated with our existing third-party strategic partners. In the event of termination of a collaboration agreement, termination negotiations may result in less than favorable terms.

There can be no assurance that we will be successful in establishing collaborative arrangements on acceptable terms or at all, that collaborative partners will not terminate funding before the completion of projects, that our collaborative arrangements will result in successful product commercialization, or that we will derive any revenues from such arrangements. Potential collaborators may reject collaborations based upon their assessment of our financial, regulatory or intellectual property position and our internal capabilities. Additionally, the negotiation, documentation and implementation of collaborative arrangements are complex and time-consuming. Our discussions with potential collaborators may not lead to new collaborations on favorable terms and may have the potential to provide collaborators with access to our key intellectual property rights.

Our success depends in part on the efforts of our current and possible future collaborators, who will likely have substantial control and discretion over the continued development and commercialization of drug candidates that are the subject of our collaborations.

Our current collaborators and future collaborators will have significant discretion in determining the effort and amount of resources that they dedicate to our collaborations. Our collaborators may determine not to proceed with clinical development or commercialization of a particular drug candidate for a number of reasons that are beyond our control, even under circumstances where we might have continued such a program, currently including PRS-060/AZD1402 and PRS-344/S095012. In addition, our rights to receive milestone payments and royalties from our collaborators will depend in part on our collaborators' abilities to establish the safety and efficacy of our drug candidates, obtain regulatory approvals and achieve market acceptance of products developed from our drug candidates. We may also depend on our collaborators to manufacture clinical scale quantities of some of our drug candidates and, possibly, for commercial scale manufacture, distribution and sales. Our collaborators may not be successful in manufacturing our drug candidates or successfully commercializing them.

We face additional risks in connection with our existing and future collaborations, including the following:

- our collaborators may develop and commercialize, either alone or with others, products that are similar to or competitive with the products that are the subject of the collaboration with us;
- our collaborators may underfund, not commit sufficient resources to, or conduct in an unsatisfactory manner the development, testing, marketing, distribution or sale of our drug candidates;

- our collaborators may not properly maintain or defend our intellectual property rights or utilize our proprietary information in such a way as to invite litigation that could jeopardize or potentially invalidate our intellectual property or proprietary information or expose us to potential liability;
- our collaborators may encounter conflicts of interest, changes in business strategy or other business issues that could adversely affect their willingness or ability to fulfill their obligations to us (for example, pharmaceutical and biotechnology companies historically have re-evaluated their priorities following mergers and consolidations, which have been common in recent years in these industries);
- we do not control the conduct and communications of our collaborators, and, thus, we are subject to the risk that their actions may negatively impact our reputation and potentially harm our business;
- disputes may arise between us and our collaborators delaying or terminating the research, development, manufacture or commercialization of our drug candidates, resulting in significant litigation or arbitration that could be time-consuming and expensive, or causing collaborators to act in their own self-interest and not in the interest of our stockholders;
- we might not have the financial or human resources to meet our obligations or take advantage of our rights under the terms of our existing and future collaborations; and
- our existing collaborators may exercise their respective rights to terminate their collaborations with us without cause, in which event, we might not be able to complete development and commercialization of our drug candidates on our own.

Certain of our research and development and manufacturing activites take place in China through third-party manufacturers. A significant disruption in the operation of those manufacturers could materially adversely affect our business and results of operations.

We have relied on certain third parties located in China to manufacture and supply certain drug substance for our drug product candidates, and we expect to continue to use such third-party manufacturers for such purposes. A natural disaster, epidemic or pandemic, including the ongoing COVID-19 pandemic, trade war, trade sanctions, political unrest, economic conditions, changes in legislation, including the passage of the People's Republic of China Biosecurity law, which became effective on April 15, 2021, or other events in China could disrupt the business or operations of manufacturers or other third parties with whom we conduct business now or in the future. Any disruption in China that significantly impacts such third parties, including our manufacturers' ability to produce drug substance or drug product in adequate quantities to meet our needs could impede, delay, limit or prevent the research, development or commercialization of our current and future products or product candidates. In addition, for any activities conducted in China, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the U.S. or Chinese governments, political unrest or unstable economic conditions including sanctions on China or any of our China-based vendors. Separately, we may also be exposed to fluctuations in the value of the local currency in China for goods and services. Our costs for any of these services or activities could also increase as a result of future appreciation of the local currency in China or increased labor costs if the demand for skilled laborers increases and/or the availability of skilled labor declines in China.

Our collaborative relationships may not produce the financial benefits that we are anticipating, which could cause our business to suffer.

Part of our strategy is to partner with, or out-license selective products to, other pharmaceutical companies in order to mitigate the cost of developing a drug through clinical trials to commercialization. Our exclusive option agreement with ASKA Pharmaceuticals Co., Ltd., or ASKA, entered into on February 27, 2017, is an example of this strategy. In January 2020, following the phase 2a study we conducted, ASKA had an option to obtain an exclusive license to develop and commercialize PRS-080, our anemia drug, in Japan, South Korea and certain other Asian markets under the option agreement, which they did not exercise for strategic reasons. Exercising this option could have made us eligible to receive more than $80 million in combined option exercise fee and milestones associated with development and commercialization of PRS-080 in the first indication in Japan with further development milestones in additional indications from Japan and other countries within the ASKA territory. If our collaboration with other similar partners is not successful our future revenues and business will be harmed.

We may not receive any further milestone, royalty or license payments under our current collaborations.

Although we have received upfront, milestone and other payments to date under our current drug development collaborations, we may not receive any royalty payments or additional license and milestone fees under such agreements. In general, our receipt of milestone, royalty or license payments depends on many factors, including whether our collaborators want and are

able to continue to pursue potential drug candidates, intellectual property issues, unforeseen complications in the development or commercialization process, and the ultimate commercial success of the drugs.

Risks Related to the Commercialization of Our Drug Candidates

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

If the FDA or a comparable foreign regulatory authority approves any of our drug candidates, activities such as the manufacturing processes, labeling, packaging, distribution, AE reporting, storage, advertising, promotion and record keeping for the products will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP. The FDA or a comparable foreign regulatory authority may also impose requirements for costly post-marketing nonclinical studies or clinical trials (often called "Phase 4 trials") and post-marketing surveillance to monitor the safety or efficacy of the product. If we or a regulatory authority discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, production problems or issues with the facility where the product is manufactured or processed, such as product contamination or significant non-compliance with applicable cGMPs, a regulator may impose restrictions on that product, the manufacturing facility or us. If we or our third-party providers, including our CMOs, fail to comply fully with applicable regulations, then we may be required to initiate a recall or withdrawal of our products.

In addition, later discovery of previously unknown problems with a product, including AEs of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in the following, among other things:

- restrictions on the manufacturing of the product, the approved manufacturers or the manufacturing process;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- withdrawal of the product from the market;
- product recalls;
- warning or untitled letters from the FDA or comparable notice of violations from foreign regulatory authorities;
- refusal of the FDA or other applicable regulatory authority to approve pending applications or supplements to approved applications;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- suspension of any of our ongoing clinical trials;
- product seizure or detention or refusal to permit the import or export of products; and
- consent decrees, injunctions or the imposition of civil or criminal penalties.

In addition, regulatory authorities' policies (such as those of the FDA or EMA) may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are otherwise not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance can also result in significant financial penalties. Similarly, failure to comply with the European Union requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay marketing approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing

approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Our commercial success depends upon attaining significant market acceptance of our drug candidates, if approved, among physicians, patients, third-party payors and other members of the medical community.

Even if we obtain regulatory approval for our drug candidates, the approved products may nonetheless fail to gain sufficient market acceptance among physicians, third-party payors, patients and other members of the medical community, which is critical to commercial success. If an approved product does not achieve an adequate level of acceptance, we may not generate significant product revenues or any profits from operations. The degree of market acceptance of any drug candidate for which we receive approval depends on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments or competitive products;
- perceptions by the medical community, physicians and patients regarding the safety and effectiveness of our products and the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the size of the market for such drug candidate, based on the size of the patient subsets that we are targeting, in the territories for which we gain regulatory approval and have commercial rights;
- the safety of the drug candidate as demonstrated through broad commercial distribution;
- the ability to offer our product candidates for sale at competitive prices;
- the availability of adequate reimbursement and pricing for our products from governmental health programs and other third-party payors;
- relative convenience and ease of administration compared to alternative treatments;
- the prevalence and severity of any side effects;
- the adequacy of supply of our product candidates;
- the timing of any such marketing approval in relation to other product approvals;
- any restrictions on concomitant use of other medications;
- support from patient advocacy groups; and
- the effectiveness of sales, marketing and distribution efforts by us and our licensees and distributors, if any.

If our drug candidates are approved but fail to achieve an adequate level of acceptance by key market participants, we will not be able to generate significant revenues, and we may not become or remain profitable, which may require us to seek additional financing.

Our ability to negotiate, secure and maintain third-party coverage and reimbursement for our product candidates may be affected by political, economic, legal and regulatory developments in the United States, the European Union and other jurisdictions. Governments continue to impose cost containment measures, and third-party payors are increasingly challenging prices charged for medicines and examining their cost effectiveness, in addition to their safety and efficacy. These and other similar developments could significantly limit the degree of market acceptance of any product candidate of ours that receives marketing approval in the future.

Our product candidates have never been manufactured on a commercial scale, and there are risks associated with scaling up manufacturing to commercial scale.

Our product candidates have never been manufactured on a commercial scale, and there are risks associated with scaling up manufacturing to commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, lot consistency and timely availability of raw materials. There is no assurance that our manufacturers will be successful in establishing a larger-scale commercial manufacturing process for PRS-060/AZD1402, cinrebafusp alfa, PRS-344/S095012 or other product candidates that achieves our objectives for manufacturing capacity and cost of goods. Even if we could otherwise obtain regulatory approval for any product candidate, there is no assurance that our manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product or to meet potential future demand. If our manufacturers are unable to produce sufficient quantities of the approved product for commercialization, our commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

Biologics carry unique risks and uncertainties, which could have a negative impact on future results of operations.

The successful discovery, development, manufacturing and sale of biologics is a long, expensive and uncertain process. There are unique risks and uncertainties with biologics. For example, access to and supply of necessary biological materials, such as cell lines, may be limited and governmental regulations restrict access to and regulate the transport and use of such materials. In addition, the development, manufacturing and sale of biologics is subject to regulations that are often more complex and extensive than the regulations applicable to other pharmaceutical products. Manufacturing biologics, especially in large quantities, is often complex and may require the use of innovative technologies. Such manufacturing also requires facilities specifically designed and validated for this purpose and sophisticated quality assurance and quality control procedures. Biologics are also frequently costly to manufacture because production inputs are derived from living animal or plant material, and some biologics cannot be made synthetically. Failure to successfully discover, develop, manufacture and sell our biological product candidates would adversely impact our business and future results of operations.

Our product candidates for which we intend to seek approval may face follow-on or biosimilar competition sooner than anticipated.

Even if we are successful in achieving regulatory approval to commercialize a product candidate ahead of our competitors, our product candidates may face competition from biosimilar products. In the United States, our Anticalin-based product candidates are expected to be regulated by the FDA as biological products and we intend to seek approval for these product candidates pursuant to the BLA pathway. The BPCIA created an abbreviated pathway for FDA approval of biosimilar and interchangeable biological products based on a previously licensed reference product. Under the BPCIA, an application for a biosimilar biological product cannot be approved by the FDA until 12 years after the original reference biological product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

We believe that any of our product candidates approved as a biological product under a BLA should qualify for the 12-year period of exclusivity available to reference biological products. 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 product candidates to be reference biological products pursuant to its interpretation of the exclusivity provisions of the BPCIA for competing products, potentially creating the opportunity for generic follow-on biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar product, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing including whether a future competitor seeks an interchangeability designation for a biosimilar of one of our products. Under the BPCIA as well as state pharmacy laws, only interchangeable biosimilar products are considered substitutable for the reference biological product without the intervention of the health care provider who prescribed the original biological product. However, as with all prescribing decisions made in the context of a patient-provider relationship and a patient's specific medical needs, health care providers are not restricted from prescribing biosimilar products in an off-label manner. In addition, a competitor could decide to forego the abbreviated approval pathway available for biosimilar products and to submit a full BLA for product licensure after completing its own preclinical studies and clinical trials. In such a situation, any exclusivity to which we may be eligible under the BPCIA would not prevent the competitor from marketing its biological product as soon as it is approved.

In Europe, the European Commission has granted marketing authorizations for several biosimilar products pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In addition, companies may be developing biosimilar products in other countries that could compete with our products, if approved.

If competitors are able to obtain marketing approval for biosimilars referencing our product candidates, if approved, our future products may become subject to competition from such biosimilars, whether or not they are designated as interchangeable, with the attendant competitive pressure and potential adverse consequences. Such competitive products may be able to immediately compete with us in each indication for which our product candidates may have received approval.

Even if we are able to commercialize any of our drug candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices or health care reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug and biological products vary widely from country to country. Current and future legislation may change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted and, in some markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we may obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the

revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize any product candidates successfully also will depend in part on the extent to which coverage and reimbursement for these product candidates and related treatments will be available from government authorities, private health insurers and other organizations. In the United States, reimbursement varies from payor to payor. Reimbursement agencies in Europe may be more conservative than federal health care programs or private health plans in the United States. For example, a number of cancer drugs are generally covered and paid for in the United States, but have not been approved for reimbursement in certain European countries. A primary trend in the U.S. health care industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of payments for particular products. For example, payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. Payors may require use of alternative therapies or a demonstration that a product is medically necessary for a particular patient before use of a product will be covered. Additionally, payors may seek to control utilization by imposing prior authorization requirements.
Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for products. We cannot be sure that coverage will be available for any product candidate that we commercialize and, if coverage is available, what the level of reimbursement will be. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. Patients are unlikely to use our products, if they are approved for marketing, unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of such products. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs and biologics, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by federal health care 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. In the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. In the European Union, reference pricing systems and other measures may lead to cost containment and reduced prices. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Further, there have been, and may continue to be, legislative and regulatory proposals at the U.S. federal and state levels and in foreign jurisdictions directed at broadening the availability and containing or lowering the cost of healthcare. The continuing efforts of the government, insurance companies, managed care organizations and other third-party payors to contain or reduce costs of healthcare may adversely affect our ability to set prices for our products that would allow us to achieve or sustain profitability. In addition, governments may impose price controls on any of our products that obtain marketing approval, which may adversely affect our future profitability.

In some foreign countries, particularly the member states of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can be a long and expensive process after the receipt of marketing approval for a drug candidate. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we may be required to conduct additional clinical trials that compare the cost-effectiveness of our drug candidates to other available therapies in order to obtain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount in a particular country, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability for sales of any of our drug candidates that are approved for marketing in that country and our business could be adversely affected.

We have no experience selling, marketing or distributing products and currently have no internal marketing and sales force. If we are unable to establish effective marketing and sales capabilities or enter into agreements with third parties to market and sell our drug candidates, we may not be able to effectively market and sell our drug candidates, if approved, or generate product revenues.

We currently have no sales, marketing or distribution capabilities and have no experience as a company in the sale or marketing of pharmaceutical products. There can be no assurance that we will be able to market and sell our products in the United States or overseas. In order to commercialize any drug candidates, we must build on a territory-by-territory basis marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. Therefore, with respect to the commercialization of all or certain of our drug candidates, we may choose to collaborate, either globally or on a territory-by-territory basis, with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If so, our success will depend, in part, on our ability to enter into and maintain collaborative relationships for such capabilities, such collaborators' strategic interest in the products under development and such collaborators' ability to successfully market and sell any such products.

If we are unable to enter into such arrangements when needed on acceptable terms or at all, we may not be able to successfully commercialize any of our drug candidates that receive regulatory approval, or any such commercialization may experience delays or limitations. Further, to the extent that we depend on third parties for marketing and distribution, any revenues we receive will depend upon the efforts of such third parties, and there can be no assurance that such efforts will be successful.

To the extent that we decide not to, or are unable to, enter into collaborative arrangements with respect to the sales and marketing of our products, we may in the future need to establish an internal sales and marketing team with technical expertise and supporting distribution capabilities to commercialize our drug candidates, which could be expensive, time-consuming and requiring significant attention of our executive officers to manage. Further, we may not have sufficient resources to allocate to the sales and marketing of our products.

Any failure or delay in the development of sales, marketing and distribution capabilities, through collaboration with one or more third parties or through internal efforts, would adversely impact the commercialization of any of our products that we obtain approval to market. As a result, our future product revenue will suffer and we may incur significant additional losses.

In addition, certain of our collaboration agreements that provide us with co-commercialization rights with respect to certain partnered programs contain specific commercialization obligations. If we fail to meet those obligations, our commercialization rights could be impaired.

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

Although we do not currently have any products on the market, upon commercialization of our drug candidates, if approved, we will be subject to additional health care statutory and regulatory requirements and oversight by federal and state governments in the United States as well as foreign governments in the jurisdictions in which we conduct our business. Physicians, other health care providers and third-party payors will play a primary role in the recommendation, prescription and use of any product candidates for which we obtain marketing approval. Our future arrangements with such third parties may expose us to broadly applicable fraud and abuse and other health care laws and regulations that may constrain our business or financial arrangements and relationships through which we market, sell and distribute any products for which we may obtain marketing approval. Restrictions under applicable domestic and foreign health care laws and regulations include, but are not limited to, the following:

- the U.S. federal Anti-Kickback Statute, or AKS, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, or the furnishing, recommending, or arranging of a good or service, for which payment may be made under a federal health care program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the AKS or specific intent to violate it to have committed a violation. Certain arrangements are protected from enforcement through AKS safe harbors and exceptions, but an arrangement must meet every element of the applicable safe harbor or exception in order to obtain this protection. The fact that an arrangement does not meet the requirements of a safe harbor or exception does not mean that it violates the AKS; such arrangements would be subject to a facts and circumstances analysis to determine compliance with the AKS or lack thereof. The definition of "remuneration" has been broadly interpreted to include anything of value, including such items as gifts, discounts, the furnishing of supplies or equipment, credit arrangements, waiver of payments, and providing anything at less than its fair market value. The AKS is broadly interpreted and aggressively enforced with the result that beneficial commercial

arrangements can be criminalized in the healthcare industry because of the AKS. The penalties for violating the federal AKS include imprisonment for up to ten years, fines of up to $100,000 per violation and possible exclusion from federal health care programs such as Medicare and Medicaid. Additionally, a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the False Claims Act;

- the U.S. False Claims Act, or FCA, prohibits knowingly presenting, or causing to be presented a false claim or the knowing use of false statements or records to obtain payment from the federal government. The FCA also prohibits the knowing retention of overpayments (sometimes referred to as "reverse false claims"). When an entity is determined to have violated the FCA, it must pay three times the actual damages sustained by the government, plus mandatory and substantial civil penalties for each separate false claim. The entity also faces the possibility of exclusion from federal healthcare programs. Suits filed under the False Claims Act, known as "qui tam" actions, can be brought by any individual on behalf of the government and such individuals (known as "relators" or, more commonly, as "whistleblowers") may share in any amounts paid by the entity to the government in fines or settlement. Claims for payment by federal health care programs for items and services which results from a violation of the federal AKS may also constitute a false or fraudulent claims for purposes of the False Claims Act;
- the U.S. Civil Monetary Penalties Law, or CMPL, authorizes the imposition of substantial civil money penalties and the possibility of exclusion against an individual or entity that engages in certain prohibited activities including but not limited to violations of the AKS, knowing submission of a false or fraudulent claim, employment of an excluded individual, and the provision or offer of anything of value to a Medicare or Medicaid beneficiary that the transferring party knows or should know is likely to influence beneficiary selection of a particular provider for which payment may be made in whole or part by a federal health care program, commonly known as the Beneficiary Inducement CMP;
- the U.S. Health Insurance Portability and Accountability Act of 1996, as amended by the American Recovery and Reinvestment Act of 2009, and implementing regulations, or HIPAA, which created two new federal crimes: health care fraud and false statements relating to health care matters. The health care fraud statute prohibits knowingly and willfully executing a scheme to defraud any health care benefit program, including private payors. A violation of this statute is a felony and may result in fines, imprisonment or exclusion from government sponsored programs. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up 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; similar to the AKS, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- analogous state and foreign laws and regulations relating to health care fraud and abuse, such as state anti-kickback and false claims laws, that may apply to sales or marketing arrangements and claims involving health care items or services reimbursed by non-governmental third-party payors, including private insurers. Penalties for violating these laws can range from fines to criminal sanctions;
- the FCPA and other anti-corruption laws and regulations pertaining to our financial relationships and interactions with foreign government officials;
- the U.S. federal physician payment transparency requirements, sometimes referred to as the Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid or the Children's Health Insurance Program to track and annually report to the Centers for Medicare & Medicaid Services, or CMS, information related to certain payments and other transfers of value made to U.S.-licensed physicians (defined broadly to include doctors, dentists, optometrists, podiatrists, chiropractors, and certain advanced non-physician health care practitioners) and teaching hospitals. Manufacturers are also required to report certain ownership and investment interests held by physicians and their immediate family members. The law carries penalties of up to $1.15 million per year for violations, depending on the circumstances, and payments reported also have the potential to draw scrutiny on payments to and relationships with physicians, which may have implications under the AKS and other healthcare laws;
- analogous state and foreign laws that require pharmaceutical companies to track, report and disclose to the government and/or the public information related to payments, gifts, and other transfers of value or remuneration to physicians and other health care providers, marketing activities or expenditures, or product pricing or transparency information, or that require pharmaceutical companies to implement compliance programs that meet certain standards or to restrict or limit interactions between pharmaceutical manufacturers and members of the health care industry;
- the U.S. federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under federal health care programs;
- HIPAA, which imposes obligations on certain covered entity health care providers, health plans, and health care clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information; and
- state and foreign laws that govern the privacy and security of health information in certain circumstances, including state security breach notification laws, state health information privacy laws and federal and state consumer protection

laws, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable health care laws and regulations will involve substantial costs. If the FDA or a comparable foreign regulatory authority approves any of our product candidates, we will be subject to an expanded number of these laws and regulations and will need to expend resources to develop and implement policies and processes to promote ongoing compliance. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other health care laws and regulations, resulting in government enforcement actions.

If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from federal health care programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other health care providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from federal health care programs.

Risks Related to Our Intellectual Property

If we breach any of the agreements under which we license from third parties the intellectual property rights or commercialization rights to our drug candidates, particularly our license agreements with TUM, Enumeral and Kelun, we could lose license rights that are important to our business and our operations could be materially harmed.

We in-license significant intellectual property related to our Anticalin platforms from TUM. Under the terms of the TUM License, TUM assigns to us certain materials and records resulting from the research. We retain rights to inventions made by our employees, and TUM assigns to us all inventions made under the agreement jointly by our employees and TUM personnel, provided that our employees have made a certain inventive contribution. With respect to all other inventions made in the course of the research, TUM grants to us worldwide exclusive license rights under patents and patent applications claiming such inventions. TUM retains rights to practice these inventions for research and teaching purposes. We bear the costs of filing, prosecuting and maintaining the patents assigned or licensed to us under the TUM License.

As consideration for the assignments and licenses, we are obliged to pay milestone payments to TUM on development of our proprietary products claimed by patents assigned or licensed to us by TUM. We are also obliged to pay low single-digit royalties, including annual minimum royalties, on the sales of such products. Should we grant licenses or sublicenses to those patents to third parties, we are obliged to pay to TUM certain undisclosed fees as a function of out-licensing revenues in connection with those patents, or Out-License Fees, where such Out-License Fees are creditable against annual license payments to TUM. Our payment obligations are reduced by our proportionate contribution to a joint invention. Payment obligations terminate on expiration or annulment of the last patent covered by the TUM License that covers a proprietary product or is sublicensed, as applicable.

Pieris and TUM initiated discussions in the second quarter of 2018, and are in the process of negotiating an amendment to our license agreement, to clarify, expand and restructure the TUM License, including the parties' obligations under such license agreement. The contemplated amendment relates to revised commercial terms. We recorded the probable expected impact of the amendment in research and development expense in 2019, although the final expense could be different than what we currently have recorded. These discussions may also lead to an increase in our collaborative research activities with TUM.

Under the PD-1 In-License with Enumeral, we in-licensed intellectual property related to an Enumeral-generated antibody against PD-1 and are granted an option to in-license up to two additional antibodies against undisclosed targets. Under the terms of the PD-1 In-License, we acquired a non-exclusive worldwide license under the applicable Enumeral patents and know-how to research, develop and commercialize fusion proteins incorporating Enumeral's PD-1 antibody and one or more Anticalin proteins. On January 29, 2018, Enumeral filed a voluntary petition for relief under Chapter 11 of the United States Bankruptcy Code in the Bankruptcy Court. In connection with those proceedings, Enumeral transferred the intellectual property related to the PD-1 In-License to Acquisition Group, who have assumed the rights and obligations of Enumeral with respect to the PD-1 In-License.

As consideration, we are obliged to pay to Acquisition Group development and sales milestones on development of products incorporating the Enumeral antibody. We are also obliged to pay low to lower-middle single-digit royalties as a percentage of net sales depending on the amount of net sales in the applicable years. In the event that we are required to pay a license fee or royalty to any third party related to the licensed products, our royalty payment obligations to Acquisition Group are reduced by

the amount of such third-party fees or payments, up to 50% of the royalty payment for each calendar year due to Acquisition Group. Payment obligations terminate on a product-by-product and country-by-country basis on the later of 10 years from the first commercial sale of a product incorporating the Enumeral antibody or the last to expire, lapse or be abandoned of a claim from the licensed Enumeral patents filed as of the effective date of the PD-1 In-License that cover the manufacture, use, offer for sale, sale or import of a product incorporating the Enumeral antibody.

In connection with our efforts to develop multispecific Anticalin-based proteins designed to engage immunomodulatory targets, during the second quarter of 2017, we entered into the Kelun Agreement. Under the Kelun Agreement, Kelun has granted to us a non-exclusive worldwide license (with the right to sublicense) under certain intellectual property owned or controlled by Kelun to research, develop, manufacture and commercialize bi- and multi- specific fusion proteins that include an antibody developed by Kelun specific for an undisclosed target and one or more Anticalin proteins.

In addition to the TUM License and the PD-1 In-License, we have other in-license agreements and may seek to enter into additional agreements with other third parties in the future granting similar license rights with respect to other potential drug candidates. If we fail to comply with any of the conditions or obligations or otherwise breach the terms of the TUM License, the PD-1 In-License, the Kelun Agreement or any future license agreement we may enter on which our business or drug candidates are dependent, TUM, Enumeral, Kelun or other licensors may have the right to terminate the applicable agreement in whole or in part and thereby extinguish our rights to the licensed technology and intellectual property and/or any rights we have acquired to develop and commercialize certain drug candidates, including, with respect to the TUM License and PD-1 In-License, our Anticalin-based drug therapies. Under the TUM License, we can terminate the licenses to any or all licensed patents upon specified advance notice to TUM. TUM may terminate the license provisions of the agreement only for cause. Termination of the TUM License does not terminate our rights in patents assigned to us but would terminate our rights to patents licensed to us under the agreement. Under the PD-1 In-License, we can terminate the agreement upon 30 days' notice to Enumeral. Enumeral may terminate the PD-1 In-License only upon a material breach by us that is not cured. The loss of the rights licensed to us under our license agreement with TUM or Enumeral, or any future license agreement that we may enter granting us rights on which our business or drug candidates are dependent, would eliminate our ability to further develop the applicable drug candidates and may materially harm our business, prospects, financial condition and results of operations.

If our efforts to protect the proprietary nature of the intellectual property related to our technologies are not adequate, we may not be able to compete effectively and our business could be harmed.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies. Any disclosure to, or misappropriation by, third parties of our proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding any competitive advantage we may derive from the proprietary information.

The strength of patents in the biotechnology and pharmaceutical fields can be uncertain and involve complex legal and scientific questions. No consistent policy regarding the breadth of claims allowed in patents has emerged to date in the United States. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced, or that the scope of any patent rights could provide a sufficient degree of protection that could permit us to gain or keep our competitive advantage with respect to these products and technologies. For example, we cannot predict:

- the degree and range of protection any patents will afford us against competitors, including whether third parties will find ways to make, use, sell, offer to sell or import competitive products without infringing our patents;
- if and when patents will be issued;
- how laws in the various jurisdictions, such as the USPTO or the European Patent Office, or the EPO, will change thus affecting our ability to obtain patents or maintain and enforce existing patents;
- whether or not others will obtain patents claiming inventions similar to those covered by our patents and patent applications; or
- whether we will need to initiate litigation or administrative proceedings (for example, at the USPTO or the EPO) in connection with patent rights, which may be costly whether we win or lose.

As a result, the patent applications we own or license may fail to result in issued patents in the United States or in foreign countries. Third parties may challenge the validity, enforceability or scope of any issued patents we own or license or any applications that may issue as patents in the future, which may result in those patents being narrowed, invalidated or held unenforceable. Even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from developing similar products that do not fall within the scope of our patents. If the breadth or strength of protection provided by the patents we hold or pursue is threatened, our ability to commercialize any drug candidates

with technology protected by those patents could be threatened. Further, if we encounter delays in our clinical trials, the period of time during which we would have patent protection for any covered drug candidates that obtain regulatory approval would be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain at the time of filing that we are the first to file any patent application related to our drug candidates.

While patent term extensions under the Hatch-Waxman Act in the United States and under supplementary protection certificates in Europe may be available to extend our patent exclusivity for our drug candidates, the applicable patents may not meet the specified conditions for eligibility for any such term extension and, even if eligible, we may not be able to obtain any such term extension. Further, because filing, prosecuting, defending and enforcing patents in multiple jurisdictions can be expensive, we may elect to pursue patent protection relating to our drug candidates in only certain jurisdictions. As a result, competitors would be permitted to use our technologies in jurisdictions where we have not obtained patent protection to develop their own products, any of which could compete with our drug candidates.

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our discovery platform and drug development processes that involve proprietary know-how, information or technology that is not covered by patents or not amenable to patent protection. Although we require all of our employees and certain consultants, third-parties and advisors to assign inventions to us, and require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, our trade secrets and other proprietary information may be disclosed or competitors may otherwise gain access to such information or independently develop or reverse engineer substantially equivalent information. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant difficulty in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the trade secrets and other intellectual property related to our technologies to third parties, we may not be able to establish or maintain the competitive advantage that we believe is provided by such intellectual property, adversely affecting our market position and business and operational results.

Claims that we infringe the intellectual property rights of others may prevent or delay our drug discovery and development efforts.

Our research, development and commercialization activities, as well as any drug candidates or products resulting from those activities, may infringe or be accused of infringing a patent or other form of intellectual property under which we do not hold a license or other rights. Third parties may assert that we are employing their proprietary technology without authorization.

There may be third-party patents of which we are currently unaware with claims that cover the use or manufacture of our drug candidates or the practice of our related methods. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our drug candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our drug candidates infringes upon one or more claims of these patents. If our activities or drug candidates infringe the patents or other intellectual property rights of third parties, the holders of such intellectual property rights may be able to block our ability to commercialize such drug candidates or practice our methods unless we obtain a license under the intellectual property rights or until any applicable patents expire or are determined to be invalid or unenforceable.

Defense of any intellectual property infringement claims against us, regardless of their merit, would involve substantial litigation expense and would be a significant diversion of resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, obtain one or more licenses from third parties, limit our business to avoid the infringing activities, pay royalties and/or redesign our infringing drug candidates or alter related formulations, processes, methods or other technologies, any or all of which may be impossible or require substantial time and monetary expenditure. Further, if we were to seek a license from the third-party holder of any applicable intellectual property rights, we may not be able to obtain the applicable license rights when needed or on reasonable terms, or at all. Some of our competitors may be able to sustain the costs of complex patent litigation or proceeding more effectively than us due to their substantially greater resources. The occurrence of any of the above events could prevent us from continuing to develop and commercialize one or more of our drug candidates and our business could materially suffer.

We may desire to, or be forced to, seek additional licenses to use intellectual property owned by third parties, and such licenses may not be available on commercially reasonable terms, or at all.

Third parties may also hold intellectual property, including patent rights that are important or necessary to the development of our drug candidates, in which case we would need to obtain a license from that third party or develop a different formulation of

the product that does not infringe upon the applicable intellectual property, which may not be possible. Additionally, we may identify drug candidates that we believe are promising and whose development and other intellectual property rights are held by third parties. In such a case, we may desire to seek a license to pursue the development of those drug candidates. Any license that we may desire to obtain or that we may be forced to pursue may not be available when needed on commercially reasonable terms, or at all. Inability to secure any license that we need or desire could have a material adverse effect on our business, financial condition and prospects.

The patent protection covering some of our drug candidates may be dependent on third parties, who may not effectively maintain that protection.

While we expect the right to fully prosecute any patents covering drug candidates we may in-license from third-party owners, there may be instances when the prosecution and maintenance of issued patents and pending patent applications that cover our drug candidates remain controlled by our licensors. Similarly, some of our future licensing partners may retain the right, or may seek the rights, to prosecute patents covering the drug candidates we license to them and we may grant such rights to those partners for business reasons. If such third parties fail to appropriately maintain that patent protection, we may not be able to prevent competitors from developing and selling competing products or practicing competing methods and our ability to generate revenue from any commercialization of the affected drug candidates may suffer.

Certain technologies and patents have been developed with partners and we may face restrictions on this jointly developed intellectual property.

We have entered into agreements with a number of commercial partners, including university partners, which cover intellectual property. We have, in some cases individually and in other cases along with our partners, filed for patent protection for a number of technologies developed under these agreements and may in the future file for further intellectual property protection and/or seek to commercialize such technologies. Under some of these agreements, certain intellectual property developed by us and the relevant partner may be subject to joint ownership and our commercial use of such intellectual property may be restricted, or may require written consent from, or a separate agreement with, the partner. In other cases, we may not have any rights to use intellectual property solely developed and owned by the partner. If we cannot obtain commercial use rights for such jointly owned intellectual property or partner-owned intellectual property, our future product development and commercialization plans may be adversely affected.

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

Competitors may infringe our patents or the patents of our current or potential licensors. To attempt to stop infringement or unauthorized use, we may need to enforce one or more of our patents, which can distract our management and divert our limited time and resources. Our standing to enforce such patents may sometimes be dependent on the licensor joining such suit, and a licensor's failure to join such suit may prevent us from enforcing the patent. If we pursue any litigation, a court may decide that a patent of ours or any of our licensors' is not valid or is unenforceable or may refuse to stop the other party from using the relevant technology on the grounds that our patents do not cover the technology in question. Further, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, which could reduce the likelihood of success of, or the amount of damages that could be awarded resulting from, any infringement proceeding we pursue in any such jurisdiction. An adverse result in any infringement litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing, which could limit our ability to exclude competitors from directly competing with us in those jurisdictions.

Interference proceedings may also be provoked or suggested by third parties, or brought by the USPTO or at its foreign counterparts (such as the EPO), to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to use it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms, or at all.

Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees.

If we are unsuccessful in obtaining or maintaining patent protection for intellectual property in development, our business and competitive position would be harmed.

We are seeking patent protection of our technology and for our drug candidates. Patent prosecution is a challenging process and is not assured of success. If we are unable to secure patent protection for our technology and drug candidates, our business may be adversely impacted.

Furthermore, issued patents and pending applications require regular maintenance. Failure to maintain our portfolio may result in loss of rights that may adversely impact our intellectual property rights, such as rendering issued patents unenforceable or terminating pending applications prematurely.

In addition, under the European Union regulation on classification, labeling and packaging of substances and mixtures, or CLP, and under other regulations in the United States or other countries related to the clinical development of our drug candidates (including, for example, submissions to regulatory authorities such as the FDA and EMA as well as submissions related to obtaining a non-proprietary, or INN and USAN, name for our clinical drug candidates to the World Health Organization, or the WHO, and United States Adopted Name Council, or the USAN Council), we may be required to publicly disclose the composition of our proprietary products or substances, which may facilitate infringement or avoidance of our intellectual property by third parties and may potentially reduce the margin we are able to charge for our products by allowing competitors to more accurately determine our production costs. Future development of these regulations may have a further negative impact on our revenues and a substantial negative impact on our business.

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

In addition to seeking patents for our Anticalin-brand technology and some of our drug candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We currently, and expect in the future to continue to, seek to protect these trade secrets, in part by entering into confidentiality agreements with parties who have access to them, such as our employees, collaborators, CMOs, consultants, advisors, investigators and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for any such disclosure. 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, we would have no right to prevent them, or those to whom they disclose the trade secrets, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

If we fail to protect our trademark rights, competitors may be able to take advantage of our goodwill, which would weaken our competitive position, reduce our revenues and increase our costs.

We believe that the protection of our trademark rights is an important factor in product recognition, maintaining goodwill, and maintaining or increasing market share. We may expend substantial cost and effort in an attempt to register, maintain and enforce our trademark rights. If we do not adequately protect our rights in our trademarks from infringement, any goodwill that we have developed in those trademarks could be lost or impaired.

Third parties may claim that the sale or promotion of our products, when and if we have any, may infringe on the trademark rights of others. Trademark infringement problems occur frequently in connection with the sale and marketing of pharmaceutical products. If we become involved in any dispute regarding our trademark rights, regardless of whether we prevail, we could be required to engage in costly, distracting and time-consuming litigation that could harm our business. If the trademarks we use are found to infringe upon the trademark of another company, we could be liable for damages and be forced to stop using those trademarks, and as result, we could lose all of the goodwill that has been developed in those trademarks.

The future growth of our business may expose our intellectual property to a high risk of counterfeiting or unauthorized use.

As part of our business strategy, we intend to license our Anticalin-based technology and sell our potential products, if any, in many different countries. As a result, we may do business with third parties in countries where intellectual property rights have been or are routinely disregarded, and the future growth of our business may expose our intellectual property to a high risk of counterfeiting or unauthorized use. Although we attempt to obtain broad international intellectual property rights for our Anticalin technology and proteins, we cannot guarantee that such rights, to the extent we can obtain them, will be enforceable in a timely fashion or at all in any particular country or jurisdiction, or that if enforced, will offer us adequate commercial protection or adequate redress for any harm suffered. Counterfeiting or unauthorized use of our technologies or products may

also expose our business to harm for which no adequate monetary redress exists, and to the extent we are unable to stop such use, may cause us to lose rights with respect to intellectual property that is crucial to our business. Any such misuse of our intellectual property may have a substantial negative impact on our business and revenues and may cause our business to fail.

Risks Related to Our Employees

If we are not able to attract and retain highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified personnel. We are highly dependent on our management, scientific and medical personnel, especially Stephen S. Yoder, our Chief Executive Officer and President, whose services are critical to the successful implementation of our drug candidate development, our business development and partnerships, and our regulatory and commercialization strategies. Further, as our approach is built upon the drug discovery and development experience of our drug development team, which we believe is a significant contributor to our competitive advantage, we are dependent on the maintenance and growth of that team with qualified members containing high levels of expertise in specific scientific fields. We may in the future hire additional employees for research and development or general and administrative activities.

We are not aware of any present intention of any of our executive officers or other members of our senior management team to leave our company. However, our industry tends to experience a high rate of turnover of management personnel and our employees are generally able to terminate their relationships with us on short notice. Pursuant to German employment law, our employment arrangements with employees of Pieris GmbH are governed by employment contracts, which provide certain defined terms for either party to terminate the employment relationship.

The loss of the services of any of our executive officers, in particular Mr. Yoder, or other key employees and our inability to find suitable replacements could potentially harm our business, financial condition and prospects. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior and mid-level managers as well as junior and mid-level scientific and medical personnel.

Moreover, there is intense competition for a limited number of qualified personnel among biopharmaceutical, biotechnology, pharmaceutical and other related businesses. Many of the other companies against which we compete for qualified personnel have greater financial and other resources, different risk profiles, longer histories in the industry and greater ability to provide valuable cash or stock incentives to potential recruits than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than what we are able to offer as an early stage company. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can develop and commercialize our drug candidates will be limited.

We may be subject to labor claims brought by our employees against us.

In the United States, an employment relationship with no specified duration is presumed to be employment "at-will" and the employer or employee may terminate the employment relationship at any time, with or without cause, except for public policy reasons including discrimination, participating in union activity, or refusing to carry out an activity that violates the law.
In contrast, in Germany, there is no analogous doctrine of "employment at will." By law, German employees must have written employment contracts that reflect the key aspects of the employment relationship. Our relations between German employers and employees are extensively regulated under German labor and employment laws and regulations. Employment relationships may be terminated for cause without observing the ordinary notice period. If terminated without cause, the applicable ordinary notice period must be observed. German employees have special protection against dismissals provided the employee has been employed by a company for more than six months and such company employs more than 10 full-time employees.

German employment termination law is regulated by various codes, in particular the *Kündigungsschutzgesetz,* or the German Termination Protection Act, and is intended to give the employee maximum protection against unfair dismissal, including among other things:

- the employer must observe the applicable notice period, which is ordinarily determined by law (between four weeks and seven months, depending upon the length of employment, though it is possible for the notice period to be two weeks, if a probationary period, lasting up to the first six months of employment, is agreed upon), if a longer period is not otherwise agreed by the parties, and has to deliver a written notice of termination to the employee;
- for companies with more than 10 full-time employees, the German Termination Protection Act generally restricts termination of employment if the employee has been employed for more than six months, wherein the employee may be terminated only for a particular reason, including certain behavioral or personal reasons relating to the employee or

certain developments relating to the business of the employer, such as a business restructuring which reduces the number of employee positions;

- special termination protection against unlawful dismissal applies to several other groups of employees, such as an employee that is an officially acknowledged handicapped person, an employee who was appointed as a company's data protection officer or as a member of the works council of a company, if any, an employee on maternity leave or a pregnant employee (in these cases, approval of various German authorities is required prior to termination but usually very difficult to obtain); and
- if a company engages in a mass layoff, which is deemed to occur when the employer intends to dismiss a large percentage of its employees during a 30 calendar day period, prior written notification to the German employment office is required.

In this regard, if we downsize for any reason and fail to adhere to the complex requirements articulated by the employee protection law, we could face legal actions brought by affected employees or former employees, and, as a result, we may incur operational or financial losses and divert the attention of our executive officers from managing our business.

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

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employers. Litigation may be necessary to defend against any such claims.

In addition, while it is our policy to require our employees and contractors, who may be involved in the development of intellectual property, to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who contributes to the development of intellectual property that we regard as our own. Further, the terms of such assignment agreements may be breached and we may not be able to successfully enforce their terms, which may force us to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of intellectual property rights we may regard and treat as our own.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause our business to suffer.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA or EMA regulations, provide accurate information to the FDA or EMA, comply with manufacturing standards we have established, comply with federal, state and international healthcare fraud and abuse laws and regulations as they may become applicable to our operations, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions and procedures we currently take or may establish in the future as our operations and employee base expand to detect and prevent this type of 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 by our employees to comply with such 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 and results of operations, including the imposition of significant fines or other sanctions.

Certain of our employees and their inventions are subject to German law.

Many of our employees work in Germany and are subject to German employment law. Ideas, developments, discoveries and inventions made by such employees and consultants are subject to the provisions of the Gesetz über Arbeitnehmererfindungen, or the German Act on Employees' Inventions, which regulates the ownership of, and compensation for, inventions made by employees. We face the risk that disputes can occur between us and such employees or ex-employees pertaining to alleged non-adherence to the provisions of this act. Such disputes may be costly to defend and take up our management's time and efforts whether we prevail or not. In addition, under the German Act on Employees' Inventions, certain employees retained rights to patents they invented or co-invented prior to 2009. Although most of these employees have subsequently assigned their interest in these patents to us, there is a risk that the compensation we provide to them may be deemed insufficient and we may be required under German law to increase the compensation due to such employees for the use of the patents. In those cases where employees have not assigned their interests to us, we may need to pay compensation for the use of those patents. If we are

required to pay additional compensation or face other disputes under the German Act on Employees' Inventions, our results of operations could be adversely affected.

Risks Related to the Ownership of Our Common Stock

Our share price is volatile and may be influenced by numerous factors, some of which are beyond our control.

Market prices for shares of biotechnology companies such as ours are often volatile. Thus, the quoted price of our common stock has been, and is likely to continue to be, highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report on Form 10-K, these factors include:

- the drug candidates we seek to pursue, and our ability to obtain rights to develop, commercialize and market those drug candidates;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- actual or anticipated adverse results or delays in our clinical trials;
- our failure to commercialize our drug candidates, if approved;
- unanticipated serious safety concerns related to the use of any of our drug candidates;
- adverse regulatory decisions;
- additions or departures of key scientific or management personnel;
- changes in laws or regulations applicable to our drug candidates, including without limitation clinical trial requirements for approvals;
- the perception of the pharmaceutical and biotechnology industry by the public, legislatures, regulators and the investment community;
- disputes or other developments relating to patents and other proprietary rights and our ability to obtain patent protection for our drug candidates;
- significant lawsuits, including patent and stockholder class action litigation;
- our dependence on third parties, including CROs and CMOs as well as our current and potential partners that produce companion diagnostic products;
- failure to meet or exceed any financial guidance or expectations regarding development milestones that we may provide to the public;
- actual or anticipated variations in quarterly operating results;
- failure to meet or exceed the estimates and projections of the investment community;
- overall performance of the equity markets and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies;
- conditions or trends in the biotechnology and biopharmaceutical industries;
- introduction of new products by us or our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- our ability to maintain an adequate rate of growth and manage such growth;
- issuances of debt or equity securities;
- sales of our common stock by us or our stockholders in the future, or the perception that such sales could occur;
- trading volume of our common stock;
- ineffectiveness of our internal control over financial reporting or disclosure controls and procedures;
- general political and economic conditions;
- effects of natural or man-made catastrophic events; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and the stocks of biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. Furthermore, other biotechnology companies or our competitors' programs could have positive or negative results that impact their stock prices and their results or stock fluctuations could have a positive or negative impact

on our stock price regardless of whether such impact is direct or not. The realization of any of the above risks or any of a broad range of other risks, including those described in these "Risk Factors," could have a dramatic and material adverse impact on the market price of our common stock.

We have broad discretion in how we use our cash, cash equivalents and investments, including the net proceeds from our collaborations, public and private securities offerings, and may not use these financial resources effectively, which could affect our results of operations and cause our stock price to decline.

Our management has considerable discretion in the application of our cash, cash equivalents and investments, including the fees and milestone payments from our collaborations and the net proceeds of our securities offerings. We intend to use the cash, cash equivalents and investments to advance our product candidates and for working capital and other general corporate purposes, which will include the hiring of additional personnel and capital expenditures. As a result, investors will be relying upon management's judgment with only limited information about our specific intentions for the use of the cash, cash equivalents and investments. We may use the cash, cash equivalents and investments for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the financial resources from our collaborations and securities offerings in a manner that does not produce income or that loses value.

If securities or industry analysts do not publish, or cease publishing, research or publish inaccurate or unfavorable research about our business or our market, or if they change their recommendations regarding our stock adversely, our stock price and any trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. If only a few securities or industry analysts commence coverage of our company, the trading price for our stock would likely be negatively affected and there can be no assurance that analysts will provide favorable coverage. If securities or industry analysts who initiate coverage downgrade our stock or publish inaccurate or unfavorable research about our business or our market, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and any trading volume to decline.

We have had, and have previously reported material weaknesses in our internal controls over financial reporting. If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, our ability to operate our business and investors' views of us.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain a smaller reporting company with less than $100 million in revenue, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm.

If we cannot favorably assess the effectiveness of our internal controls over financial reporting, investor confidence and, in turn, our stock price could be materially adversely affected.

As previously reported in our Annual Report on Form 10-K for the year ended December 31, 2019, we concluded that we had a material weakness in 2019 in our internal controls. No material financial statement misstatement was identified in relation to the previously reported material weaknesses in our internal control over financial reporting. While we took steps to address these material weaknesses and concluded in 2020 that the material weaknesses had been remediated, there is a reasonable possibility that material weaknesses may be identified in the future and that a material misstatement of our annual or interim consolidated financial statements may not be prevented or detected on a timely basis. Management, including our principal executive officer and principal financial officer, believes the consolidated financial statements included in this Annual Report on Form 10-K fairly represent in all material respects our financial condition, results of operations and cash flows in accordance with U.S. GAAP. However, we cannot assure you that additional material weaknesses or significant deficiencies in our internal control over financial reporting will not be identified in the future.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that will need to be evaluated frequently. Our failure to maintain the effectiveness of our internal controls in accordance with the requirements of the Sarbanes-Oxley Act could have a material adverse effect on the tradability of our common stock, which in turn would negatively impact our business. We could lose investor confidence in the accuracy and completeness of our financial reports, which could have an adverse effect on the price of our common stock. In addition, if our efforts to comply with new or changed laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Shares of our common stock that have not been registered under federal securities laws are subject to resale restrictions imposed by Rule 144 of the Securities Act, including those set forth in Rule 144(i) which apply to a former "shell company."

We were previously deemed a "shell company" under applicable SEC rules and regulations, prior to the reverse merger transaction in which we became a public company, because we had no or nominal operations and either no or nominal assets, assets consisting solely of cash and cash equivalents, or assets consisting of any amount of cash and cash equivalents and nominal other assets. Pursuant to Rule 144 of the Securities Act, sales of the securities of a former shell company, such as us, are not permitted unless at the time of a proposed sale, (i) we are subject to the reporting requirements of Section 13 or 15(d) of the Exchange Act; and (ii) we have filed all reports and other materials required to be filed by Section 13 or 15(d) of the Exchange Act, as applicable, during the preceding 12 months, other than current reports on Form 8-K. Additionally, our previous status as a shell company could also limit our use of our securities to pay for any acquisitions we may seek to pursue in the future. The lack of liquidity of our securities as a result of the inability to sell under Rule 144 for a longer period of time than a non-former shell company could cause the market price of our securities to decline.

If we issue additional shares of our capital stock in the future, our existing stockholders will be diluted.

Our Amended and Restated Articles of Incorporation authorize the issuance of up to 300,000,000 shares of our common stock and up to 10,000,000 shares of preferred stock with the terms, limitations, voting rights, relative rights and preferences and variations of each series that our Board of Directors may determine from time to time. Possible business and financial uses for our authorized capital stock include, without limitation, equity financing, future stock splits, acquiring other companies, businesses or products in exchange for shares of our capital stock, issuing shares of our capital stock to partners or other collaborators in connection with strategic alliances, attracting and retaining employees by the issuance of additional securities under our equity compensation plan, or other transactions and corporate purposes that our Board of Directors deems are in the interests of our company. Furthermore, issuances of shares of our capital stock could have the effect of delaying or preventing changes in control or our management. Any future issuances of shares of our capital stock may not be made on favorable terms or at all, they may have rights, preferences and privileges that are superior to those of our common stock and may have an adverse effect on our business or the trading price of our common stock. The issuance of any additional shares of our common stock will reduce the book value per share and may contribute to a reduction in the market price of the outstanding shares of our common stock. Additionally, any such issuance will reduce the proportionate ownership and voting power of all of our current stockholders.

Sales of a substantial number of shares of our common stock in the public market, or the perception that such sales could occur, could cause our stock price to fall.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. As of December 31, 2021, a total of 72,222,661 shares of our common stock were outstanding. Any sales of those shares or any perception in the market that such sales may occur could cause the trading price of our common stock to decline.

In addition, shares of our common stock that are either subject to outstanding options or reserved for future issuance under our equity incentive plan, or issuable upon the conversion of our outstanding preferred stock or upon the exercise of our outstanding warrants, will be eligible for sale in the public market to the extent permitted by the provisions of applicable vesting schedules and/or terms of such securities. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

The resale of shares covered by our effective resale registration statements could adversely affect the market price of our common stock in the public market, which result would in turn negatively affect our ability to raise additional equity capital.

The sale, or availability for sale, of our common stock in the public market may adversely affect the prevailing market price of our common stock and may impair our ability to raise additional equity capital. Pursuant to registration statements filed with the SEC, we previously registered for resale shares of our common stock, which included all of the shares of our common stock issued in our private placements and in connection with the closing of the reverse merger transaction in which we became a public company. For example, in March 2021, we registered for resale 3,706,174 shares of common stock in connection with a private placement transaction with Seagen, and 3,584,320 shares of common stock in connection with a private placement transaction with AstraZeneca. The resale registration statements permit the resale of these shares at any time without restriction.

The resale of a substantial number of shares of our common stock in the public market could adversely affect the market price for our common stock and make it more difficult for investors to sell shares of our common stock at times and prices that investors feel are appropriate. Furthermore, because there are a large number of shares registered pursuant to the resale registration statements, we may continue to offer shares covered by the resale registration statements for a significant period of time, the precise duration of which cannot be predicted. Accordingly, the adverse market and price pressures resulting from an

offering pursuant to the resale registration statement may continue for an extended period of time and continued negative pressure on the market price of our common stock could have a material adverse effect on our ability to raise additional equity capital.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans or otherwise, could result in dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

Even after giving effect to the funds raised in the past, we expect that significant additional capital will be needed in the future to continue our planned operations. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner, in which we may determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors in a prior transaction may be materially diluted. Additionally, new investors could gain rights, preferences and privileges senior to those of existing holders of our common stock. Further, any future sales of our common stock by us or resales of our common stock by our existing stockholders could cause the market price of our common stock to decline.

As of December 31, 2021, there were 3,282,399 shares reserved for future issuance under our equity compensation plans, and 12,211,713 shares reserved for issuance upon the exercise of outstanding equity awards. Pursuant to our 2018 Employee Stock Purchase Plan, we are authorized to sell 500,000 shares to our employees. Any future grants of options, warrants or other securities exercisable or convertible into our common stock, or the exercise or conversion of such shares, and any sales of such shares in the market, could have an adverse effect on the market price of our common stock.

Anti-takeover provisions in our organizational documents could delay or prevent a change of control.

Certain provisions of our Amended and Restated Articles of Incorporation and Amended and Restated Bylaws may have an anti-takeover effect and may delay, defer or prevent a merger, acquisition, tender offer, takeover attempt or other change of control transaction that a stockholder might consider to be in its interests, including attempts that might result in a premium over the market price for the shares held by our stockholders.

These provisions provide, among other things:

- a classified Board of Directors with staggered three-year terms;
- the ability of our Board of Directors to issue one or more series of preferred stock with voting or other rights or preferences that could have the effect of impeding the success of an attempt to acquire us or otherwise effect a change of control;
- advance notice for nominations of directors by stockholders and for stockholders to include matters to be considered at stockholder meetings;
- certain limitations on convening special stockholder meetings and the prohibition of stockholder action by written consent; and
- directors may only be removed for cause and only by the affirmative vote of the holders of at least 80% of the voting power of all of the then-outstanding shares of our capital stock entitled to vote at an election of directors, voting together as a single class.

These anti-takeover provisions, including those noted above, could make it more difficult for a third party to acquire us, even if the third party's offer may be considered beneficial by many of our stockholders. As a result, our stockholders may be limited in their ability to obtain a premium for their shares.

We may incur significant costs from class action litigation due to our expected stock volatility.

Our stock price may fluctuate for many reasons, including as a result of public announcements regarding the progress of our development efforts or the development efforts of future collaborators or competitors, the addition or departure of our key personnel, variations in our quarterly operating results and changes in market valuations of biopharmaceutical and biotechnology companies.

This risk is especially relevant to us because biopharmaceutical and biotechnology companies have experienced significant stock price volatility in recent years. When the market price of a stock has been volatile as our stock price may be, holders of that stock have occasionally brought securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, could result in substantial costs

defending the lawsuit and diversion of the time, attention and resources of our Board of Directors and management, which could significantly harm our profitability and reputation.

Our Amended and Restated Articles of Incorporation designates the Eighth Judicial District Court of Clark County, Nevada, as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, and therefore limit our stockholders' ability to choose a forum for disputes with us or our directors, officers, employees or agents.

Our Amended and Restated Articles of Incorporation provide that, to the fullest extent permitted by law, and unless we consent to the selection of an alternative forum, the Eighth Judicial District Court of Clark County, Nevada shall be the sole and exclusive forum for any (i) derivative action or proceeding brought in the name or right of the corporation or on its behalf, (ii) action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or agents to the corporation or any of our stockholders, (iii) any action arising or asserting a claim arising pursuant to any provision of Chapters 78 or 92A of the Nevada Revised Statutes or any provision of our articles of incorporation or bylaws, (iv) any action to interpret, apply, enforce or determine the validity of our articles of incorporation or bylaws or (v) any action asserting a claim governed by the internal affairs doctrine. Our Amended and Restated Articles of Incorporation further provide that any person purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed, to the fullest extent permitted by law, to have notice of and consented to the foregoing provision.

We believe the choice-of-forum provision in our Amended and Restated Articles of Incorporation will help provide for the orderly, efficient and cost-effective resolution of Nevada-law issues affecting us by designating courts located in the State of Nevada (our state of incorporation) as the exclusive forum for cases involving such issues. However, this provision may limit a stockholder's ability to bring a claim in a judicial forum that it believes to be favorable for disputes with us or our directors, officers, employees or agents, which may discourage such actions against us and our directors, officers, employees and agents. While we are not aware of any Nevada case law addressing the enforceability of this type of provision, Nevada courts have on prior occasion found persuasive authority in Delaware case law in the absence of Nevada statutory or case law specifically addressing an issue of corporate law. The Court of Chancery of the State of Delaware ruled in June 2013 that choice-of-forum provisions of a type similar to those included in our Amended and Restated Articles of Incorporation are not facially invalid under corporate law and constitute valid and enforceable contractual forum selection clauses. However, if a court were to find the choice-of-forum provision in our Amended and Restated Articles of Incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business, financial condition or results of operations.

The elimination of personal liability of our directors and officers under Nevada law and the existence of indemnification rights held by our directors, officers and employees may result in substantial expenses.

Our Amended and Restated Articles of Incorporation eliminate to the furthest extent permitted under Nevada law the personal liability of our directors and officers to us, our stockholders and creditors for damages as a result of any act or failure to act in his or her capacity as a director or officer. Further, our Amended and Restated Articles of Incorporation, our Amended and Restated Bylaws and individual indemnification agreements that we have entered with each of our directors and officers provide that we are obligated to indemnify, subject to certain exceptions, each of our directors or officers to the fullest extent authorized by Nevada law and, subject to certain conditions, to advance the expenses incurred by any director or officer in defending any action, suit or proceeding prior to its final disposition. Those indemnification obligations could expose us to substantial expenditures to cover the cost of settlement or damage awards against our directors or officers, which we may be unable to afford. Further, those provisions and resulting costs may discourage us or our stockholders from bringing a lawsuit against any of our current or former directors or officers for such damages, even if such actions might otherwise benefit our stockholders.

We do not intend to pay cash dividends on our capital stock in the foreseeable future.

We have never declared or paid any cash dividends on our common stock and do not anticipate paying any dividends in the foreseeable future. We currently intend to retain all future earnings to fund the development and growth of our business. Any future payment of cash dividends in the future will be at the discretion of our Board of Directors and will depend on, among other things, our earnings, financial condition, capital requirements, level of indebtedness, statutory and contractual restrictions applying to the payment of dividends and other considerations that the Board of Directors deems relevant. Our stockholders should not expect that we will ever pay cash or other dividends on our outstanding capital stock. Any return to our stockholders will therefore be limited to the appreciation of their stock.

We can issue and have issued shares of preferred stock, which may adversely affect the rights of holders of our common stock.

Our amended and restated Certificate of Incorporation authorizes us to issue up to 10,000,000 shares of preferred stock with designations, rights, and preferences determined from time-to-time by our Board of Directors. Accordingly, our Board of Directors is empowered, without stockholder approval, to issue preferred stock with dividend, liquidation, conversion, voting or other rights superior to those of holders of our common stock. For example, an issuance of shares of preferred stock could:

- adversely affect the voting power of the holders of our common stock;
- make it more difficult for a third party to gain control of us;
- discourage bids for our common stock at a premium;
- limit or eliminate any payments that the holders of our common stock could expect to receive upon our liquidation; or
- otherwise adversely affect the market price or our common stock.

We have in the past issued, and we may at any time in the future issue, shares of preferred stock. In connection with our June 2016 private placement, we issued 4,963 shares of our Series A convertible preferred stock to certain affiliates of Biotechnology Value Fund, L.P., or BVF, each share of which is convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. In January 2019, we entered into an exchange agreement with BVF to exchange 5,000,000 shares of our common stock previously held by BVF for 5,000 shares of our Series B convertible preferred stock, each share of which is convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. In connection with our November 2019 private placement, we issued 3,522 shares of our Series C convertible preferred stock to certain affiliates of BVF each share of which is convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. In March 2020, we entered into another exchange agreement with BVF to exchange 3,000,000 shares of our common stock previously held by BVF for 3,000 shares of our Series D convertible preferred stock, each share of which is convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. In May 2021, we entered into another exchange agreement with BVF to exchange 5,000,000 shares of our common stock previously held by BVF for 5,000 shares of our Series E convertible preferred stock, each share of which is convertible into 1,000 shares of our common stock, subject to certain ownership restrictions. If the holders of our shares of preferred stock convert their shares into common stock, existing holders of our common stock will experience dilution.

Requirements associated with being a public company have increased our costs significantly and have diverted significant company resources and management attention.

Since we are no longer an "emerging growth company" as defined in the JOBS Act, we are no longer able to take advantage of certain exemptions from various reporting requirements that were previously available to us, but which were not available to other public companies that are not emerging growth companies. Accordingly, we are now required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, increased disclosure obligations regarding executive compensation in our periodic reports and proxy statements and the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. As a result, we will incur greater expenses associated with such reporting requirements. These expenses would further increase if we ceased to be a "smaller reporting company."

Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased and will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

Having availed ourselves of scaled disclosure available to smaller reporting companies, we cannot be certain if such reduced disclosure will make our common stock less attractive to investors.

Under Rule 12b-2 of the Exchange Act, a "smaller reporting company" is a company that is not an investment company, an asset-backed issuer or a majority-owned subsidiary of a parent company that is not a smaller reporting company, and had a public float of less than $250 million as of the last business day of its most recently completed second fiscal quarter or, if such public float is less than $700 million, had annual revenues of less than $100 million during the most recently completed fiscal year. Smaller reporting companies are permitted to provide simplified executive compensation disclosure in their filings; and they have certain other decreased disclosure obligations in their SEC filings, including, among other things, only being required to provide two years of audited financial statements in annual reports. We qualify as a smaller reporting company. For as long as we continue to be a smaller reporting company, we expect that we will take advantage of the reduced disclosure obligations available to us as a result of those respective classifications. Decreased disclosure in our SEC filings as a result of our having

availed ourselves of scaled disclosure may make it harder for investors to analyze our results of operations and financial prospects.

Item 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

Item 2. PROPERTIES

In October 2018, Pieris GmbH entered into a lease initially comprising of approximately 96,400 square feet of mixed laboratory and office space in Hallbergmoos, Germany, which became our location for all German operations in February 2020. This agreement, or the Lease Agreement, provides for an initial term of 150 months, commencing on the date the lessor first delivers the leased property to Pieris GmbH as agreed under the Lease Agreement, which occurred in February 2020. Pieris GmbH and the lessor are each entitled to terminate the Lease Agreement for due cause.

We lease 3,950 square feet of office space in Boston, Massachusetts under a sublease, or the Sublease, that houses our executive offices, clinical operations and other operational functions. The Sublease was scheduled to expire on February 27, 2022 or such earlier date pursuant to the termination provisions of the Sublease. In July 2021, the Company extended the lease for this office space for an additional 10 months through December 31, 2022.

We believe that our facilities are sufficient to meet our needs and will look for suitable additional space as and when needed.

Item 3. LEGAL PROCEEDINGS

As of the date of this Annual Report on Form 10-K, we are not currently involved in any material legal proceedings. However, from time to time, we could be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Regardless of the outcome, legal proceedings can have an adverse impact on us because of defense and settlement costs, diversion of management resources, and other factors.

Item 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

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

Market Information

Our common stock is listed on The Nasdaq Stock Market LLC under the symbol "PIRS" and on June 30, 2015 our common stock began trading on The Nasdaq Capital Market.

Stockholders

As of February 24, 2022, there were 40 and 4 stockholders of record of our common stock and preferred stock, respectively. Because many of our shares are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of beneficial holders represented by these record holders.

Unregistered Sales of Securities

None.

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 consolidated financial statements and the related notes and other financial information included in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties as described under the heading "Forward-Looking Statements" elsewhere in this Annual Report on Form 10-K. You should review the disclosure under the heading "Risk Factors" in this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage biotechnology company that discovers and develops Anticalin-based drugs to target validated disease pathways in unique and transformative ways. Our clinical pipeline includes an inhaled IL-4Rα antagonist Anticalin protein to treat uncontrolled asthma, an immuno-oncology, or IO, bispecific targeting HER2 and 4-1BB, and an IO bispecific targeting PD-L1 and 4-1BB. Proprietary to us, Anticalin proteins are a novel class of therapeutics validated in the clinic and through partnerships with leading pharmaceutical companies. In particular, we have alliances with AstraZeneca and Genentech to treat respiratory diseases, with Genentech also in ophthalmology and with Servier, Seagen, and Boston Pharmaceuticals in IO. Our discovery and development programs are in varying stages and include:

- *PRS-060/AZD1402*, our lead respiratory program partnered with AstraZeneca for the treatment of asthma, is a drug candidate that antagonizes IL-4Rα, thereby inhibiting the downstream action of IL-4 and IL-13, two cytokines known to be key mediators in the inflammatory cascade that drive the pathogenesis of asthma and other inflammatory diseases.
    - PRS-060/AZD1402 was tested in a nebulized formulation and an IV arm for pharmacokinetic, or PK, assessment in 54 healthy volunteers at nominal dose levels ranging from 0.25 mg to 400 mg in a phase 1 SAD, study. Data from that study were presented at the American Thoracic Society International Conference in May 2019 showing that PRS-060/AZD1402 was well-tolerated when given as single inhaled or intravenous doses to healthy volunteers and there was systemic target engagement (as measured by pSTAT6 inhibition). We presented interim data from the PRS-060/AZD1402 phase 1 MAD study at the European Respiratory Society International Congress in October 2019 and reported that PRS-060/AZD1402 was safe and well-tolerated at all doses, led to a statistically significant

reduction in FeNO, a validated biomarker for eosinophilic airway inflammation, and showed dose-dependent systemic target engagement in patients with mild asthma and elevated levels of FeNO (≥ 35ppb).

- The phase 2a asthma study is ongoing in multiple sites globally. This phase 2a study is a two-part, multi-center, placebo-controlled clinical study of PRS-060/AZD1402 that will evaluate PRS-060/AZD1402 at up to three dose levels using a dry powder formulation administered twice daily. In part 1a (1 mg and 3 mg dose safety) of the study, 31 asthma patients, controlled on standard of care (medium dose inhaled corticosteroids (ICS) with long-acting beta agonists (LABA)), received PRS-060/AZD1402 twice daily over four weeks to establish the safety profile and pharmacokinetics of the dry powder formulation of PRS-060/AZD1402. A safety review following completion of part 1a included an evaluation, compared to placebo, of the incidence of adverse events, changes in laboratory markers (immuno-biomarkers, clinical chemistry, and hematology), and forced expiratory volume in one second (FEV1). AstraZeneca began enrollment of part 2a (1 mg and 3 mg dose efficacy) of the study to evaluate efficacy, safety, and pharmacokinetics of PRS-060/AZD1402 administered twice daily to asthma patients, uncontrolled on medium dose ICS LABA, that have a blood eosinophil count of ≥ 150 cells/μL and FeNO ≥ 25 ppb in the 1 mg and 3 mg arms and a placebo arm. Following a four-week run-in period, patients will be dosed and monitored over four weeks. FEV1 improvement compared to placebo will be the primary endpoint in this portion of the study. AstraZeneca began enrollment of part 1b (10 mg dose safety) of the study to evaluate the safety of the10 mg dose in asthma patients controlled on standard of care who will receive PRS-060/AZD1402 twice daily over four weeks. We expect to announce topline data from the phase 2a study this year, although we are actively evaluating the feasibility of study timelines in the current geopolitical environment and will update guidance in the orderly course of business, if needed. Upon receipt of the topline data and notice from AstraZeneca, including a product development plan and budget, the Company will have 30 days to opt into co-development of the program with AstraZeneca. The Company also retains a separate option to co-commercialize PRS-060/AZD1402 with AstraZeneca in the United States.

- Four discovery-stage respiratory programs were included in the AstraZeneca alliance beyond PRS-060/AZD1402, the targets and disease areas of which are undisclosed. In January2022, the Company and AstraZeneca jointly discontinued one of the four discovery-stage programs in the collaboration beyond PRS-060/AZD1402, for which they were not able to validate an exploratory target. Pieris retains co-development and co-commercialization options for two of the three remaining active discovery programs.

- Our lead fully proprietary respiratory asset, PRS-220, an oral inhaled Anticalin protein targeting connective tissue growth factor, or CTGF, is being developed as a local treatment for idiopathic pulmonary fibrosis, or IPF, and has passed the drug candidate nomination stage. We received a €14.2 million grant from the Bavarian Ministry of Economic Affairs, Regional Development and Energy supporting research and development of the program for post-acute sequelae of SARS-CoV-2 infection (PASC) pulmonary fibrosis, or PASC-PF, also known as post-COVID-19 syndrome pulmonary fibrosis, or “long COVID”.

  - PRS-220 is currently in the IND-enabling stage. We presented initial preclinical data for PRS-220 at the European Respiratory Society International Congress 2021, or ERS, demonstrating a more potent and durable target engagement profile compared to a clinical-stage, systemically delivered anti-CTGF antibody benchmark. Additionally, the targeting of CTGF locally in the lung showed increased attenuation of fibrotic lung remodeling *in vivo* compared to the systemically delivered antibody. This outcome correlates with superior lung tissue exposure of PRS-220 compared to that of the systemically administered antibody in head-to-head studies, where intratracheally administered PRS-220 efficiently penetrates the fibrotic, interstitial lung tissue of mice. Clinical development for the program is expected to begin in 2022.

- We entered into a multi-program research collaboration and license agreement with Genentech, a member of the Roche Group, to discover, develop and commercialize locally delivered respiratory and ophthalmology therapies. We have initiated joint discovery activities in each of the two committed programs.

- *Cinrebafusp alfa,* our lead IO program, is a fusion protein, comprising a HER2-targeting antibody genetically linked to 4-1BB-targeting Anticalin proteins. Cinrebafusp alfa is designed to drive tumor localized T cell activation through tumor-targeted drug clustering mediated by HER2 expressed on tumor cells. This program was the first bispecific T cell co-stimulatory agonist to enter clinical development.

  In January 2022, we dosed the first patient in our two-arm phase 2 study for cinrebafusp alfa in gastric cancer in the United States. Supported by additional data we presented from the phase 1 monotherapy study of cinrebafusp alfa in an oral presentation at the American Association for Cancer Research Virtual Congress, or AACR, in April 2021, the first arm of the phase 2 study includes the combination with ramucirumab and paclitaxel in HER2-high gastric cancer, while the second arm is in combination with tucatinib in HER2-low gastric cancer. Collaboration partners Lilly and Seagen are

supplying ramucirumab and tucatinib, respectively. The criteria for advancement of this program will evaluate a composite of measures, including a minimum target of 50% ORR in the HER2-high arm and a minimum target of 40% ORR in the HER2-low arm, duration of response, and safety. The Company expects to report initial data from the arm evaluating cinrebafusp alfa in combination with tucatinib in HER2-low gastric cancer in 2022 and expects to report data from the arm evaluating cinrebafusp alfa in combination with ramucirumab and paclitaxel in HER2-high gastric cancer in 2023. In June 2021, FDA granted orphan drug designation to cinrebafusp alfa for the treatment of HER2-high and HER2-low expressing gastric cancers.

  - The supporting data presented at AACR included an evaluation of 78 patients who had been enrolled in the monotherapy study as of the February 2021 cutoff date, including four additional patients enrolled in the active dose cohorts (≥2.5 mg/kg) since the data were presented at the ESMO Virtual Congress in September 2020. Out of 42 response-evaluable patients at the time of the data cutoff of February 25, 2021, according to RECIST 1.1, one patient with stage 4 rectal adenocarcinoma achieved a confirmed complete response at the 18 mg/kg Q2W dose (cohort 13b), four patients achieved a partial response (three at the 8 mg/kg Q2W dose (cohort 11b) and one at the 18 mg/kg Q2W dose (cohort 13b)), and stable disease was observed in 17 patients as best response out of 42 evaluable patients across the predicted active dose ranges (cohorts 9-13b), translating to an ORR of 12% and a DCR of 52%. Consistent with the mechanism of action of cinrebafusp alfa, dose-dependent immune activation was demonstrated by showing an increase in CD8+, T cell, NK cells and cytotoxic activity in the tumor microenvironment and an increase of soluble 4-1BB in the blood, indicating target engagement of 4-1BB and activation of immune cells. Cinrebafusp alfa demonstrated durable anti-tumor activity in a heavily pre-treated patient population. Additionally, clinical benefit was observed in patients with “cold” tumors as well as those with low HER2 expression who were enrolled into the study on the basis of archived HER2-status and were later re-assessed on the basis of a pre-treatment biopsy. Cinrebafusp alfa also showed an acceptable safety profile at all doses and schedules tested in the clinical study with no dose-limiting toxicities. The totality of response data generated in cohorts 11b (8 mg/kg Q2W) and 13b support the recommended phase 2 dose of a two-cycle loading dose of 18 mg/kg (Q2W), following by an 8 mg/kg dose (Q2W) in subsequent cycles.

  - The last update of the atezolizumab combination study of cinrebafusp alfa was presented at the ESMO Virtual Congress in September 2020. As of the July 2020 cutoff date, 41 patients had been enrolled and seven dose cohorts have been evaluated at a Q3W dosing schedule ranging from 0.05 mg/kg to 8 mg/kg in combination with a fixed 1200 mg dose of atezolizumab. In that trial, under RECIST 1.1, four patients achieved a confirmed partial response at active dose levels and an acceptable safety profile was observed at all doses and schedules tested in the clinical study.

- *PRS-344/S095012*, a bispecific Anticalin-antibody fusion protein comprising a PD-L1-targeting antibody genetically fused to Anticalin proteins specific for 4-1BB, is being developed as part of our IO collaboration with Servier. The first patient was dosed in the phase 1/2 study of PRS-344/S095012, a 4-1BB/PD-L1 bispecific, in November 2021.

- We are also developing additional IO drug candidates beyond cinrebafusp alfa and PRS-344/S095012 that are multi-specific Anticalin-based fusion proteins designed to engage immunomodulatory targets, comprising a variety of multifunctional biotherapeutics. Other IO drug candidates are being developed as part of our collaborations Servier, Seagen, and Boston Pharmaceuticals.

  - Servier has obtained *in vivo* proof of concept for PRS-352, an Anticalin-based bispecific beyond 4-1BB, triggering an undisclosed milestone payment to Pieris. Servier is responsible for further development of the program.

  - We achieved a key development milestone during 2020 for one of the programs in the Seagen collaboration, a bispecific tumor-targeted costimulatory agonist, triggering a $5.0 million milestone. We also handed the program over to Seagen, who is responsible for further advancement and funding of the asset. The program is one of up to three potential programs in the Seagen alliance, and we believe the achieved milestone further validates our approach and leadership in IO bispecifics, complementing the encouraging clinical data seen with cinrebafusp alfa. During the third quarter of 2021, we initiated the second program within the collaboration with Seagen. We retain a co-promotion option for one of the three programs in the Seagen collaboration in the United States.

  - We are supporting IND-readiness for PRS-342/BOS-342, a 4-1BB/GPC3 bispecific that we have exclusively licensed to Boston Pharmaceuticals, who will oversee future development of that asset.

Since inception, we have devoted nearly all of our efforts and resources to our research and development activities and have incurred significant net losses. For the years ended December 31, 2021 and 2020, we reported net losses of $45.7 million and

$37.2 million, respectively. As of December 31, 2021, we had an accumulated deficit of $257.1 million. We expect to continue incurring substantial losses for the next several years as we continue to develop our clinical and preclinical drug candidates and programs. Our operating expenses are comprised of research and development expenses and general and administrative expenses.

We have not generated any revenues from product sales to date, and we do not expect to generate revenues from product sales for the foreseeable future. Our revenues for the fiscal years ended December 31, 2021 and 2020 were from license and collaboration agreements with our partners.

A significant portion of our operations are conducted in countries other than the United States. Since we conduct our business in U.S. dollars, our main exposure, if any, results from changes in the exchange rates between the euro and the U.S. dollar. At each period end, we remeasure assets and liabilities to the functional currency of that entity (for example, U.S. dollar payables recorded by Pieris Pharmaceuticals GmbH). Remeasurement gains and losses are recorded in the statement of operations line item 'Other income (expense), net'. All assets and liabilities denominated in euros are translated into U.S. dollars at the exchange rate on the balance sheet date. Revenues and expenses are translated at the weighted average rate during the period. Equity transactions are translated using historical exchange rates. All adjustments resulting from translating foreign currency financial statements into U.S. dollars are included in accumulated other comprehensive income (loss).

Key Financial Terms and Metrics

The following discussion summarizes the key factors our management believes are necessary for an understanding of our consolidated financial statements.

Revenues

We have not generated any revenues from product sales to date and we do not expect to generate revenues from product sales for the foreseeable future. Our revenues for the last two years have been from the license and collaboration agreements with AstraZeneca, Servier, Seagen, Genentech and Boston Pharmaceuticals.

The revenues from AstraZeneca, Servier, Seagen, Genentech and Boston Pharmaceuticals. have been comprised primarily of upfront payments, research and development services and milestone payments. For additional information about our revenue recognition policy, see "Note 2-Summary of Significant Accounting Policies".

Research and Development Expenses

The process of researching and developing drugs for human use is lengthy, unpredictable, and subject to many risks. We expect to continue incurring substantial expenses for the next several years as we continue to develop our clinical and preclinical drug candidates and programs. We are unable, with any certainty, to estimate either the costs or the timelines in which those expenses will be incurred. Our current development plans focus on the following programs: our lead respiratory program, PRS-060/AZD1402 and our proprietary respiratory program, PRS-220, our IO programs, currently comprised of cinrebafusp alfa as well as multiple additional proprietary and partnered programs, including PRS-344/S095012. These programs consume a large proportion of our current, as well as projected, resources.

Our research and development costs include costs that are directly attributable to the creation of certain of our Anticalin drug candidates and are comprised of:

- internal recurring costs, such as personnel-related costs (salaries, employee benefits, equity compensation and other costs), materials and supplies, facilities and maintenance costs attributable to research and development functions; and
- fees paid to external parties who provide us with contract services, such as preclinical testing, manufacturing and related testing and clinical trial activities.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, employee benefits, equity compensation, and other personnel-related costs associated with executive, administrative and other support staff. Other significant general and administrative expenses include the costs associated with professional fees for accounting, auditing, insurance costs, consulting and legal services, along with facility and maintenance costs attributable to general and administrative functions.

Results of Operations

Comparison of Years Ended December 31, 2021 and December 31, 2020

The following table sets forth our revenues and operating expenses for the fiscal years ended December 31, 2021 and 2020 (in thousands):

	Years ended December 31,	
	2021	2020
Revenues	$ 31,418	$ 29,323
Research and development expenses	66,656	46,531
General and administrative expenses	16,593	16,713
Total operating expenses	83,249	63,244
Interest income	4	511
Grant income	3,685	—
Other (expense) income , net	2,404	(3,656)
Loss before income taxes	(45,738)	(37,066)
Benefit for income tax	—	164
Net loss	$ (45,738)	$ (37,230)

Revenues

The following table provides a comparison of revenues for the years ended December 31, 2021 and 2020 (in thousands):

	Years ended December 31,		
	2021	2020	Increase/(Decrease)
Customer revenue	$ 27,940	$ 23,911	$ 4,029
Collaboration revenue	3,478	5,412	$ (1,934)
Total Revenue	$ 31,418	$ 29,323	$ 2,095

- The $4.0 million increase in customer revenue for the year ended December 31, 2021 compared to the year ended December 31, 2020 is driven by the following:
  - Higher revenue in the current year for the phase 2a milestone ($13.0 million) recognized for PRS-060/AZD1402 under the AstraZeneca collaboration, revenue attributed to two new collaboration agreements, Genentech ($2.0 million) and Boston Pharmaceuticals ($5.7 million) and the achievement of a preclinical milestone on PRS-352.
  - Lower Seagen revenue as there was an achievement of a $5.0 million milestone on the first collaboration program recorded in 2020 along with the impact of the execution of a contractual amendment (approximately $3.5 million) in the same year.
  - Lower Servier revenue as the prior year included recognition of amounts for a preclinical stage product that is not being pursued under the Servier collaboration.
- Collaboration revenue decreased by $1.9 million in the year ended December 31, 2021 compared to the year ended December 31, 2020. The decrease relates to revenue recognized in the prior year on a preclinical stage product that Servier declined to pursue further, offset slightly by higher Servier cost-sharing revenue generated from higher levels of manufacturing costs incurred on PRS-344/S095012.

Research and Development Expenses

The following table provides a comparison of the research and development expenses for the years ended December 31, 2021 and 2020 (in thousands):

	Years ended December 31,		
	2021	2020	Increase/(Decrease)
Immuno-oncology	$ 23,210	$ 12,386	$ 10,824
Respiratory	17,158	9,677	$ 7,481
Other R&D activities	26,288	24,468	$ 1,820
Total	$ 66,656	$ 46,531	$ 20,125

- The $10.8 million increase in our immuno-oncology program spending period-over-period is due primarily to an increase in clinical and manufacturing costs for cinrebafusp alfa and higher manufacturing costs for PRS-344/S095012, all partially offset by lower preclinical costs across a number of programs.
- The $7.5 million increase for our respiratory programs period-over-period is due to higher manufacturing costs for PRS-220, increased preclinical work on a number of early stage programs as well as higher license fees, offset partially by lower clinical and manufacturing costs with respect to activities for PRS-060/AZD1402.
- The $1.8 million increase in other research and development activities expenses is mainly due primarily to higher personnel and recruiting costs due to higher headcount, higher external consulting and higher license fees, offset slightly by lower lab consumable costs and lower facility costs due to the move to the new R&D facility in Hallbergmoos, Germany in the prior year.

General and Administrative Expenses

General and administrative expenses was $16.6 million for the year ended December 31, 2021 as compared to $16.7 million for the year ended December 31, 2020. The period-over-period decrease is due primarily to lower legal, accounting and project management costs, along with lower one-time office and building equipment costs related to the move to the new R&D facility in Hallbergmoos, Germany in the prior year. These reductions in cost were offset by higher fixed and variable compensation and higher insurance costs.

Other income (expense), net

Our other income was $6.1 million for the year ended December 31, 2021 as compared to a other expense of $3.1 million for the year ended December 31, 2020. This period-over-period increase was primarily due to $3.7 million of grant income recorded on PRS-220 as well as foreign exchange realized gains due to a strengthening U.S. dollar compared to the same period in the prior year.

Liquidity and Capital Resources

We are subject to risks common to companies in the biotechnology industry, including but not limited to, the need for additional capital, risks of failure of preclinical studies and clinical trials, the need to obtain marketing approval and reimbursement for any drug product candidate that we may identify and develop, the need to successfully commercialize and gain market acceptance of our product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development of technological innovations by competitors, reliance on third-party manufacturers and the ability to transition from pilot-scale production to large-scale manufacturing of products.

Through December 31, 2021, we have funded our operations with $568.0 million of cash that has been obtained from the following main sources: $276.0 million from sales of equity; $270.6 million in total payments received under license and collaboration agreements, including $52.9 million for research and development services costs received from our collaboration partners; $14.8 million from government grants and $6.5 million from loans.

As of December 31, 2021, we had a total of $117.8 million in cash and cash equivalents. We have incurred losses in every period since inception including the years ended December 31, 2021 and 2020, respectively, and have a total accumulated deficit of $257.1 million as of December 31, 2021. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. We expect to continue to incur operating losses for at least the next several years.

The following table provides a summary of operating, investing, and financing cash flows for the years ended December 31, 2021 and 2020 respectively (in thousands):

	Years ended December 31,	
	2021	2020
Net cash used in operating activities	$ (7,660)	$ (45,896)
Net cash (used in) provided by investing activities	(949)	39,212
Net cash provided by financing activities	59,127	10,115

Net cash used in operating activities for the year ended December 31, 2021 and 2020 was $7.7 million and $45.9 million, respectively. Lower operating cash used in 2021 was benefited by higher deferred revenue, primarily driven by the new collaboration agreement with Genentech, and higher accounts payable and accrued expenses, offset partially by higher accounts receivables and prepaid expenses. This compares to the impact of lower accounts payable, accrued expenses and deferred revenue, primarily driven by revenue recognized for the discontinued Servier programs and the satisfaction of a performance obligation under the Seagen agreements, for the year ended December 31, 2020. Offsetting the impact from changes in operating assets and liabilities was an increase in the net loss in 2021 compared to the same timeframe in 2020.

The change in net cash used in investing activities for the year ended December 31, 2021 compared to net cash provided by investing activities the same period in 2020 is mainly attributable to the impact of net investments changes (purchases and maturities of available-for-sale securities) for which there is no activity in the comparable current year period. Additionally, purchases of property and equipment were lower as the 2020 purchases primarily related to our move to a new R&D facility.

Financing activities for the year ended December 31, 2021 and 2020 provided cash of $59.1 million and $10.1 million, respectively. The increase in 2021 compared to 2020 is driven by equity investments from both Seagen and AstraZeneca (see Note 3), higher sales activity under our ATM programs and higher proceeds received from warrant and option exercises. There was limited option exercise activity for the same period in 2020.

In August 2019, we entered into a sales agreement pursuant to which we may offer and sell shares of its common stock, from time to time, up to an aggregate gross sales proceeds of $50.0 million through an “at the market offering” program, or the 2019 ATM Program, under a shelf registration statement on Form S-3 (File No. 333-226725). In August 2021, the 2019 ATM Program expired.

In August 2021, we established a second ATM offering program, or the 2021 ATM Program, under the existing sales agreement with Jefferies LLC, pursuant to which the Company may offer and sell shares of its common stock, from time to time, up to an aggregate amount of gross sales proceeds of $50.0 million. The 2021 ATM Program is offered under a shelf registration statement on Form S-3 that was filed with and declared effective by the SEC in August 2021. For the year ended December 31, 2021, we sold 8.2 million shares for gross proceeds of $39.7 million under both ATM programs at an average stock price of $4.85. For the year ended December 31, 2020, we sold 3.6 million shares at a price of $2.80 per share resulting in gross proceeds of $10.0 million under the 2019 ATM Program only.

In March 2021, we amended our strategic collaboration agreement with Seagen which resulted in their purchase of $13.0 million of our common stock (See Note 3). In March 2021, we also earned a $13.0 million milestone from AstraZeneca related to the initiation of the phase 2a study for PRS-060/AZD1402 and AstraZeneca agreed to purchase $10.0 million of our common stock (See Note 3).

Our future success is dependent on our ability to identify and develop our product candidates, expand our corporate infrastructure and ultimately upon our ability to attain profitable operations. We have devoted substantially all of our financial resources and efforts to research and development and general and administrative expenses to support such research and development. We have several research and development programs underway in varying stages of development and we expect that these programs will continue to require increasing amounts of cash for development, conducting clinical trials, and testing and manufacturing of product material. Cash necessary to fund operations will increase significantly over the next several years as we continue to conduct these activities necessary to pursue governmental regulatory approval of clinical-stage programs and other product candidates.

Any requirements for additional capital will depend on many factors, including the following:

- the scope, rate of progress, results and cost of our clinical studies, preclinical testing and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our drug candidates and any products that we may develop;
- the number and characteristics of drug candidates that we pursue;
- the cost, timing and outcomes of regulatory approvals;

- the cost and timing of establishing sales, marketing and distribution capabilities;
- the terms and timing of any collaborative, licensing and other arrangements that we may establish;
- the timing, receipt and amount of sales, profit sharing or royalties, if any, from our potential products;
- the cost of preparing, filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the extent to which we acquire or invest in businesses, products or technologies, although we currently have no commitments or agreements relating to any of these types of transactions; and
- the effects of the COVID-19 pandemic and the cost and timing of actions taken to contain it.

In addition, any unfavorable development or delay in the progress of our core clinical-stage programs including cinrebafusp alfa and PRS-060/AZD1402 could have a material adverse impact on our ability to raise additional capital.

We plan to raise additional capital to fulfill our operating and capital requirements through public or private equity financings, utilization of our ATM program, strategic collaborations, licensing arrangements, and/or the achievement of milestones under our collaborative agreements. The funding requirements of our operating plans, however, are based on estimates that are subject to risks and uncertainties and may change as a result of many factors currently unknown. Although we continue to pursue these funding plans, there is no assurance that we will be successful in obtaining sufficient funding on terms acceptable to us to fund continuing operations, if at all. Until such time as we can generate substantial product revenues, if ever, we expect to finance our cash needs through a combination of equity offerings, debt financings, strategic partnerships and licensing arrangements. The terms of any future financing may adversely affect the holdings or the rights of our existing stockholders.

We believe that our currently available funds will be sufficient to fund our operations through at least the next twelve months from the issuance of this Annual Report on Form 10-K. Our belief with respect to our ability to fund operations is based on estimates that are subject to risks and uncertainties. If actual results are different from our estimates, we may need to seek additional funding. If we are unable to obtain additional funding on acceptable terms when needed, we may be required to defer or limit some or all of our research, development, and/or clinical projects

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements, as defined under applicable SEC rules.

Critical Accounting Policies and Estimates

The discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these financial statements requires management to make estimates and judgments that affect reported amounts of assets and liabilities as of the date of the balance sheet and reported amounts of revenues and expenses for the periods presented. Management makes estimates and exercises judgment in revenue recognition, accrued and prepaid clinical trial expenses, share-based payments and income taxes. Judgments must also be made about the disclosure of contingent liabilities, and these estimates and assumptions form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. Actual results may differ from those estimates and under different assumptions or conditions.

While our significant accounting policies are more fully described in the notes to our consolidated financial statements, we have identified the following accounting policies that we believe require application of management's most subjective judgments, often requiring the need to make estimates about the effect of matters that are inherently uncertain and may change in subsequent periods. Our actual results could differ from these estimates and such differences could be material.

Revenue Recognition

Pieris has entered into several licensing agreements with collaboration partners for the development of Anticalin therapeutics against a variety of targets. The terms of these agreements provide for the transfer of multiple goods or services which may include: (i) licenses, or options to obtain licenses, to Pieris' Anticalin technology and/or specific programs and (ii) research and development activities to be performed on behalf of or with a collaborative partner. Payments to Pieris under these agreements may include upfront fees (which include license and option fees), payments for research and development activities, payments

based upon the achievement of certain milestones, and royalties on product sales. There are no performance, cancellation, termination or refund provisions in any of the arrangements that could result in material financial consequences to Pieris.

The Company accounts for revenue recognition pursuant to FASB ASC Topic 606, Revenue Recognition, or ASC 606. The standard requires a company to recognize revenue when it transfers goods or services to customers in an amount that reflects the consideration that the company expects to receive for those goods or services.

Collaborative Arrangements

We consider the nature and contractual terms of an arrangement and assess whether the arrangement involves a joint operating activity pursuant to which we are an active participant and are exposed to significant risks and rewards with respect to the arrangement. If we are an active participant and are exposed to the significant risks and rewards with respect to the arrangement, we account for these arrangements pursuant to ASC 808, *Collaborative Arrangements*, or ASC 808, and apply a systematic and rational approach to recognize revenue. We classify payments received as revenue and payments made as a reduction of revenue in the period in which they are earned.

Revenue from Contracts with Customers

In accordance with ASC 606, revenue is recognized when a customer obtains control of promised goods or services. The amount of revenue recognized reflects the consideration to which we expect to be entitled in exchange for these goods and services. To achieve this core principle, we apply the following five steps: 1) identify the customer contract; 2) identify the contract's performance obligations; 3) determine the transaction price; 4) allocate the transaction price to the performance obligations; and 5) recognize revenue when or as a performance obligation is satisfied.

We evaluate all promised goods and services within a customer contract and determines which of such goods and services are separate performance obligations. This evaluation includes an assessment of whether the good or service is capable of being distinct and whether the good or service is separable from other promises in the contract. In assessing whether promised goods or services are distinct, we consider factors such as the stage of development of the underlying intellectual property and the capabilities of the customer to develop the intellectual property on their own or whether the required expertise is readily available.

Licensing arrangements are analyzed to determine whether the promised goods or services, which often include licenses, research and development services and governance committee services, are distinct or whether they must be accounted for as part of a combined performance obligation. If the license is considered not to be distinct, the license would then be combined with other promised goods or services as a combined performance obligation. If we are involved in a governance committee, we assess whether our involvement constitutes a separate performance obligation. When governance committee services are determined to be separate performance obligations, we determine the fair value to be allocated to this promised service.

Certain contracts contain optional and additional items, which are considered marketing offers and are accounted for as separate contracts with the customer if such option is elected by the customer, unless the option provides a material right which would not be provided without entering into the contract. An option that is considered a material right is accounted for as a separate performance obligation.

The transaction price is determined based on the consideration to which we will be entitled in exchange for transferring goods and services to the customer. A contract may contain variable consideration, including potential payments for both milestone and research and development services. For certain potential milestone payments, we estimate the amount of variable consideration by using the most likely amount method. In making this assessment, we evaluate factors such as the clinical, regulatory, commercial and other risks that must be overcome to achieve the milestone. Each reporting period we re-evaluate the probability of achievement of such variable consideration and any related constraints. We will include variable consideration, without constraint, in the transaction price to the extent it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. For potential research and development service payments, we estimate the amount of variable consideration by using the expected value method, including any approved budget updates arising from additional research or development services.

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price among the performance obligations on a relative standalone selling price basis unless a portion of the transaction price is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct good or service that forms part of a single performance obligation.

We allocate the transaction price based on the estimated standalone selling price of the underlying performance obligations or in the case of certain variable consideration to one or more performance obligations. We must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. We utilize key assumptions to determine the stand-alone selling price, which may include other comparable transactions, pricing considered in negotiating the transaction and the estimated costs to complete the respective performance obligation. Certain variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration relate to the satisfaction of the performance obligation and the resulting amounts allocated to each performance obligation are consistent with the amount we would expect to receive for each performance obligation.

When a performance obligation is satisfied, revenue is recognized for the amount of the transaction price, excluding estimates of variable consideration that are constrained, that is allocated to that performance obligation on a relative standalone selling price basis. Significant management judgment is required in determining the level of effort required under an arrangement and the period over which we are expected to complete its performance obligations under an arrangement.

For performance obligations consisting of licenses and other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non- refundable, up-front fees. We evaluate the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we will recognize revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license.

Milestones and Royalties

We aggregate milestones into four categories: (i) research milestones, (ii) development milestones, (iii) commercial milestones, and (iv) sales milestones. Research milestones are typically achieved upon reaching certain success criteria as defined in each agreement related to developing an Anticalin protein against the specified target. Development milestones are typically reached when a compound reaches a defined phase of clinical research or passes such phase or upon gaining regulatory approvals. Commercial milestones are typically achieved when an approved pharmaceutical product reaches the status for commercial sale, including regulatory approval. Sales milestones are certain defined levels of net sales by the licensee, such as when a product first achieves global sales or annual sales of a specified amount.

There is uncertainty that the events to obtain the research and development milestones will be achieved given the nature of clinical development and the stage of our technology. We have thus determined that all research and development milestones will be constrained until it is deemed probable that a significant revenue reversal will not occur. For revenues from research and development milestones, payments will be recognized consistent with the recognition pattern of the performance obligation to which they relate.

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, 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). Commercial milestones and sales royalties are determined by sales or usage-based thresholds and will be accounted for under the royalty recognition constraint as constrained variable consideration.

Contract Balances

We recognize a contract asset when we transfer goods or services to a customer before the customer pays consideration or before payment is due, excluding any amounts presented as a receivable (i.e., accounts receivable). A contract asset is an entity’s right to consideration in exchange for goods or services that the entity has transferred to a customer. The contract liabilities (i.e., deferred revenue) primarily relate to contracts where we have received payment but has not yet satisfied the related performance obligations.

Contingencies

Accruals are recorded for loss contingencies when it is probable that a liability has been incurred and the amount of the related loss can be reasonably estimated. We evaluate, on a quarterly basis, developments in legal proceedings and other matters that could cause an increase or decrease in the amount of the liability that has been accrued previously. Considering facts known at the time of the assessment, we determine whether potential losses are considered reasonably possible or probable and whether

they are estimable. Based upon this assessment, we carry out an evaluation of disclosure requirements and consider possible accruals in the financial statements.

Research and Development Expense

Research and development costs are charged to expense as incurred in performing research and development activities. Research and development expenses are comprised of costs incurred in performing research and development activities, including salaries and benefits, facilities costs, pre-clinical and clinical costs, contract services, consulting, depreciation and amortization expense, and other related costs. Costs associated with acquired technology, in the form of upfront fees or milestone payments, are charged to research and development expense as incurred.

Income Taxes

Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases, and operating losses and tax credit carry forwards. Deferred tax assets and liabilities are measured using enacted statutory tax rates expected to apply to taxable income in the jurisdictions and years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

We evaluate the realizability of our net deferred tax assets, including considering the level of historical operating results and projections of taxable income for the future. We record a full valuation allowance to reduce our net deferred tax assets when it is determined that it is more likely than not that our net deferred tax assets will not be realized.

We recognize, measure, present and disclose in our financial statements any uncertain tax positions that we have taken or expect to take on a tax return. We operate in multiple jurisdictions, both within and outside the United States, and may be subject to audits from various tax authorities. Management's judgment is required in determining our provision for income taxes, our deferred tax assets and liabilities, liabilities for uncertain tax positions, and any valuation allowance recorded against our net deferred tax assets. We will monitor the extent to which our deferred tax assets may be realized and adjust the valuation allowance accordingly.

Our policy is to classify interest and penalties related to unrecognized tax benefits as income tax expense.

Recently Issued Accounting Pronouncements

We review new accounting standards to determine the expected financial impact, if any, that the adoption of each standard will have. For the recently issued accounting standards that we believe may have an impact on our consolidated financial statements, see "Note 2—Summary of Significant Accounting Policies" in our consolidated financial statements.

Smaller Reporting Company Status

Currently, we qualify as a smaller reporting company.

As a smaller reporting company, we are eligible and have taken advantage of certain exemptions from various reporting requirements that are not available to public reporting companies that do not qualify for this classification, including, but not limited to:

- An opportunity for reduced disclosure obligations regarding executive compensation in our periodic and annual reports, including without limitation exemption from the requirement to provide a compensation discussion and analysis describing compensation practices and procedures,
- An opportunity for reduced financial statement disclosure in registration statements and in annual reports on Form 10-K, which only requires two years of audited financial statements rather than the three years of audited financial statements that are required for other public companies,
- An opportunity for reduced audit and other compliance expenses as we are not subject to the requirement to obtain an auditor's report on internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act of 2002, and
- An opportunity to utilize the non-accelerated filer time-line requirements beginning with our annual report for the year ending December 31, 2020 and quarterly filings thereafter.

For as long as we continue to be a smaller reporting company, we expect that we will take advantage of both the reduced internal control audit requirements and the disclosure obligations available to us as a result of this classification.

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.

Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Our Consolidated Financial Statements required by this Item are as set forth in Item 15 beginning on page F-3 of this Annual Report on Form 10-K.

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

Not applicable.

Item 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management is responsible for establishing and maintaining "disclosure controls and procedures" as such term is defined in Rule 13a-15(e) of the Exchange Act, as well as for establishing and maintaining "adequate internal control over financial reporting" as such term is defined in Rule 13a-15(f) under the Exchange Act. Our system of internal controls over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of the consolidated financial statements in accordance with generally accepted accounting principles.

Because of the inherent limitations surrounding internal controls over financial reporting, our disclosure controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the disclosure controls and procedures are met. Additionally, in designing disclosure controls and procedures, our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible disclosure controls and procedures. The design of any disclosure controls and procedures also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions.

A material weakness is a deficiency, or a combination of deficiencies, in internal controls over financial reporting, such that there is a reasonable possibility that a material misstatement of a company's annual or interim consolidated financial statements would not be prevented or detected on a timely basis.

Our management, under the supervision of and with the participation of our principal executive officer and principal financial officer, assessed the effectiveness of our internal control over financial reporting and disclosure controls and procedures as of December 31, 2021. In making this assessment, management used the updated criteria set forth in 2013 by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, in Internal Control-Integrated Framework.

Based on our assessment under the COSO Internal Control-Integrated Framework, management believes that, as of December 31, 2021, our disclosure controls and procedures and internal control over financial reporting were effective.

Management, including our principal executive officer and principal financial officer, has concluded that the financial statements and other financial information included in this Annual Report on Form 10-K fairly present in all material respects our financial condition, results of operations and cash flows as of, and for, the periods presented.

Changes in Internal Control over Financial Reporting

There have been no changes in internal control over financial reporting identified in connection with the evaluation of such internal control required by Rules 13a-15(d) and 15d-15(d) under the Exchange Act that occurred during the fourth quarter of 2021 have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. OTHER INFORMATION

Not applicable.

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 10 is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2021.

Item 11. EXECUTIVE COMPENSATION

The information required by this Item 11 is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2021.

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

The information required by this Item 12 is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2021.

Item 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this Item 13 is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2021.

Item 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item 14 is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2021.

PART IV

Item 15. **EXHIBITS, FINANCIAL STATEMENT SCHEDULES**

Item 15(a). The following documents are filed as part of this Annual Report on Form 10-K:

Item 15(a)(1) and (2) See "Index to Consolidated Financial Statements" on page F-1 to this Annual Report on Form 10-K. Other financial statement schedules have not been included because they are not applicable or the information is included in the financial statements or notes thereto.

Item 15(a)(3) Exhibits

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Number	Exhibit Description		Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
2.1	Acquisition Agreement, dated as of December 17, 2014, by and among the Registrant, Pieris AG and the former stockholders of Pieris AG named therein		Form 8-K (Exhibit 2.1)	December 18, 2014	333-190728
3.1	Amended and Restated Articles of Incorporation of the Registrant		Form 8-K (Exhibit 3.1)	December 18, 2014	333-190728
3.2	Certificate of Designation of Series A Convertible Preferred Stock		Form 10-Q (Exhibit 3.1)	August 11, 2016	001-37471
3.3	Certificate of Designation of Series B Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	February 4, 2019	001-37471
3.4	Certificate of Designation of Series C Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	November 4, 2019	001-37471
3.5	Certificate of Designation of Series D Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	April 6, 2020	001-37471
3.6	Certificate of Designation of Series E Convertible Preferred Stock		Form 8-K (Exhibit 3.1)	May 21, 2021	001-37471
3.7	Amended and Restated Bylaws of the Registrant		Form 8-K (Exhibit 3.2)	December 18, 2014	333-190728
3.8	Amendment to the Amended and Restated Bylaws of the Registrant		Form 8-K (Exhibit 3.1)	September 3, 2019	001-37471
4.1	Form of Common Stock certificate		Form 8-K (Exhibit 4.1)	December 18, 2014	333-190728
4.2	Form of Common Stock certificate		Form 10-K (Exhibit 4.2)	March 23, 2016	001-37471
4.3	Description of Registered Securities		Form 10-K (Exhibit 4.3)	March 13, 2020	001-37471
10.1	2014 Employee, Director and Consultant Equity Incentive Plan	#	Form 8-K (Exhibit 10.1)	December 18, 2014	333-190728
10.2	Form of Stock Option Award Agreement under the Registrant's 2014 Employee, Director and Consultant Equity Incentive Plan	#	Form 8-K (Exhibit 10.2)	December 18, 2014	333-190728
10.3	2016 Employee, Director and Consultant Equity Incentive Plan	#	Form 8-K (Exhibit 10.1)	July 1, 2016	001-37471
10.4	Form of Stock Option Award Agreement under the Registrant's 2016 Employee, Director and Consultant Equity Incentive Plan	#	Form 10-K (Exhibit 10.4)	March 30, 2017	001-37471
10.5	2018 Employee, Director and Consultant Equity Incentive Plan	#	Form 8-K (Exhibit 10.1)	July 26, 2018	001-37471

10.6	Form of Stock Option Award Agreement under the Registrant's 2018 Employee, Director and Consultant Equity Incentive Plan	#	Form S-8 (Exhibit 10.2)	August 9, 2018	333-226733
10.7	Form of Stock Option Award Agreement under the Registrant's 2020 Employee, Director and Consultant Equity Incentive Plan	#	Form S-8 (Exhibit 10.2)	August 5, 2021	333-258502
10.8	2018 Employee Stock Purchase Plan	#	Form 8-K (Exhibit 10.2)	July 26, 2018	001-37471
10.9	2019 Employee, Director and Consultant Equity Incentive Plan	#	Form 8-K (Exhibit 10.1)	July 31, 2019	001-37471
10.10	2020 Employee, Director and Consultant Equity Incentive Plan	#	Form 8-K (Exhibit 10.1)	June 29, 2020	001-37471
10.11	2020 Employee, Director and Consultant Equity Incentive Plan, as amended	#	Form 8-K (Exhibit 10.1)	June 29, 2021	001-37471
10.12	Research and Licensing Agreement by and between Pieris AG and Technische Universität München, dated as of July 26, 2007	±	Form 10-K (Exhibit 10.10)	March 30, 2015	333-190728
10.13	License and Transfer Agreement by and between the Company and Enumeral Biomedical Holdings, Inc dated as of April 18, 2016	±	Form 10-Q/A (Exhibit 10.1)	July 20, 2016	001-37471
10.14	Definitive License and Transfer Agreement by and between the Company and Enumeral Biomedical Holdings, Inc. dated as of June 6, 2016	±	Form 10-Q (Exhibit 10.1)	August 11, 2016	001-37471
10.15	Amendment No.1 to Definitive License and Transfer Agreement by and between the Company and Enumeral Biomedical Holdings, Inc. effective as of January 3, 2017		Form 10-K (Exhibit 10.14)	March 30, 2017	001-37471
10.16	Collaboration Agreement by and among the Registrant, Pieris Pharmaceuticals GmbH, Les Laboratoires Servier and Institut de Recherches Internationales Servier, dated as of January 4, 2017	±	Form 10-K/A (Exhibit 10.15)	April 26, 2018	001-37471
10.17	Non-Exclusive Anticalin Platform Technology License Agreement by and among the Registrant, Pieris Pharmaceuticals GmbH, Les Laboratoires Servier and Institut de Recherches Internationales Servier, dated as of January 4, 2017	±	Form 10-K/A (Exhibit 10.16)	April 26, 2018	001-37471
10.18	First Amendment to the License and Collaboration Agreement by and between Les Laboratoires Servier, Institut de Recherches Internationales Servier, Pieris Pharmaceuticals, Inc. and Pieris Pharmaceuticals GmbH, effective as of June 16, 2017	±	Form 10-Q/A (Exhibit 10.4)	April 26, 2018	001-37471
10.19	Letter Amendment to the License and Collaboration Agreement by and between Les Laboratoires Servier, Institut de Recherches Internationales Servier, Pieris Pharmaceuticals, Inc. and Pieris Pharmaceuticals GmbH, effective as of January 3, 2020	+	Form 10-K (Exhibit 10.16)	March 13, 2020	001-37471

10.20	License & Collaboration Agreement by and between Pieris Pharmaceuticals Inc., Pieris Pharmaceuticals GmbH & Pieris Australia Pty. Limited and AstraZeneca AB, dated as of May 2, 2017	±	Form 10-Q/A (Exhibit 10.1)	April 26, 2018	001-37471
10.21	Amendment No. 2, dated March 29, 2021, to the License & Collaboration Agreement by and between the Registrant and AstraZeneca AB	±	Form 10-Q (Exhibit 10.4)	May 17, 2021	001-37471
10.22	Non-Exclusive Anticalin® Platform Technology License Agreement, by and between Pieris Pharmaceuticals Inc., Pieris Pharmaceuticals GmbH and Pieris Australia Pty. Limited and AstraZeneca AB, dated as of May 2, 2017	±	Form 10-Q/A (Exhibit 10.2)	April 26, 2018	001-37471
10.23	Amendment No. 1, dated March 29, 2021, to the Non-Exclusive Anticalin® Platform Technology License Agreement, dated May 2, 2017, by and between the Registrant and AstraZeneca AB	±	Form 10-Q (Exhibit 10.5)	May 17, 2021	001-37471
10.24	Subscription Agreement, dated March 29, 2021, by and between the Registrant and AstraZeneca AB	±	Form 10-Q (Exhibit 10.6)	May 17, 2021	001-37471
10.25	License and Collaboration Agreement by and among the Registrant, Pieris GmbH and Seagen, Inc., dated February 8, 2018	±	Form 10-Q (Exhibit 10.1)	May 10, 2018	001-37471
10.26	Amendment No. 1 to License and Collaboration Agreement by and among the Registrant, Pieris GmbH and Seagen, Inc., dated June 2, 2020		Form 10-Q (Exhibit 10.3)	August 10, 2020	001-37471
10.27	Amended and Restated License and Collaboration Agreement, dated March 24, 2021, by and between the Registrant and Seagen Inc.		Form 10-Q (Exhibit 10.1)	May 17, 2021	001-37471
10.28	Combination Study Agreement, dated March 24, 2021, by and between the Registrant and Seagen Inc.		Form 10-Q (Exhibit 10.2)	May 17, 2021	001-37471
10.29	Subscription Agreement, dated March 24, 2021, by and between the Registrant and Seagen Inc.		Form 10-Q (Exhibit 10.3)	May 17, 2021	001-37471
10.30	Non-Exclusive Anticalin Platform Technology License Agreement by and among the Registrant, Pieris Pharmaceuticals GmbH and Seagen, Inc., dated February 8, 2018	±	Form 10-Q (Exhibit 10.2)	May 10, 2018	001-37471
10.31	Amendment No. 1 to Non-Exclusive Anticalin Platform Technology License Agreement by and among the Registrant, Pieris Pharmaceuticals GmbH and Seagen, Inc., dated June 2, 2020		Form 10-Q (Exhibit 10.3	August 10, 2020	001-37471
10.32	Clinical Trial Collaboration and Supply Agreement by and among the Registrant and Eli Lilly and Company, dated August 10, 2020		Form 10-Q (Exhibit 10.1)	November 4, 2020	001-37471
10.33	Exclusive Product License Agreement, dated April 24, 2021, by and among the Registrant, Pieris Pharmaceuticals GmbH and BP Asset XII, Inc.		Form 10-Q (Exhibit 10.1)	August 5, 2021	001-37471

10.34	Research Collaboration and License Agreement, dated May 19, 2021, by and among the Registrant, Pieris Pharmaceuticals GmbH and Genentech, Inc.		Form 10-Q (Exhibit 10.3)	August 5, 2021	001-37471
10.35	Form of Indemnification Agreement by and between the Registrant and each of its current directors and executive officers	#	Form 8-K (Exhibit 10.10)	December 18, 2014	333-190728
10.36	Employment Agreement by and between the Registrant and Stephen S. Yoder, dated as of December 17, 2014	#	Form 8-K (Exhibit 10.15)	December 18, 2014	333-190728
10.37	Employment Agreement by and between the Registrant and Ahmed Mousa, dated as of October 7, 2021	#	Form 10-Q (Exhibit 10.1)	November 2, 2021	001-37471
10.38	Employment Agreement by and between the Registrant and Tom Bures, dated as of October 7, 2021	#	Form 10-Q (Exhibit 10.2)	November 2, 2021	001-37471
10.39	Non-Employee Director Compensation Policy, as amended	*#			
10.40	Agreement of Sublease by and between Berenberg Capital Markets LLC and the Registrant, dated as of August 27, 2015		Form 10-Q (Exhibit 10.3)	November 13, 2015	001-37471
10.41	Subtenant Recognition and Attornment Agreement, by and among Pieris Pharmaceuticals, Inc., 225 State Street, LLC, and Berenberg Capital Markets LLC, dated as of May 31, 2019		Form 10-Q (Exhibit 10.29.1)	August 9, 2019	001-37471
10.42	Lease Agreement by and between Pieris GmbH and Hallbergmoos Grundvermögen GmbH, dated October 24, 2018		Form 10-K (Exhibit 10.30)	March 18, 2019	001-37471
10.43	Amendment No. 1 to Lease Agreement by and between Pieris GmbH and Hallbergmoos Grundvermögen GmbH, dated May 21, 2019 (English translation)		Form 10-K (Exhibit 10.31)	March 13, 2020	001-37471
10.44	Amendment No. 2 to Lease Agreement by and between Pieris GmbH and Hallbergmoos Grundvermögen GmbH, dated February 13, 2020 (English translation)		Form 10-K (Exhibit 10.32)	March 13, 2020	001-37471
10.45	Form of Securities Purchase Agreement, dated December 17, 2014, by and among the Registrant and the Purchasers		Form 8-K (Exhibit 10.1)	December 23, 2014	333-190728
10.46	Form of Registration Rights Agreement, dated December 17, 2014, by and among the Registrant and the investors party thereto		Form 8-K (Exhibit 10.2)	December 23, 2014	333-190728
10.47	Form of Warrant to Purchase Common Stock, dated December 17, 2014, issued by the Registrant		Form 8-K (Exhibit 10.3)	December 23, 2014	333-190728
10.48	Securities Purchase Agreement, dated June 2, 2016, by and among the Registrant and the Investors named therein		Form 8-K (Exhibit 10.1)	June 6, 2016	001-37471
10.49	Registration Rights Agreement, dated June 2, 2016, by and among the Registrant and the Investors named therein		Form 8-K (Exhibit 10.3)	June 6, 2016	001-37471
10.50	Form of Warrant to purchase Common Stock, dated June 2, 2016, issued by the Registrant		Form 8-K (Exhibit 10.2)	June 6, 2016	001-37471

10.51	Securities Purchase Agreement, dated November 2, 2019, by and among the Company and the Investors named therein		Form 8-K (Exhibit 10.1)	November 4, 2019	001-37471
10.52	Registration Rights Agreement, dated November 2, 2019, by and among the Company and the Investors named therein		Form 8-K (Exhibit 10.3)	November 4, 2019	001-37471
10.53	Form of Warrant to purchase Common Stock, dated November 2, 2019, issued by the Registrant		Form 8-K (Exhibit 10.2)	November 4, 2019	001-37471
10.54	Exchange Agreement, dated January 30, 2019, by and among the Registrant and Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., and Biotechnology Value Trading Fund OS, L.P.		Form 8-K (Exhibit 10.1)	February 4, 2019	001-37471
10.55	Exchange Agreement, dated March 31, 2020, by and among the Registrant and Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., and Biotechnology Value Trading Fund OS, L.P.		Form 8-K (Exhibit 10.1)	April 6, 2020	001-37471
10.56	Exchange Agreement by and among the Registrant and Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., Biotechnology Value Trading Fund OS, L.P., and MSI BVF SPV, L.L.C., dated as of May 20, 2021		Form 8-K (Exhibit 10.1)	May 21, 2021	001-37471
10.57	Open Market Sale Agreement, dated as of August 9, 2019, by and between Pieris Pharmaceuticals, Inc. and Jefferies LLC		Form 10-Q (Exhibit 10.1)	August 9, 2019	001-37471
10.58	Managing Director Services Agreement by and between Pieris Pharmaceuticals GmbH and Hitto Kaufmann, Ph.D., dated as of August 30, 2019	#	Form 10-Q (Exhibit 10.2)	November 12, 2019	001-37471
10.59	Non-Qualified Stock Option Agreement by and between the Registrant and Hitto Kaufmann, Ph.D., dated as of August 30, 2019	#	Form 10-Q (Exhibit 10.3)	November 12, 2019	001-37471
10.6	Form of Non-Qualified Stock Option Agreement by and between the Registrant and Tim Demuth, M.D., Ph.D.		Form S-8 (Exhibit 10.3)	August 5, 2021	333-258502
14.1	Corporate Code of Ethics and Conduct and Whistleblower Policy		Form 10-K (Exhibit 14.1)	March 31, 2021	001-37471
21.1	List of Subsidiaries	*			
23.1	Consent of Ernst & Young LLP	*			
31.1	Certification of Stephen S. Yoder, Chief Executive Officer and President, pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	*			
31.2	Certification of Thomas Bures, Chief Financial Officer, pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	*			
32.1	Certification of Stephen S. Yoder, Chief Executive Officer and President, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350	**			

32.2	Certification of Thomas Bures, Chief Financial Officer, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350	**
101.INS	XBRL Instance Document	*
101.SCH	XBRL Taxonomy Extension Schema Document	*
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	*
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	*
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	*
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	*
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	*

*	Filed herewith
**	Furnished herewith
±	Confidential treatment received as to portions of the exhibit. Confidential materials omitted and filed separately with the SEC.
+	Portions of the exhibit are omitted pursuant to Regulation S-K Item 601(b)(10)(iv). Copies of the unredacted exhibit will be furnished to the SEC upon request.
#	Indicates a management contract or compensatory plan

Item 16. FORM 10-K SUMMARY

We may voluntarily include a summary of information required by Form 10-K under this Item 16. We have elected not to include such summary information.

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.

PIERIS PHARMACEUTICALS, INC.

March 1, 2022

By: /s/ Stephen S. Yoder
Stephen S. Yoder
Chief Executive Officer and President

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

Signature	Title	Date
/s/ Stephen S. Yoder Stephen S. Yoder	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 1, 2022
/s/ Thomas Bures Thomas Bures	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 1, 2022
/s/ James Geraghty James Geraghty	Chairman of the Board of Directors	March 1, 2022
/s/ Michael Richman Michael Richman	Director	March 1, 2022
/s/ Maya R. Said, Sc.D. Maya R. Said, Sc.D.	Director	March 1, 2022
/s/ Peter Kiener, D.Phil. Peter Kiener, D.Phil.	Director	March 1, 2022
/s/ Christopher Kiritsy Christopher Kiritsy	Director	March 1, 2022
/s/ Ann Barbier, M.D., Ph.D. Ann Barbier, M.D., Ph.D.	Director	March 1, 2022
/s/ Matthew L. Sherman, M.D. Matthew L. Sherman, M.D.	Director	March 1, 2022

PIERIS PHARMACEUTICALS, INC.

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Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Pieris Pharmaceuticals, Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2021, 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, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (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 consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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 consolidated 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.

	Accrued and Prepaid Clinical Trial Expenses
Description of the Matter	As discussed in Note 2 to the consolidated financial statements, the Company records research and development expenses, which include expenses related to clinical trials, as incurred. The Company's determination of clinical trial costs incurred, as well as the related accrued and prepaid expenses at each reporting period incorporates judgment and utilizes various assumptions. Such judgments and assumptions include an evaluation of the information provided to the Company by third parties on actual costs incurred but not yet billed, estimated project timelines and patient enrollment. Payments for these activities are based on the terms of the individual arrangements, which differ from the pattern of costs incurred. Auditing the Company's accrued and prepaid clinical trial expenses was especially challenging due to the large volume of information received from multiple sources that perform service on the Company's behalf. While the Company's estimates of accrued and prepaid clinical trial expenses are primarily based on information received related to each study from its vendors, the Company may need to make an estimate for additional costs incurred based on management judgment. Additionally, due to the duration of the work performed under clinical trials and the timing of invoices received from vendors, the actual amounts incurred are not typically known at the time the financial statements are issued.
How We Addressed the Matter in Our Audit	To evaluate the accrued and prepaid clinical trial expenses, our audit procedures included, among others, testing the accuracy and completeness of the underlying data used in the estimates and evaluating the significant assumptions that are used by management to estimate the recorded accruals and prepayments. We corroborated the progress of research and development activities associated with clinical trials through discussion with the Company's research and development personnel that oversee the research and development activities. We inspected the Company's third-party contracts, amendments, and any pending change orders to assess the impact on amounts recorded. We also reviewed information received by the Company directly from certain third parties, which indicated the third parties' estimate of costs incurred to date. In addition, we performed analytics over fluctuations in accruals and prepaids by vendor throughout the period subject to audit and compared subsequent invoices received from third parties to amounts accrued.

/s/ Ernst & Young LLP
We have served as the Company's auditor since 2016.
Boston, Massachusetts
March 1, 2022

PIERIS PHARMACEUTICALS, INC.

CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share data)

	December 31,	
	2021	**2020**
Assets		
Current assets:		
Cash and cash equivalents	$ 117,764	$ 70,436
Accounts receivable	3,313	1,706
Prepaid expenses and other current assets	6,548	3,579
Total current assets	127,625	75,721
Property and equipment, net	19,122	22,046
Operating lease right-of-use assets	3,909	3,934
Other non-current assets	2,904	3,309
Total assets	$ 153,560	$ 105,010
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 8,609	$ 1,787
Accrued expenses and other current liabilities	16,836	7,731
Deferred revenues, current portion	25,116	12,627
Total current liabilities	50,561	22,145
Deferred revenue, net of current portion	38,403	35,900
Operating lease liabilities	13,841	15,932
Other long-term liabilities	—	6
Total liabilities	102,805	73,983
Stockholders' equity:		
Convertible preferred stock, $0.001 par value per share, 10,000,000 shares authorized and 15,617 and 14,429 shares issued and outstanding at December 31, 2021 and 2020, respectively	—	—
Common stock, $0.001 par value per share, 300,000,000 shares authorized and 72,222,661 and 56,002,815 shares issued and outstanding at December 31, 2021 and 2020, respectively	72	56
Additional paid-in capital	306,998	242,672
Accumulated other comprehensive income (loss)	829	(295)
Accumulated deficit	(257,144)	(211,406)
Total stockholders' equity	50,755	31,027
Total liabilities and stockholders' equity	$ 153,560	$ 105,010

The accompanying notes are an integral part of these consolidated financial statements.

PIERIS PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except per share data)

	Years Ended December 31,	
	2021	**2020**
Revenue		
Customer revenue	$ 27,940	$ 23,911
Collaboration revenue	3,478	5,412
Total revenue	31,418	29,323
Operating expenses		
Research and development	66,656	46,531
General and administrative	16,593	16,713
Total operating expenses	83,249	63,244
Loss from operations	(51,831)	(33,921)
Other income (expense)		
Interest income	4	511
Grant income	3,685	—
Other income (expense), net	2,404	(3,656)
Loss before income taxes	(45,738)	(37,066)
Income tax provision	—	164
Net loss	$ (45,738)	$ (37,230)
Foreign currency translation	1,124	1,630
Unrealized gain on available-for-sale securities	—	70
Comprehensive loss	$ (44,614)	$ (35,530)
Net loss per share:		
Basic and diluted	$ (0.71)	$ (0.68)
Weighted average number of common shares outstanding used in net loss per share attributable to common stockholders		
Basic and diluted	64,547	54,481

The accompanying notes are an integral part of these consolidated financial statements.

PIERIS PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY

(In thousands)

	Convertible preferred shares		Common shares		Additional paid-in capital	Accumulated other comprehensive income (loss)	Accumulated deficit	Total equity
	No. of shares	Share capital	No. of shares	Share capital				
Balance as of January 1, 2020	11	—	55,212	55	227,468	(1,995)	(174,176)	51,352
Net loss	—	—	—	—	—	—	(37,230)	(37,230)
Foreign currency translation adjustment	—	—	—	—	—	1,630	—	1,630
Unrealized gain on investments	—	—	—	—	—	70	—	70
Stock based compensation expense	—	—	—	—	5,090	—	—	5,090
Issuance of common stock resulting from exercise of stock options	—	—	149	—	291	—	—	291
Issuance of common stock resulting from purchase of employee stock purchase plan shares	—	—	70	—	200	—	—	200
Issuance of common stock resulting from exercise of warrants	—	—	—	—	—	—	—	—
Issuance of common stock pursuant to ATM, net of $ 0.4 million in offering costs	—		3,571	4	9,620	—	—	9,624
Preferred stock conversion (Series D)	3	—	(3,000)	(3)	3	—	—	—
Balance as of December 31, 2020	14	$ —	56,003	$ 56	$ 242,672	$ (295)	$ (211,406)	$ 31,027
Net loss	—	—	—	—	—	—	(45,738)	(45,738)
Foreign currency translation adjustment	—	—	—	—	—	1,124	—	1,124
Stock based compensation expense	—	—	—	—	5,215	—	—	5,215
Issuance of common stock resulting from exercise of stock options	—	—	482	—	1,024	—	—	1,024
Issuance of common stock resulting from purchase of employee stock purchase plan shares	—	—	64	—	165	—	—	165
Issuance of common stock resulting from exercise of warrants	—	—	1,391	1	836	—	—	837
Issuance of common stock resulting from conversion of preferred stock	(4)	—	3,812	4	(4)	—	—	—
Preferred stock conversion (Series E)	5	—	(5,000)	(5)	5	—	—	—
Issuance of common stock pursuant to at the market offering program, net of $ 1.5 million in offering costs	—		8,180	8	38,180	—	—	38,188
Issuance of common stock pursuant to private placement offering, net of $0.1 million in offering costs	—	—	7,290	8	18,905	—	—	18,913
Balance as of December 31, 2021	16	—	72,222	72	306,998	829	(257,144)	50,755

The accompanying notes are an integral part of these consolidated financial statements.

PIERIS PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

	Years Ended December 31,	
	2021	**2020**
Operating activities:		
Net loss	$ (45,738)	$ (37,230)
Adjustments to reconcile net loss to net cash (used in) operating activities:		
Depreciation and amortization	2,459	2,311
Right-of-use asset amortization	(91)	(184)
Stock-based compensation	5,215	5,090
Other non-cash transactions	(30)	(133)
Realized investment gain/loss	—	471
Deferred tax expense	—	164
Foreign currency re-measurement loss	—	(8)
Changes in operating assets and liabilities:		
Accounts receivable	(1,813)	5,343
Prepaid expenses and other assets	(3,154)	(500)
Deferred revenue	19,555	(14,496)
Accounts payable	7,049	(4,354)
Accrued expenses and other current liabilities	9,876	(1,655)
Lease liabilities	(988)	(715)
Net cash used in operating activities	(7,660)	(45,896)
Investing activities:		
Purchase of property and equipment	(949)	(2,726)
Proceeds from maturities of investments	—	83,437
Purchase of investments	—	(41,499)
Net cash (used in) provided by investing activities	(949)	39,212
Financing activities:		
Proceeds from exercise of options	1,024	291
Proceeds from employee stock purchase plan	165	200
Proceeds from exercise of warrants	837	—
Proceeds from issuance of common stock resulting from ATM sales, net of $1.5 million in transaction costs	38,188	9,624
Proceeds from issuance of common stock from private placement, net of $0.1 million in issuance costs	18,913	—
Net cash provided by financing activities	59,127	10,115
Effect of exchange rate change on cash and cash equivalents	(3,190)	4,745
Net increase in cash and cash equivalents	47,328	8,176
Cash and cash equivalents at beginning of year	70,436	62,260
Cash and cash equivalents at end of year	$ 117,764	$ 70,436
Supplemental cash flow disclosures:		
Property and equipment included in accounts payable	$ 237	$ 131

The accompanying notes are an integral part of these consolidated financial statements.

PIERIS PHARMACEUTICALS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Corporate Information

Pieris Pharmaceuticals, Inc., was founded in May 2013, and acquired 100% interest in Pieris Pharmaceuticals GmbH (formerly Pieris AG, a German company which was founded in 2001) in December 2014. Pieris Pharmaceuticals, Inc. and its wholly-owned subsidiaries, hereinafter collectively Pieris, or the Company, is a clinical-stage biopharmaceutical company that discovers and develops Anticalin-based drugs to target validated disease pathways in unique and transformative ways. Pieris' corporate headquarters is located in Boston, Massachusetts and its research facility, as of December 31, 2021, was located in Hallbergmoos, Germany.

Pieris' clinical pipeline includes an inhaled IL-4Rα antagonist Anticalin protein to treat moderate-to-severe asthma and an immuno-oncology, or IO, bispecific targeting 4-1BB and HER2.

The Company's core Anticalin technology and platform was developed in Germany, and the Company has partnership arrangements with several major multi-national pharmaceutical companies.

The Company is subject to risks common to companies in the biotechnology industry, including but not limited to, the need for additional capital, risks of failure of preclinical studies and clinical trials, the need to obtain marketing approval and reimbursement for any drug product candidate that it may identify and develop, the need to successfully commercialize and gain market acceptance of its product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development of technological innovations by competitors, reliance on third party manufacturers and the ability to transition from pilot-scale production to large-scale manufacturing of products.

As of December 31, 2021, cash and cash equivalents were $117.8 million. The Company's net loss was $45.7 million and $37.2 million for the years ended December 31, 2021 and 2020, respectively. The Company has incurred net losses since inception and had an accumulated deficit of $257.1 million as of December 31, 2021. Net losses and negative cash flows have had, and will continue to have, an adverse effect on the Company's stockholders' equity and working capital. The Company expects to continue to incur operating losses for at least the next several years.

The future success of the Company is dependent on its ability to identify and develop its product candidates, expand its corporate infrastructure and ultimately upon its ability to attain profitable operations. The Company has devoted substantially all of its financial resources and efforts to research and development and general and administrative expenses to support such research and development. The Company has several research and development programs underway in varying stages of development and it expects that these programs will continue to require increasing amounts of cash for development, conducting clinical trials, and testing and manufacturing of product material. Cash necessary to fund operations will increase significantly over the next several years as the Company continues to conduct these activities necessary to pursue governmental regulatory approval of clinical-stage programs and other product candidates.

The Company plans to raise additional capital to fulfill its operating and capital requirements through public or private equity financings, utilization of its current ATM program, strategic collaborations, licensing arrangements, government grants and/or the achievement of milestones under its collaborative agreements. The funding requirements of the Company's operating plans, however, are based on estimates that are subject to risks and uncertainties and may change as a result of many factors currently unknown. Although management continues to pursue these funding plans, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all. Until such time as the Company can generate substantial product revenues, if ever, the Company expects to finance its cash needs through a combination of equity offerings, debt financings, strategic partnerships, government grants and licensing arrangements. The terms of any future financing may adversely affect the holdings or the rights of the Company's existing stockholders.

The Company believes that its currently available funds will be sufficient to fund the Company's operations through at least the next twelve months from the issuance of this Annual Report on Form 10-K. The Company's belief with respect to its ability to fund operations is based on estimates that are subject to risks and uncertainties. If actual results are different from management's estimates, the Company may need to seek additional funding. If the Company is unable to obtain additional funding on acceptable terms when needed, it may be required to defer or limit some or all of its research, development, and/or clinical projects.

2. Summary of Significant Accounting Policies

Basis of Presentation and Use of Estimates

The accompanying consolidated financial statements of Pieris Pharmaceuticals, Inc. and its wholly-owned subsidiaries were prepared in accordance with U.S. GAAP. The consolidated financial statements include the accounts of all subsidiaries. All intercompany balances and transactions have been eliminated.

The preparation of the financial statements in accordance with U.S. GAAP requires management to make estimates, judgments, and assumptions that affect the reported amounts of assets, liabilities, revenues, expenses and the related disclosures at the date of the financial statements and during the reporting period. Significant estimates are used for, but are not limited to, revenue recognition; deferred tax assets, deferred tax liabilities and valuation allowances; determination of the incremental borrowing rate to calculate right-of-use assets and lease liabilities; beneficial conversion features; fair value of stock options, preferred stock, and warrants; and prepaid and accrued clinical trial expenses. Management evaluates its estimates on an ongoing basis. Actual results and outcomes could differ materially from management's estimates, judgments, and assumptions.

Foreign Currency Translation

The financial statements of the Company's foreign subsidiaries are translated from local currency into reporting currency, which is U.S. dollars, using the current exchange rate at the balance sheet date for assets and liabilities, and the weighted average exchange rate prevailing during the period for revenues and expenses. The functional currency for Pieris' foreign subsidiaries is considered to be the local currency for each entity and, accordingly, translation adjustments for these subsidiaries are included in accumulated other comprehensive loss within stockholders' equity.

Realized and unrealized gains and losses resulting from foreign currency transactions denominated in currencies other than the functional currency are reflected as other (expense) income, net in the consolidated statements of operations. Foreign currency gains and losses on available-for-sale investment transactions are recorded to other comprehensive income (loss) on the Company's balance sheet per Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 830, *Foreign Currency Matters.*

Cash, Cash Equivalents and Investments

The Company determines the appropriate classification of its investments at the time of purchase. All liquid investments with original maturities of 90 days or less from the purchase date and for which there is an active market are considered to be cash equivalents. The Company's investments are comprised of money market, asset backed securities, government treasuries, and corporate bonds that are classified as available-for-sale in accordance with FASB ASC 320, *Investments—Debt and Equity Securities*. The Company classifies investments available to fund current operations as current assets on its balance sheets.

Available-for-sale investments are recorded at fair value, with unrealized gains or losses included in accumulated other comprehensive income (loss) on the Company's balance sheets. Realized gains and losses are determined using the specific identification method and are included as a component of other income (expense).

The Company reviews investments for other-than-temporary impairment whenever the fair value of an investment is less than the amortized cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. To determine whether an impairment is other-than temporary, the Company considers its intent to sell, or whether it is more likely than not that the Company will be required to sell the investment before recovery of the investment's amortized cost basis. Evidence considered in this assessment includes reasons for the impairment, the severity and the duration of the impairment, and changes in value subsequent to period end.

Concentration of Credit Risk and Off-Balance Sheet Risk

The Company has no financial instruments with off-balance sheet risk such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that subject Pieris to concentrations of credit risk include cash and cash equivalents, investments, and accounts receivable. The Company's cash, cash equivalents, and investments are held in accounts with financial institutions that management believes are creditworthy. The Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimizes the exposure to concentration of credit risk. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds. Accounts receivable primarily consist of amounts due under strategic partnership and other license agreements with major multi-national pharmaceutical companies for which the Company does not obtain collateral.

Fair Value Measurement

The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. FASB ASC Topic 820, *Fair Value Measurement and Disclosures*, or ASC 820, established a hierarchy of inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available. Observable inputs are inputs that market participants would use in pricing the financial instrument based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the financial instrument and are developed based on the best information available in the circumstances. The fair value hierarchy applies only to the valuation inputs used in determining the reported or disclosed fair value of the financial instruments and is not a measure of the investment credit quality. Fair value measurements are classified and disclosed in one of the following three categories:

- Level 1 inputs are quoted prices in active markets for identical assets or liabilities that the reporting entity has the ability to access at the measurement date.
- Level 2 utilizes quoted market prices in markets that are not active, broker or dealer quotations, or alternative pricing sources with reasonable levels of price transparency.
- Level 3 inputs are unobservable inputs for the asset or liability in which there is little, if any, market activity for the asset or liability at the measurement date.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Financial instruments measured at fair value on a recurring basis include cash equivalents and investments, if any (*Note 6*).

An entity may elect to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in net loss. The Company did not elect to measure any additional financial instruments or other items at fair value.

Fair Values of Financial Instruments

The fair value of cash, accounts receivable, and accounts payable approximates the carrying value of these financial instruments because of the short-term nature of any maturities. The Company determines the estimated fair values of other financial instruments, using available market information and valuation methodologies, primarily input from independent third party pricing sources.

Accounts Receivable

Accounts receivable are recorded net of allowances for doubtful accounts and represent amounts due from strategic partners. The Company monitors and evaluates collectability of receivables on an ongoing basis and considers whether an allowance for doubtful accounts is necessary. The Company determined that no such reserve is needed as of December 31, 2021 and 2020. Historically, Pieris has not had collectability issues.

Property and Equipment

Property and equipment are recorded at acquisition cost, less accumulated depreciation and impairment. Depreciation on property and equipment is calculated using the straight-line method over the remaining estimated useful lives of the assets. Maintenance and repairs to these assets are charged to expenses as occurred. During the year ended December 31, 2020, the Company added material assets related to the February 2020 move to a new research and development facility in Hallbergmoos, Germany. Substantially all of the Company's fixed assets are located in Germany. The estimated useful life of the different groups of property and equipment is as follows:

Asset Classification	Estimated useful life (in years)
Leasehold improvements	shorter of useful life or remaining life of the lease
Laboratory furniture and equipment	8 - 14
Office furniture and equipment	5 - 13
Computer and equipment	3 - 7

Impairment of Long-lived Assets

The Company reviews its long-lived assets to be held and used for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. The Company evaluates the realizability of its long-lived assets based on profitability and cash flow expectations for the related asset. Any write-downs are treated as permanent reductions in the carrying amount of the assets. The Company believes that, as of each of the balance sheets presented, none of the Company's long-lived assets were impaired.

Revenue Recognition

Pieris has entered into several licensing agreements with collaboration partners for the development of Anticalin therapeutics against a variety of targets. The terms of these agreements provide for the transfer of multiple goods or services which may include: (i) licenses, or options to obtain licenses, to Pieris' Anticalin technology and/or specific programs and (ii) research and development activities to be performed on behalf of or with a collaborative partner. Payments to Pieris under these agreements may include upfront fees (which include license and option fees), payments for research and development activities, payments based upon the achievement of certain milestones, and royalties on product sales. There are no performance, cancellation, termination or refund provisions in any of the arrangements that could result in material financial consequences to Pieris. As the Company's intellectual property is located in Germany, the Company records all consolidated revenue in its Pieris Pharmaceuticals, GmbH subsidiary.

Collaborative Arrangements

The Company considers the nature and contractual terms of an arrangement and assess whether the arrangement involves a joint operating activity pursuant to which it is an active participant and exposed to significant risks and rewards with respect to the arrangement. If the Company is an active participant and exposed to the significant risks and rewards with respect to the arrangement, it accounts for these arrangements pursuant to ASC 808, *Collaborative Arrangements*, or ASC 808, and applies a systematic and rational approach to recognize revenue. The Company classifies payments received as revenue and payments made as a reduction of revenue in the period in which they are earned. Revenue recognized under a collaborative arrangement involving a participant that is not a customer is presented as Collaboration Revenue in the Statement of Operations.

In November 2018, the FASB issued ASU 2018-18, which makes targeted improvements to U.S. GAAP for collaborative arrangements, including: clarification that certain transactions between collaborative arrangement participants should be accounted for as revenue under ASC 606, *Revenue from Contracts with Customers*, or ASC 606, when the collaborative arrangement participant is a customer in the context of a unit of account; adding unit-of-account guidance in ASC 808 to align with the guidance in ASC 606; and a requirement that in a transaction with a collaborative arrangement participant that is not directly related to sales to third parties, presenting the transaction together with revenue recognized under ASC 606 is precluded if the collaborative arrangement participant is not a customer. The guidance per ASU 2018-18 was adopted retrospectively to the date of initial application of ASC 606. The Company adopted ASU 2018-18 in the first quarter of 2020. The adoption of this standard did not have a material impact on the Company's consolidated financial statements; however, revenue recognized under a collaborative arrangement involving a participant that is not a customer (Collaboration revenue) is now presented separately from Customer revenue. All amounts presented herein are in conformity with ASU 2018-18.

Revenue from Contracts with Customers

In accordance with ASC 606, revenue is recognized when a customer obtains control of promised goods or services. The amount of revenue recognized reflects the consideration to which the Company expects to be entitled in exchange for these goods and services. To achieve this core principle, the Company applies the following five steps: 1) identify the customer contract; 2) identify the contract's performance obligations; 3) determine the transaction price; 4) allocate the transaction price to the performance obligations; and 5) recognize revenue when or as a performance obligation is satisfied.

The Company evaluates all promised goods and services within a customer contract and determines which of such goods and services are separate performance obligations. This evaluation includes an assessment of whether the good or service is capable

of being distinct and whether the good or service is separable from other promises in the contract. In assessing whether promised goods or services are distinct, the Company considers factors such as the stage of development of the underlying intellectual property and the capabilities of the customer to develop the intellectual property on their own or whether the required expertise is readily available.

Licensing arrangements are analyzed to determine whether the promised goods or services, which often include licenses, research and development services and governance committee services, are distinct or whether they must be accounted for as part of a combined performance obligation. If the license is considered not to be distinct, the license would then be combined with other promised goods or services as a combined performance obligation. If the Company is involved in a governance committee, it assesses whether its involvement constitutes a separate performance obligation. When governance committee services are determined to be separate performance obligations, the Company determines the fair value to be allocated to this promised service.

Certain contracts contain optional and additional items, which are considered marketing offers and are accounted for as separate contracts with the customer if such option is elected by the customer, unless the option provides a material right which would not be provided without entering into the contract. An option that is considered a material right is accounted for as a separate performance obligation.

The transaction price is determined based on the consideration to which the Company will be entitled in exchange for transferring goods and services to the customer. A contract may contain variable consideration, including potential payments for both milestone and research and development services. For certain potential milestone payments, the Company estimates the amount of variable consideration by using the most likely amount method. In making this assessment, the Company evaluates factors such as the clinical, regulatory, commercial and other risks that must be overcome to achieve the milestone. Each reporting period the Company re-evaluates the probability of achievement of such variable consideration and any related constraints. Pieris will include variable consideration, without constraint, in the transaction price to the extent it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. For potential research and development service payments, the Company estimates the amount of variable consideration by using the expected value method, including any approved budget updates arising from additional research or development services.

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price among the performance obligations on a relative standalone selling price basis unless a portion of the transaction price is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct good or service that forms part of a single performance obligation.

The Company allocates the transaction price based on the estimated standalone selling price of the underlying performance obligations or in the case of certain variable consideration to one or more performance obligations. The Company must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. The Company utilizes key assumptions to determine the stand-alone selling price, which may include other comparable transactions, pricing considered in negotiating the transaction and the estimated costs to complete the respective performance obligation. Certain variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration relate to the satisfaction of the performance obligation and the resulting amounts allocated to each performance obligation are consistent with the amount the Company would expect to receive for each performance obligation.

When a performance obligation is satisfied, revenue is recognized for the amount of the transaction price, excluding estimates of variable consideration that are constrained, that is allocated to that performance obligation on a relative standalone selling price basis. Significant management judgment is required in determining the level of effort required under an arrangement and the period over which the Company is expected to complete its performance obligations under an arrangement.

For performance obligations consisting of licenses and other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non- refundable, up-front fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. If the license to the Company’s intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company will recognize revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license.

Revenue recognized under an arrangement involving a participant that is a customer is presented as Customer Revenue.

Milestones and Royalties

The Company aggregates milestones into four categories (i) research milestones, (ii) development milestones, (iii) commercial milestones and (iv) sales milestones. Research milestones are typically achieved upon reaching certain success criteria as defined in each agreement related to developing an Anticalin protein against the specified target. Development milestones are typically reached when a compound reaches a defined phase of clinical research or passes such phase, or upon gaining regulatory approvals. Commercial milestones are typically achieved when an approved pharmaceutical product reaches the status for commercial sale, including regulatory approval. Sales milestones are certain defined levels of net sales by the licensee, such as when a product first achieves global sales or annual sales of a specified amount.

There is uncertainty that the events to obtain the research and development milestones will be achieved given the nature of clinical development and the stage of the Company's technology. The Company has thus determined that all research and development milestones will be constrained until it is deemed probable that a significant revenue reversal will not occur. For revenues from research and development milestones, payments will be recognized consistent with the recognition pattern of the performance obligation to which they relate.

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and for which the license is deemed to be the predominant item to which the royalties relate, the Company recognizes 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). Commercial milestones and sales royalties are determined by sales or usage-based thresholds and will be accounted for under the royalty recognition constraint as constrained variable consideration.

The Company calculates the maximum amount of potential milestones achievable under each collaboration agreement and discloses such potential future milestones for all current collaborations using such a maximum calculation.

Contract Balances

The Company recognizes a contract asset when the Company transfers goods or services to a customer before the customer pays consideration or before payment is due, excluding any amounts presented as a receivable (i.e., accounts receivable). A contract asset is an entity's right to consideration in exchange for goods or services that the entity has transferred to a customer. The contract liabilities (i.e., deferred revenue) primarily relate to contracts where the Company has received payment but has not yet satisfied the related performance obligations.

In the event of an early termination of a collaboration agreement, any contract liabilities would be recognized in the period in which all Company obligations under the agreement have been fulfilled.

Costs to Obtain and Fulfill a Contract with a Customer

Certain costs to obtain customer contracts, including success-based fees paid to third-party service providers, and costs to fulfill customer contracts are capitalized in accordance with FASB ASC 340, *Other Assets and Deferred Costs*, or ASC 340. These costs are amortized to expense on a systemic basis that is consistent with the transfer to the customer of the goods or services to which the asset relates. The Company will expense the amortization of costs to obtain customer contracts to general and administrative expense and costs to fulfill customer contracts to research and development expense.

Research and Development

Research and development expenses are charged to the statement of operations as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities, including salaries and benefits, facilities costs, pre-clinical and clinical costs, contract services, consulting, depreciation and amortization expense, and other related costs. Costs associated with acquired technology, in the form of upfront fees or milestone payments, are charged to research and development expense as incurred.

Income Taxes

The Company applies ASC Topic 740 *Income Taxes*, which established financial accounting and reporting requirements for the effects of income taxes that result from the Company's activities during the current and preceding years. Deferred tax assets and

liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases, and operating losses and tax credit carry forwards. Deferred tax assets and liabilities are measured using enacted statutory tax rates expected to apply to taxable income in the jurisdictions and years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. Where the Company determines that it is more likely than not that some portion or all of the deferred tax assets will not be realized in the future, the deferred tax assets are reduced by a valuation allowance. The Company records interest and penalties related to uncertain tax positions as part of income tax expense.

The Tax Cuts and Jobs Act (TCJA) subjects a U.S. shareholder to tax on global-intangible low tax income (GILTI) earned by certain foreign subsidiaries. The Company has made an accounting policy election to provide for the tax expense related to GILTI in the year the tax is incurred as a period expense only.

Stock-based Compensation

The Company measures share-based payments in accordance with ASC Topic 718,*Stock Compensation*. Pieris records its stock-based compensation expense over the requisite service period and records forfeitures as they occur. Determining the appropriate fair value model and related assumptions requires judgment, including estimating share price volatility and expected terms of the awards. For employee options, the fair value measurement date is generally on the date of grant and the related compensation expense is recognized on a straight-line basis over the requisite service period of the awards, less expense for actual forfeitures.

The Company uses the Black-Scholes option pricing model to determine the estimated fair value for stock-based awards. Option-pricing models require the input of various subjective assumptions, including the option's expected life, expected dividend yield, price volatility, risk free interest rate and forfeitures of the underlying stock. Due to the limited operating history of the Company as a public entity and a lack of company specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. When selecting these public companies on which it has based its expected stock price volatility, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected term of the stock-based awards. The Company computes historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Due to the lack of Company specific historical option activity, the Company has estimated the expected term of its employee stock options using the "simplified" method, whereby, the expected term equals the arithmetic average of the vesting term and the original contractual term of the option. The expected term for non-employee awards is the remaining contractual term of the option. The risk-free interest rates are based on the U.S. Treasury securities with a maturity date commensurate with the expected term of the associated award. The Company has never paid, and does not expect to pay dividends in the foreseeable future.

All excess tax benefits and tax deficiencies are recorded as income tax expense or benefit in the Company's statement of operations and comprehensive loss.For the years ended December 31, 2021 and 2020, the Company did not record an income statement benefit for excess tax benefits as a valuation allowance is also required on these amounts.

Government Grants

The Company recognizes grants from governmental agencies when there is reasonable assurance that the Company will comply with the conditions attached to the grant arrangement and the grant will be received. The Company evaluates the conditions of each grant as of each reporting period to evaluate whether the Company has reached reasonable assurance of meeting the conditions of each grant arrangement and that it is expected that the grant will be received as a result of meeting the necessary conditions. Grants are recognized in the consolidated statements of operations on a systematic basis over the periods in which the Company recognizes the related costs for which the government grant is intended to compensate. Specifically, grant income related to research and development costs is recognized as such expenses are incurred. Grant income is included as a separate caption within Other income (expense), net in the consolidated statements of operations.

Leases

The Company accounts for leases pursuant to ASC 842 *Leases (Topic 842)*, or ASC 842. As a lessee, the Company is required to recognize (i) a lease liability, which is a lessees obligation to make lease payments arising from a lease, measured on a discounted basis; and (ii) a right-of-use asset, which is an asset that represents the lessee's right to use, or control the use of, a specified asset for the lease term for all leases (with the exception of short-term leases) at the commencement date. Any variable components of lease costs are excluded from lease payments and are recognized in the period incurred.

The Company determines if an arrangement is a lease at inception. The Company's contracts are determined to contain a lease within the scope of ASC 842 when all of the following criteria based on the specific circumstances of the arrangement are met: (1) there is an identified asset for which there are no substantive substitution rights; (2) the Company has the right to obtain substantially all of the economic benefits from the identified asset; and (3) the Company has the right to direct the use of the identified asset. In addition, the Company does not apply the recognition requirements in the lease standard to short-term leases (a lease that at commencement date has a lease term of 12 months or less and does not contain a purchase option that it is reasonably certain to exercise) and does not separate lease and non-lease components for all asset classes. Any variable components of lease costs are excluded from lease payments and are recognized in the period incurred.

At the commencement date, operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of future lease payments over the expected lease term. The Company's lease agreements do not provide an implicit rate. As a result, the Company utilizes an estimated incremental borrowing rate to discount lease payments, which is based on the rate of interest the Company would have to pay to borrow a similar amount on a collateralized basis over a similar term and based on observable market data points. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or lease incentives received. Operating lease cost is recognized over the expected term on a straight-line basis.

The Company typically only includes an initial lease term in its assessment of a lease agreement. Options to renew a lease are not included in the Company's assessment unless there is reasonable certainty that the Company will renew. The expected lease term includes noncancelable lease periods and, when applicable, periods covered by an option to extend the lease if the Company is reasonably certain to exercise that option, as well as periods covered by an option to terminate the lease if the Company is reasonably certain not to exercise that option.

Assumptions made by the Company at the commencement date are re-evaluated upon occurrence of certain events, including a lease modification. A lease modification results in a separate contract when the modification grants the lessee an additional right of use not included in the original lease and when lease payments increase commensurate with the standalone price for the additional right of use. When a lease modification results in a separate contract, it is accounted for in the same manner as a new lease.

Contingencies

Accruals are recorded for loss contingencies when it is probable that a liability has been incurred and the amount of the related loss can be reasonably estimated. The Company evaluates, on a quarterly basis, developments in legal proceedings and other matters that could cause an increase or decrease in the amount of the liability that has been accrued previously. Considering facts known at the time of the assessment, the Company determines whether potential losses are considered reasonably possible or probable and whether they are estimable. Based upon this assessment, the Company carries out an evaluation of disclosure requirements and considers possible accruals in the financial statements.

Segment Reporting

Operating segments are identified as components of an enterprise where separate discrete financial information is evaluated by the chief operating decision maker in making decisions on how to allocate resources and assess performance. The Company operates as a single segment dedicated to the discovery and development of biotechnological applications and the Company's chief operating decision maker, or CODM, makes decisions based on the Company as a whole. The Company has determined that its CODM is its Chief Executive Officer.

Earnings per Share

Basic earnings per share attributable to common stockholders is calculated by dividing net loss attributable to common stockholders by the weighted average shares outstanding during the period, without consideration for common stock equivalents.

Diluted earnings per share attributable to common stockholders is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock and if-converted methods. For purposes of the diluted net loss per share attributable to common stockholders' calculation, preferred stock, stock options, unvested restricted stock, and warrants are considered to be common stock equivalents but have been excluded from the calculation of diluted net loss per share attributable to common stockholders, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented.

Recent Accounting Pronouncement Adopted

In December 2019, the FASB issued ASU No. 2019-12,*Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*which amends and aims to simplify accounting disclosure requirements regarding a number of topics including intraperiod tax allocation, accounting for deferred taxes when there are changes in consolidation of certain investments, tax basis step up in an acquisition and the application of effective rate changes during interim periods, among other improvements. This standard is effective for fiscal years beginning after December 15, 2020 and was adopted by the Company on January 1, 2021. Adoption of this new standard did not have a material impact on the Company.

In November 2021, the FASB issued ASU No. 2021-10,*Government Assistance (Topic 832)*, or ASU 2021-10. ASU 2021-10 provides clarity on increasing transparency over the disclosure of certain government assistance including the disclosure of (1) the types of assistance, (2) an entity's accounting for the assistance, and (3) the effect of the assistance on an entity's financial statements. Diversity currently exists in the recognition, measurement, presentation, and disclosure of government assistance received by business entities because of the lack of specific authoritative guidance in generally accepted accounting principles. The guidance in ASU 2021-10 is effective for the Company for financial statements issued for fiscal years beginning after December 15, 2021, with early adoption permitted. The Company adopted this standard for the period ended December 31, 2021 on a prospective basis and concluded that we have made the required disclosure in Footnote 5 below.

Recent Accounting Pronouncements Not Yet Adopted

In June 2016, the FASB issued ASU No. 2016-13,*Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Statements,* or ASU 2016-13. ASU 2016-13 significantly changes the impairment model for most financial assets and certain other instruments. The new standard requires that expected credit losses relating to financial assets measured on an amortized cost basis and available-for-sale debt securities be recorded through an allowance for credit losses. It also limits the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value, and requires the reversal of previously recognized credit losses if fair value increases. The allowance for credit losses is a valuation account that is deducted from the amortized cost basis of the financial asset(s) to present the net carrying value at the amount expected to be collected on the financial asset.

Subsequently, in November 2018, the FASB issued ASU No. 2018-19,*Codification Improvements to Topic 326, Financial Instruments-Credit Losses*, which clarifies codification and corrects unintended application of the guidance. In November 2019, the FASB issued ASU No. 2019-11, *Codification Improvements to Topic 326, Financial Instruments-Credit Losses*, which clarifies or addresses specific issues about certain aspects of ASU 2016-13. In November 2019 the FASB also issued ASU No. 2019-10*Financial Instruments-Credit Losses (Topic 326), Derivatives and Hedging (Topic 815), and Leases (Topic 842): Effective Dates*, which delays the effective date of ASU 2016-13 by three years for certain smaller reporting companies such as the Company. The guidance in ASU 2016-13 is effective for the Company for financial statements issued for fiscal years beginning after December 15, 2022 and interim periods within those fiscal years, with early adoption permitted. The Company is still evaluating the impact of the adoption of this standard.

The Company has considered other recent accounting pronouncements and concluded that they are either not applicable to the business, or that the effect is not expected to be material to the unaudited consolidated financial statements as a result of future adoption.

3. Revenue

General

The Company has not generated revenue from product sales. The Company has generated revenue from contracts with customers (option, license and collaboration agreements), which include upfront payments for licenses or options to obtain licenses, payments for research and development services and milestone payments.

During the years ended December 31, 2021 and 2020, respectively, the Company recognized revenue from the following strategic partnerships and other license agreements (in thousands):

	Years Ended December 31,	
	2021	2020
AstraZeneca	$ 18,919	$ 8,308
Seagen	768	9,702
Servier	4,070	11,313
Boston Pharmaceuticals	5,711	—
Genentech	1,950	—
Total Revenue	$ 31,418	$ 29,323

Under the Company´s existing strategic partnerships and other license agreements, the Company could receive the following potential milestone payments (in millions) as of December 31, 2021:

	Research, Development, Regulatory & Commercial Milestones	Sales Milestones
AstraZeneca	$ 1,096	$ 4,275
Servier	136	102
Seagen	754	450
Boston Pharmaceuticals	88	265
Genentech	844	600
Total potential milestone payments	$ 2,918	$ 5,692

Strategic Partnerships

Genentech

On May 19, 2021, the Company and Genentech, Inc., or Genentech, entered into a Research Collaboration and License Agreement, or the Genentech Agreement, to discover, develop and commercialize locally delivered respiratory and ophthalmology therapies that leverage the Company's proprietary Anticalin technology. Upon signing the Genentech Agreement, Genentech paid the Company a $20 million upfront fee. In addition, the Company may be eligible to receive additional milestone payments across multiple programs, as well as tiered royalty payments on net sales at percentages ranging from the mid-single to low double-digits, subject to certain standard reductions and offsets.

Under the terms of the Genentech Agreement, the Company will be responsible for discovery and preclinical development of two initial programs. The Company will be responsible for research activities following target nomination through the late-stage research go decision. The parties will then collaborate on drug candidate characterization until the development go decision. After the development go decision, Genentech will be responsible for pursuing the preclinical and clinical development of each program, and thereafter, the commercialization efforts. Each party will be responsible for the costs incurred to perform their respective responsibilities. Genentech has an option to expand the collaboration to encompass two additional programs with the payment of a $10 million fee per additional program. If Genentech exercises its option to start additional programs, payment to the Company of additional fees, milestone payments and royalties would result.

Unless earlier terminated, the term of the Genentech Agreement continues until no royalty or other payment obligations are or will become due under the Genentech Agreement. The Genentech Agreement may be terminated (i) by either party based on insolvency or breach by the other party and such insolvency proceeding is not dismissed or such breach is not cured within 90 days; or (ii) after 9 months from the effective date of the Genentech Agreement, by Genentech as a whole or on a product-by-product and/or country-by-country basis upon 90 days prior written notice before the first commercial sale of a product or upon180 days prior written notice after the first commercial sale of a product.

While the Genentech Agreement allows for up to four research programs, only two research programs are initially identified and committed in the Genentech Agreement. To reach a total of up to four research programs, the Company has granted Genentech options to nominate an additional two collaboration targets of their choosing, subject to the legal availability of the target to be researched. Genentech will have three years after the effective date to nominate the subsequent targets. The Company has also granted Genentech options to replace any of the collaboration targets identified with another target.

However, at no point will there be more than four identified collaboration targets for which there are ongoing research programs.

The arrangement with Genentech provides for the transfer of the following goods or services: (i) exclusive research and commercial license for the collaboration programs, (ii) a non-exclusive platform improvement license, (iii) research and development services, (iv) participation in a governance committee, and (v) replacement target options on the first two programs upon a screening failure which were assessed as material rights.

Management evaluated all of the promised goods or services within the contract and determined which such goods and services were separate performance obligations. The Company determined that the licenses granted, at arrangement inception, should be combined with the research and development services to be provided for the related target programs as they are not capable of being distinct. A third party would not be able to provide the research and development services due to the specific nature of the intellectual property and knowledge required to perform the services, and Genentech could not benefit from the licenses without the corresponding services. The Company determined that the participation in the governance committees was distinct as the services could be performed by an outside party.

As a result, management concluded there werefive separate performance obligations at the inception of the Genentech Agreement: (i) two combined performance obligations, each comprised of an exclusive research and commercial license, a non-exclusive platform improvement license, and research and development services for the first two Genentech programs, (ii) two performance obligations each comprised of a material right for a target swap option for the first two Genentech programs, and (iii)one performance obligation comprised of the participation on the governance committee.

The Company allocated consideration to the performance obligations based on the relative proportion of their standalone selling prices. The Company developed standalone selling prices for licenses by applying a risk adjusted, net present value, estimate of future potential cash flows approach, which included the cost of obtaining research and development services at arm's length from a third-party provider, as well as internal full-time equivalent costs to support these services. The Company developed the standalone selling price for committee participation by using management's estimate of the anticipated participation hours multiplied by a market rate for comparable participants.

The transaction price at inception is comprised of fixed consideration of $20.0 million in upfront fees and was allocated to each of the performance obligations based on the relative proportion of their standalone selling prices. The amounts allocated to the performance obligations for the two research programs will be recognized on a proportional performance basis through the completion of each respective estimated research term of the individual research programs. The amounts allocated to the material right for the target options will be recognized either at the time the material right expires or, if exercised, on a proportional performance basis over the estimated research term for that program along with any remaining deferred revenue associated with the replacement target. The amounts allocated to the participation on the committee will be recognized on a straight-line basis over the anticipated research term for all research programs. As of December 31, 2021, there was $16.6 million of aggregate transaction price allocated to remaining performance obligations.

Under the Genentech Agreement, the Company is eligible to receive various research, development, commercial and sales milestones. There is uncertainty that the events to obtain the research and development milestones will be achieved given the nature of clinical development and the stage of the Company's technology. The Company has determined that all other research and development milestones will be constrained until it is deemed probable that a significant revenue reversal will not occur.

As of December 31, 2021, there were $8.1 million and $8.5 million of current and non-current deferred revenue, respectively, related to the Genentech Agreement.

Boston Pharmaceuticals

On April 24, 2021, the Company and BP Asset XII, Inc., or Boston Pharmaceuticals, a subsidiary of Boston Pharma Holdings, LLC, entered into an Exclusive Product License Agreement, or the BP Agreement, to develop PRS-342, a 4-1BB/GPC3 preclinical immuno-oncology Anticalin-antibody bispecific fusion protein.

Under the terms of the BP Agreement, Boston Pharmaceuticals exclusively licensed worldwide rights to PRS-342. The Company received an upfront payment of $10.0 million and is further entitled to receive development, regulatory and sales-based milestone payments, tiered royalties up to low double-digits on sales of PRS-342 and a percentage of consideration received by Boston Pharmaceuticals in the event of a sublicense of a program licensed under the BP Agreement or a change of control of Boston Pharmaceuticals. The Company will also contribute up to $4.0 million toward manufacturing activities.

The term of the BP Agreement ends upon the expiration of all of Boston Pharmaceuticals' payment obligations thereunder. The BP Agreement may be terminated by Boston Pharmaceuticals in its entirety for convenience beginning nine months after its effective date upon 60 days' notice or, for any program under the BP Agreement which has received marketing approval, upon 120 days' notice. If any program is terminated by Boston Pharmaceuticals, the Company will have full rights to continue such program. The BP Agreement may also be terminated by Boston Pharmaceuticals or the Company for an uncured material breach by the other party upon 180 days' notice (60 days in the case of non-payment of undisputed amounts due and payable), subject to extension for an additional 180 days in certain cases and subject, in all cases, to dispute resolution procedures. The Agreement may also be terminated due to the other party's insolvency. The Company may also terminate the BP Agreement if Boston Pharmaceuticals challenges the validity of any patents licensed under the BP Agreement, subject to certain exceptions.

The Company does not have any obligations to assist in the research and development efforts of Boston Pharmaceuticals under the BP Agreement. However, the Company has an obligation to fund up to $4.0 million in costs, including out-of-pocket costs incurred by Boston Pharmaceuticals, in connection with the manufacture of products under the BP Agreement.
The arrangement with Boston Pharmaceuticals provides for the transfer of the following: (i) exclusive license of PRS-342, (ii) non-exclusive Pieris platform license, (iii) initial know-how, (iv) product cell line license, and (v) materials (as each such term is defined under the BP Agreement).

Management evaluated all of the promised goods or services within the BP Agreement and determined which such goods and services were separate performance obligations. The Company determined that the licenses granted, at arrangement inception, should be combined with the transfer of know-how, materials and the product cell line license. Boston Pharmaceuticals could not benefit from the exclusive and non-exclusive licenses without the corresponding transfer of know-how and materials.

As a result, management concluded there was only one combined performance obligation. The transaction price at inception is comprised of fixed consideration of $0.0 million in upfront fees, offset by $4.0 million in consideration payable to Boston Pharmaceuticals to reimburse them for expected out-of-pocket manufacturing costs, for a total transaction price of $6.0 million. Management has assessed the forms of variable consideration within the BP Agreement and concluded that the payments are either constrained by the royalty recognition constraint or because management has assessed the most likely amount associated with the payments as zero.

The amounts allocated to the performance obligations did not meet the criteria to be recognized over time on a proportional performance basis and thus will be recognized at a point in time. The Company determined that the performance obligation will be fully satisfied when all of the deliverables in the combined performance obligation are transferred to Boston Pharmaceuticals as that is the point at which Boston Pharmaceuticals can fully use and benefit from the license to PRS-342. The Company transferred all such deliverables to Boston Pharmaceuticals in the fourth quarter of 2021. As of December 31, 2021, the Company has recognized the full transaction price, or $5.7 million, as revenue and there is no remaining deferred revenue.

Seagen

On February 8, 2018, the Company entered into a license and collaboration agreement, or the Seagen Collaboration Agreement, and a non-exclusive Anticalin platform technology license agreement, or the Seagen Platform License, and together with the Seagen Collaboration Agreement, the Seagen Agreements, with Seagen, Inc., or Seagen, pursuant to which the parties will develop multiple targeted bispecific IO treatments for solid tumors and blood cancers.

Under the terms of the Seagen Agreements, the companies will pursue multiple Anticalin-antibody fusion proteins during the research phase. The Seagen Agreements provide Seagen a base option to select up to three programs for further development. Prior to the initiation of a pivotal trial, the Company may opt into global co-development and U.S. commercialization of the second program and share in global costs and profits on an equal basis. Seagen will solely develop, fund and commercialize the other two programs. Seagen may also decide to select additional candidates from the initial research phase for further development in return for the payment to us of additional fees, milestone payments, and royalties

The Seagen Platform License grants Seagen a non-exclusive license to certain intellectual property related to the Anticalin platform technology.

Upon signing the Seagen Agreements, Seagen paid the Company a $30.0 million upfront fee and an additional $4.9 million was estimated to be paid for research and development services as reimbursement to the Company through the end of the research term. In addition, the Company may receive tiered royalties on net sales up to the low double-digits and success-based research, development, commercial, and sales milestones payments across the product candidates, depending on the successful development and commercialization of those candidates. If Seagen exercises its option to select additional candidates from the initial research phase for further development, payment to Pieris of additional fees, milestone payments, and royalties would result.

The term of each of the Seagen Agreements ends upon the expiration of all of Seagen's payment obligations under each agreement. The Seagen Collaboration Agreement may be terminated by Seagen on a product-by-product basis for convenience beginning 12 months after its effective date upon 90 days' notice or, for any program where a pivotal study has been initiated, upon 180 days' notice. Any program may be terminated at Seagen's option. If any program is terminated by Seagen after a pre-defined pre-clinical stage, the Company will have full rights to continue such program. If any program is terminated by Seagen prior to such pre-defined pre-clinical stage, the Company will have the right to continue to develop such program, but will be obligated to offer a co-development option to Seagen for such program. The Seagen Collaboration Agreement may also be terminated by Seagen or the Company for an uncured material breach by the other party upon 90 days' notice, subject to extension for an additional 90 days if the material breach relates to diligence obligations and subject, in all cases, to dispute resolution procedures. The Seagen Collaboration Agreement may also be terminated due to the other party's insolvency and may in certain instances, including for reasons of safety, be terminated on a product-by-product basis. Each party may also terminate the Seagen Agreements if the other party challenges the validity of any patents licensed under the Seagen Agreements, subject to certain exceptions. The Seagen Platform License will terminate upon termination of the Seagen Collaboration Agreement, whether in its entirety or on a product-by-product basis.

The Company determined that the Seagen Agreements should be combined and evaluated as a single arrangement under ASC 606 as they were executed on the same date. The arrangement with Seagen provides for the transfer of the following goods or services: (i) three candidate research licenses that each consist of a non-exclusive platform technology license, a co-exclusive candidate research license, and research and development services, (ii) research, development and manufacturing services associated with each candidate research license, (iii) participation on various governance committees, and (iv) two antibody target swap options which were assessed as material rights.

Management evaluated all of the promised goods or services within the contract and determined which such goods and services were separate performance obligations. The Company determined that the licenses granted, at arrangement inception, should be combined with the research and development services to be provided for the related antibody target programs as they are not capable of being distinct. A third party would not be able to provide the research and development services due to the specific nature of the intellectual property and knowledge required to perform the services, and Seagen could not benefit from the licenses without the corresponding services. The Company determined that the participation on the various governance committees was distinct as the services could be performed by an outside party.

As a result, management concluded there are six separate performance obligations at the inception of the Seagen Agreements: (i) three combined performance obligations, each comprised of a non-exclusive platform technology license, a co-exclusive candidate research license, and research and development services for the first three approved Seagen antibody target programs, (ii) two performance obligations each comprised of a material right for an antibody target swap option for the first and the second approved Seagen antibody target for no additional consideration, and (iii) one performance obligation comprised of the participation on the various governance committees.

The Company allocated consideration to the performance obligations based on the relative proportion of their standalone selling prices. The Company developed standalone selling prices for licenses by applying a risk adjusted, net present value, estimate of future potential cash flows approach, which included the cost of obtaining research and development services at arm's length from a third-party provider, as well as internal full-time equivalent costs to support these services. The Company developed the standalone selling price for committee participation by using management's estimate of the anticipated participation hours multiplied by a market rate for comparable participants.

The transaction price at inception is comprised of fixed consideration of $30.0 million in upfront fees and variable consideration of $4.9 million of estimated research and development services to be reimbursed as research and development occurs through the research term. The $30.0 million upfront fee, which represents the fixed consideration in the transaction price, was allocated to each of the performance obligations based on the relative proportion of their standalone selling prices. The $4.9 million in variable consideration related to the research and development services is allocated specifically to the three target program performance obligations based upon the budgeted services for each program

The amounts allocated to the performance obligations for the three research programs will be recognized on a proportional performance basis through the completion of each respective estimated research term of the individual research programs. The amounts allocated to the material right for the antibody target swap option will be recognized either at the time the material right expires, or if exercised, on a proportional performance basis over the estimated research term for that program. The amounts allocated to the participation on each of the committees will be recognized straight-line over the anticipated research term for all research programs. As of December 31, 2021, there was $21.5 million of aggregate transaction price allocated to remaining performance obligations.

In June 2020, Seagen and the Company entered into amendments to the Seagen Agreements, or together, the First Seagen Amendment. The Seagen Amendment extended the deadline for Seagen to nominate a second and third antibody target. As a result of the Seagen Amendment, which completed the remaining performance obligations under the research term for the first antibody target, the Company recorded $4.2 million of previously deferred revenue for the year ended December 31, 2020. The Company also recorded $5.0 million of milestone revenue in June 2020.

On March 24, 2021, the Company announced that Seagen made a strategic equity investment in Pieris, and that the companies had entered into a combination study agreement, or the Combination Study Agreement, to evaluate the safety and efficacy of combining Pieris' cinrebafusp alfa with Seagen's tucatinib, a small-molecule tyrosine kinase HER2 inhibitor, for the treatment of gastric cancer patients expressing lower HER2 levels (IHC2+/ISH- & IHC1+) as part of the upcoming phase 2 study to be conducted by Pieris. The companies have also entered into an Amended and Restated License and Collaboration Agreement, or the Second Seagen Amendment, in which their existing immuno-oncology collaboration agreement has been amended relating to joint development and commercial rights for the second program in the alliance.

Specifically, under the Second Seagen Amendment, Pieris' option to co-develop and co-commercialize the second ofthree programs in the collaboration has been converted to a co-promotion option in the United States, with Seagen solely responsible for the development and overall commercialization of that program. Pieris will also be entitled to increased royalties from that program in the event that it chooses to exercise the co-promotion option. In connection with the agreements described above, the Company and Seagen entered into a subscription agreement, or the Seagen Subscription Agreement, pursuant to which the Company agreed to issue to Seagen, and Seagen agreed to acquire from the Company, 3,706,174 shares of the Company's common stock for a total purchase price of $13.0 million, or $3.51 per share, in a private placement transaction pursuant to Section 4(a)(2) of the Securities Act of 1933, as amended. The Seagen Subscription Agreement includes a provision to the effect that Seagen may ask the Company to file a registration statement to register the resale of the shares issued to Seagen, at any time beginning on the date that is 60 calendar days from the date of issuance of the shares. The Company assessed the ASC 606 implications of the Seagen Subscription Agreement and concluded that the fair value of the shares on a per share basis was $2.61 per share as of the transaction date. This resulted in a premium paid for the shares of $3.3 million, all of which was recorded in deferred revenue upon contract execution and allocated to the remaining performance obligations.

The Company has concluded that the Combination Study Agreement is within the scope of ASC 808, which defines collaborative arrangements and addresses the presentation of the transactions between the two parties in the income statement and related disclosures. However, ASC 808 does not provide guidance on the recognition of consideration exchanged or accounting for the obligations that may arise between the parties. The Company has concluded that ASC 730, *Research and Development*, should be applied by analogy. There is no financial statement impact for the Combination Study Agreement as the value of the drug supply received from Seagen is offset against the drug supply cost.

Under the Seagen Agreements, the Company is eligible to receive various research, development, commercial and sales milestones. There is uncertainty that the events to obtain the research and development milestones will be achieved given the nature of clinical development and the stage of the Company's technology. The Company has thus determined that all research and development milestones will be constrained until it is deemed probable that a significant revenue reversal will not occur.
As of December 31, 2021, there is $10.3 million and $8.2 million of current and non-current deferred revenue, respectively, related to the Seagen Agreements.

AstraZeneca

On May 2, 2017, the Company entered into a license and collaboration agreement, or the AstraZeneca Collaboration Agreement, and a non-exclusive Anticalin platform technology license agreement, or AstraZeneca Platform License, and together with the AstraZeneca Collaboration Agreement, the AstraZeneca Agreements with AstraZeneca AB, or AstraZeneca, which became effective on June 10, 2017, following expiration of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976. Under the AstraZeneca Agreements the parties will advance several novel inhaled Anticalin proteins.

In addition to the Company's lead inhaled drug candidate, PRS-060/AZD1402, or the AstraZeneca Lead Product, the Company and AstraZeneca, under the original terms of the the AstraZeneca Collaboration Agreement, would also collaborate to progress four additional novel Anticalin proteins against undisclosed targets for respiratory diseases, or the AstraZeneca Collaboration Products, and together with the AstraZeneca Lead Product, the AstraZeneca Products. The Company is responsible for advancing the AstraZeneca Lead Product through its phase 1 study, with the associated costs funded by AstraZeneca. The parties will collaborate thereafter to conduct a phase 2a study in asthma patients, with AstraZeneca continuing to fund development costs. After completion of a phase 2a study, Pieris has the option to co-develop the AstraZeneca Lead Product and

also has a separate option to co-commercialize the AstraZeneca Lead Product in the United States. For the AstraZeneca Collaboration Products, the Company will be responsible for the initial discovery of the novel Anticalin proteins, after which AstraZeneca will take the lead on continued development of the AstraZeneca Collaboration Products. The Company has the option to co-develop two of the four AstraZeneca Collaboration Products beginning at a pre-defined preclinical stage and would also have the option to co-commercialize these two programs in the United States, while AstraZeneca will be responsible for development and commercialization of the other programs worldwide.

The term of each of the AstraZeneca Agreements ends upon the expiration of all of AstraZeneca's payment obligations under such agreement. The AstraZeneca Collaboration Agreement may be terminated by AstraZeneca in its entirety for convenience beginning 12 months after its effective date upon 90 days' notice or, if the Company has obtained marketing approval for the marketing and sale of a product, upon 180 days' notice. Each program may be terminated at AstraZeneca's option; if any program is terminated by AstraZeneca, the Company will have full rights to such program. The AstraZeneca Collaboration Agreement may also be terminated by AstraZeneca or the Company for material breach upon 180 days' notice of a material breach (or 30 days with respect to payment breach), provided that the applicable party has not cured such breach by the permitted cure period (including an additional 180 days if the breach is not susceptible to cure during the initial 180-day period) and dispute resolution procedures specified in the agreement have been followed. The AstraZeneca Collaboration Agreement may also be terminated due to the other party's insolvency and may in certain instances be terminated on a product-by-product and/or country-by-country basis. Each party may also terminate an AstraZeneca Agreement if the other party challenges the validity of patents related to certain intellectual property licensed under such AstraZeneca Agreement, subject to certain exceptions for infringement suits, acquisitions and newly-acquired licenses. The AstraZeneca Platform License will terminate upon termination of the AstraZeneca Collaboration Agreement, on a product-by-product and/or country-by-country basis.

At inception, AstraZeneca is granted the following licenses: (i) research and development license for the AstraZeneca Lead Product, (ii) commercial license for the AstraZeneca Lead Product, (iii) individual research licenses for each of the four AstraZeneca Collaboration Products, (iv) individual commercial licenses for each of the four AstraZeneca Collaboration Products, and (v) individual non-exclusive platform technology licenses for the AstraZeneca Lead Product and the four AstraZeneca Collaboration Products. AstraZeneca will be granted individual development licenses for each of the four AstraZeneca Collaboration Products upon completion of the initial discovery of Anticalin proteins.

The collaboration will be managed on an overall basis by a Joint Steering Committee, or JSC, formed by an equal number of representatives from the Company and AstraZeneca. In addition to the JSC, the AstraZeneca Collaboration Agreement also requires each party to designate an alliance manager to facilitate communication and coordination of the parties' activities under the agreement, and further requires participation of both parties on a joint development committee, or JDC, and a commercialization committee. The responsibilities of these committees vary, depending on the stage of development and commercialization of each product.

Under the AstraZeneca Agreements, the Company received an upfront, non-refundable payment of $45.0 million. In addition, the Company will receive payments to conduct a phase 1 clinical study for the AstraZeneca Lead Product. The Company is also eligible to receive research, development, commercial, sales milestone payments, and royalty payments. The Company may receive tiered royalties on sales of potential products commercialized by AstraZeneca and for co-developed products, gross margin share on worldwide sales equal dependent on the Company's level of committed investment.

The Company determined that the AstraZeneca Agreements should be combined and evaluated as a single arrangement under ASC 606 as they were executed on the same date. The arrangement with AstraZeneca, including the impact of any modifications, provides for the transfer of the following goods and services: (i) five non-exclusive platform technology licenses, (ii) research and development license for the AstraZeneca Lead Product, (iii) commercial license for the AstraZeneca Lead Product, (iv) development and manufacturing services for the AstraZeneca Lead Product (or the phase 1 services), (v) technology transfer services for the AstraZeneca Lead Product, (vi) research services related to the AstraZeneca Lead Product, (vii) participation on each of the committees, (viii) four research licenses for the AstraZeneca Collaboration Products, (ix) four commercial licenses for the AstraZeneca Collaboration Products, (x) research services for the AstraZeneca Collaboration Products and (xi) certain phase 2a services for the AstraZeneca Lead Product. Additionally, as the development licenses on the four AstraZeneca Collaboration Products may be granted at a discount in the future, the Company determined such discounts should be assessed as material rights at inception.

Management evaluated all of the promised goods or services within the contract and determined which such goods and services were separate performance obligations. The Company determined that the licenses granted for the AstraZeneca Lead Product at the inception of the arrangement should be combined with the research services related to the AstraZeneca Lead Product and the licenses granted for the AstraZeneca Collaboration Products should be combined with the research services for the AstraZeneca Collaboration Products, as the licenses are not capable of being distinct. A third party would not be able to provide

the research and development services, due to the specific nature of the intellectual property and knowledge required to perform the services and AstraZeneca could not benefit from the licenses without the corresponding services. The Company also determined that each of the phase 1 services and the phase 2a services for the AstraZeneca Lead Product were distinct and that the participation on the various committees was also distinct as all of the phase 1 services, phase 2a services and the committee services could be performed by an outside party. The Company determined that the commercial licenses for the AstraZeneca Collaboration Products granted at the inception of the arrangement should be combined with the development licenses for the AstraZeneca Collaboration Products as the company would not benefit from the commercial license without the ability to develop each product.

As a result, management concluded that there were16 performance obligations: (i) combined performance obligation comprised of a non-exclusive platform technology license, research and development license, and commercial licenses for the AstraZeneca Lead Product and research services for the AstraZeneca Lead Product, (ii) combined performance obligation comprised of development and manufacturing services, and technology transfer services for the AstraZeneca Lead Product, (iii) committee participation, (iv-vii) four combined performance obligations each comprised of a non-exclusive platform technology license, research licenses, and research services for each AstraZeneca Collaboration Product (viii-xi) four performance obligations comprised of a material right to acquire the development licenses granted for the AstraZeneca Collaboration Products, (xii-xv)four performance obligations comprised of the commercial licenses granted for the AstraZeneca Collaboration Products and (xvi) phase 2a services.

The Company allocated consideration to the performance obligations based on the relative proportion of their standalone selling prices. The Company developed standalone selling prices for licenses and corresponding research services by applying a risk adjusted, net present value, estimate of future potential cash flow approach, which included the cost of obtaining research services at arm's length from a third-party provider, as well as internal full-time equivalent costs to support these services. The Company developed its standalone selling price for development and manufacturing services, and technology transfer services for the AstraZeneca Lead Product using estimated internal and external costs to be incurred.

The Company developed its standalone selling price for committee participation by using management's estimate of the anticipated participation hours multiplied by a market rate for comparable participants.

The Company developed its standalone selling price for the commercial licenses and material rights granted on the development licenses by probability weighting multiple cash flow scenarios using the income approach.

The transaction price was comprised of fixed consideration of $45.0 million in upfront fees and variable consideration of (i) $14.2 million in estimated phase 1 services, (ii) $12.5 million in milestone payments achieved upon the initiation of a phase 1 study in December 2017, and (iii) $4.7 million in estimated phase 2a services. The $45.0 million upfront fee, which represents the fixed consideration in the transaction price, was allocated to each of the performance obligations based on the relative proportion of their standalone selling prices. Variable consideration of $14.2 million is related to the phase 1 services and will be allocated entirely to the performance obligation to which they relate. Variable consideration of $12.5 million related to the phase 1 trial milestone was allocated by relative selling price to the combined performance obligation comprised of a non-exclusive platform technology license, research and development license and commercial licenses for the AstraZeneca Lead Product and research services for the AstraZeneca Lead Product, and the combined performance obligation comprised of development and manufacturing services and technology transfer services for the AstraZeneca Lead Product performance obligations. Variable consideration of $4.7 million for phase 2a services was allocated specifically to the related performance obligation.

The amounts allocated to the license performance obligation for the AstraZeneca Lead Product and thefour performance obligations for the four research licenses for AstraZeneca Collaboration Products will be recognized on a proportional performance basis as the activities are conducted over the life of the arrangement. The amounts allocated to the performance obligation for phase 1 services, technology transfer services for the AstraZeneca Lead Product will be recognized on a proportional performance basis over the estimated term of development through phase 2a study. The amounts allocated to the performance obligation for phase 2a services for the AstraZeneca Lead Product will be recognized on a proportionate performance basis over an estimated term of 12 months. The amounts allocated to the performance obligation for participation on each of the committees will be recognized on a straight-line basis over the expected term of development of the AstraZeneca Lead Product and the AstraZeneca Collaboration Products. The term of performance is approximately five years. The amounts allocated to the four performance obligations for the material rights to acquire a development license and the four performance obligations for commercial licenses for the AstraZeneca Collaboration Products will be recognized upon exercise of the specific material right and delivery of each of the development licenses. As of December 31, 2021, there was $18.7 million of aggregate transaction price allocated to remaining performance obligations.

Additionally, the Company evaluated payments required to be made between both parties as a result of the shared development costs of the AstraZeneca Lead Product and the two AstraZeneca Collaboration Products for which the Company has a co-development option. The Company will classify payments made as a reduction of revenue and will classify payments received as revenue, in the period they are earned.

Under the AstraZeneca Agreements, the Company is eligible to receive various research, development, commercial and sales milestones. There is uncertainty that the events to obtain the research and development milestones will be achieved given the nature of clinical development and the stage of the Company's technology. The Company has thus determined that all research and development milestones, other than the phase 1 initiation milestone achieved in December 2017 and included in the impact of adoption of ASC 606, will be constrained until it is deemed probable that a significant revenue reversal will not occur.

On March 29, 2021, the Company and AstraZeneca entered into (1) Amendment No. 1 to the Non-exclusive Anticalin® Platform License Agreement dated May 2, 2017 and (2) Amendment No. 2 to the License and Collaboration Agreement dated May 2, 2017, as previously amended by Amendment No. 1 dated September 14, 2020, collectively, the Amended Collaboration Agreement. Under the Amended Collaboration Agreement, the parties agreed to restructure certain commercial economics for the PRS-060/AZD1402 program by increasing potential sales milestones and reducing potential sales royalties, while fundamentally maintaining the overall value split between AstraZeneca and the Company.

In connection with the Amended Collaboration Agreement, the Company and AstraZeneca entered into a Subscription Agreement pursuant to which the Company agreed to issue to AstraZeneca, and AstraZeneca agreed to acquire from the Company, 3,584,230 shares of the Company's common stock for a total purchase price of $10.0 million, or $2.79 per share, in a private placement transaction pursuant to Section 4(a)(2) of the Securities Act of 1933, as amended. The Subscription Agreement closed on April 1, 2021 and includes a requirement that the Company file a registration statement to register the resale of the shares issued to AstraZeneca within 60 calendar days of the issuance of the shares. The Company assessed the payment under ASC 606 and concluded that the fair value of the shares on a per share basis was $2.60 per share as of the transaction date. This resulted in a premium paid for the shares of $0.7 million, which was added to the deferred revenue balance and will be recognized over time in line with our revenue recognition pattern for all remaining performance obligations.

Also in March 2021, the Company earned a $13.0 million milestone from AstraZeneca related to the initiation of the phase 2a study for PRS-060/AZD1402. The Company assessed the milestone payment under ASC 606 and determined that there no longer existed a constraint on the milestone as the performance obligation related to the phase 2a study was fully satisfied. Therefore, the Company realized the full $13.0 million as milestone revenue for the year ended December 31, 2021.

In January 2022, the Company and AstraZeneca jointly discontinued one discovery-stage programs as they were not able to validate an exploratory target. Pieris retains co-development and co-commercialization options for two of the three remaining active discovery programs.

As of December 31, 2021, there is $0.9 million and $17.0 million of current and non-current deferred revenue, respectively, related to the AstraZeneca Agreements.

The Company incurred $1.6 million of third-party success fees to obtain the contract with AstraZeneca. Upon adoption of ASC 606, the Company capitalized $1.1 million in accordance with ASC 340. As of December 31, 2021, the remaining balance of the asset recognized from transaction costs to obtain the AstraZeneca contract is $0.6 million. Amortization during the years ended December 31, 2021 and 2020 was de minimis.

Servier

On January 4, 2017, the Company entered into a license and collaboration agreement, or Servier Collaboration Agreement, and a non-exclusive Anticalin platform license agreement, or Servier Platform License, and together with the Servier Collaboration Agreement, the Servier Agreements with Les Laboratoires Servier and Institut de Recherches Internationales Servier, or Servier, pursuant to which the Company and Servier agreed to initially pursue five bispecific therapeutic programs.

Five committed programs were initially defined, which may combine antibodies from the Servier portfolio with one or more Anticalin proteins based on the Company's proprietary platform to generate innovative IO bispecific drug candidates, or the Collaboration Products. The collaboration may be expanded by up to three additional therapeutic programs. The Company had the option to co-develop and retain commercial rights in the United States for PRS-332, the initial lead program under the collaboration, or the Initial Lead, and has a similar option on up to three additional programs, or the Co-Development Collaboration Products, while Servier will be responsible for development and commercialization of the other programs worldwide, or the Servier Worldwide Collaboration Products. Each party is responsible for an agreed upon percentage of shared costs, as set forth in the budget for the collaboration plan, and as further discussed below.

The Co-Development Collaboration Products may be jointly developed, according to a collaboration plan, through marketing approval from the U.S. Food and Drug Administration or the European Medicines Agency. Servier Worldwide Collaboration Products may be jointly developed, according to a collaboration plan, through specified preclinical activities, at which point Servier becomes responsible for further development of the Collaboration Product.

At inception, Servier was granted the following licenses: (i) development license for the Initial Lead, (ii) commercial license for the Initial Lead, (iii) individual research licenses for each of the four Collaboration Products, and (iv) individual non-exclusive platform technology licenses for the Initial Lead and for each of thefour Collaboration Products. Upon achievement of certain development activities, specified by the collaboration for each Servier Agreement, Servier will be granted a development license and a commercial license. For the Initial Lead and the Co-Development Collaboration Products, the licenses granted are with respect to the entire world except for the United States. For Servier Worldwide Collaboration Products, the licenses granted are with respect to the entire world.

The Servier Agreements are managed on an overall basis by a joint executive committee, or JEC, formed by an equal number of members from the Company and Servier. Decisions by the JEC will be made by consensus; however, in the event of a disagreement, each party will have final-decision making authority as it relates to the applicable territory in which such party has commercialization rights for the applicable product. In addition to the JEC, the Servier Collaboration Agreement requires the participation of both parties on: (i) a JSC, (ii) a JDC, (iii) a joint intellectual property committee, or JIPC, and (iv) a joint research committee, or JRC. The responsibilities of these committees vary, depending on the stage of development and commercialization of the Collaboration Products.

For the Initial Lead and Co-Development Collaboration Products, the Company and Servier are responsible for an agreed upon percent of the shared costs required to develop the products through commercialization. In the event that the Company fails to exercise its option to co-develop the Co-Development Collaboration Products, Servier has the right to continue with the development and will be responsible for all costs required to develop the products through commercialization.

Under the Servier Agreements, the Company received an upfront, non-refundable payment of €30.0 million (approximately $32.0 million). In addition, the Company is eligible to receive research, development, commercial, and sales milestone payments as well as tiered royalties up to low double digits on the sales of commercialized products in the Servier territories. Since inception of the Servier Collaboration Agreement, the Company has achieved four development milestones under Servier Agreements totaling €3.8 million (approximately $4.3 million), all of which became billable on their respective achievement dates.

The initial research collaboration term, as it relates to the Initial Lead and Collaboration Products, shall continue forthree years from the effective date of the Servier agreements, and may be mutually extended for two one-year terms consecutively applied.
The term of each Servier Agreement ends upon the expiration of all of Servier's payment obligations under such Servier Agreement. The Servier Agreements may be terminated by Servier for convenience beginning 12 months after their effective date upon 180 days' notice. The Servier Agreements may also be terminated by Servier or the Company for material breach upon 90 days' or 120 days' notice under the Servier Collaboration Agreement and the Servier Platform License, respectively, provided that the applicable party has not cured such breach by the applicable 90-day or 120-day permitted cure period, and dispute resolution procedures specified in the applicable Servier Agreement have been followed. The Servier Agreements may also be terminated due to the other party's insolvency or for a safety issue and may in certain instances be terminated on a product-by-product and/or country-by-country basis. The Servier Platform License will terminate upon termination of the Servier Collaboration Agreement, on a product-by-product and/or country-by-country basis. In February 2020, the research term was extended for 12 months. The research term was then extended for another12 months in February 2021.

As the Company and Servier are considered to be active participants in the Servier Agreements and are exposed to significant risks and rewards, certain units of account within the Servier Agreements are within the scope of ASC 808. The arrangement with Servier provides for the transfer of the following goods and services: (i) five non-exclusive platform technology licenses, a development license, a commercial license and research and development services for the Initial Lead, (ii) participation on each of the committees, (iii) four research licenses for Collaboration Products, and (iv) research and development services for the Collaboration Products. Additionally, as the development and commercial licenses on the four Collaboration Products may be granted at a discount in the future, the Company determined such discounts should be assessed as material rights at inception.

Management evaluated all of the promised goods or services within the contract and determined which goods and services
were separate performance obligations. The Company determined that the licenses granted at the inception of the Servier collaboration, should be combined with the research and development services to be provided for the Initial Lead and

Collaboration Products, over the term of the Servier Agreements, as such licenses are not capable of being distinct. A third party would not be able to provide the research and development services, due to the specific nature of the intellectual property and knowledge required to perform the services, and Servier could not benefit from the licenses without the corresponding services. The Company determined that the participation on the various committees was distinct as the services could be performed by an outside party.

As a result, management concluded that there are10 performance obligations at the inception of the Servier Agreements. The following performance obligations are within the scope of ASC 808: (i) combined performance obligation comprised of a non-exclusive platform technology license, commercial license, development license and research and development services for the Initial Lead, (ii) two separate performance obligations each comprised of a combined non-exclusive platform technology license, research license, and research and development services for each Co-Development Collaboration Product (iii) one performance obligation comprised of participation in the various governance committees, and (iv) two combined performance obligations comprised of the development and commercial licenses granted for the Co-Development Collaboration Products (and corresponding discounts) upon the achievement of specified preclinical activities, resulting in material rights. Revenue recognized associated with these performance obligations are presented as Collaboration Revenue within the Statement of Operations. The following performance obligations are within the scope of ASC 606: (i) two separate performance obligations each comprised of a combined non-exclusive platform technology license, research license and research and development services for each Servier Worldwide Collaboration Product, and (ii) two combined performance obligations comprised of the development and commercial licenses granted for the Servier Worldwide Collaboration Products (and corresponding discounts) upon the achievement of specified preclinical activities, resulting in material rights. Revenue recognized associated with these performance obligations are presented as Customer Revenue within the Statement of Operations.

The Company allocated consideration to the performance obligations based on the relative proportion of their standalone selling prices. The Company developed its standalone selling prices for licenses by applying a risk adjusted, net present value, estimate of future potential cash flows approach, which included the cost of obtaining research and development services at arm's length from a third-party provider, as well as internal full-time equivalent costs to support these services.

The Company developed its estimate of standalone selling price for committee participation by using management's estimate of the anticipated participation hours multiplied by a market rate for comparable participants.

The Company developed its estimate of standalone selling price for the material rights granted on the development and commercial licenses granted for the Collaboration Products by probability weighting multiple cash flow scenarios using the income approach.

The transaction price at inception is comprised of the fixed upfront fee of €30.0 million (approximately $32.0 million) and was allocated to the performance obligations based on the relative proportion of their standalone selling prices.

The amounts allocated to the performance obligation for the Initial Lead and thefour performance obligations for the four research and development licenses for Collaboration Products will be recognized on a proportional performance basis as the activities are conducted over the life of the arrangement. The term of the performance at inception of the Servier Agreements for the Initial Lead and each of the Co-Development Collaboration Products may be through approval of certain regulatory bodies; a period which could be many years. The term of the performance for each of the other two Servier Worldwide Collaboration Products is through the initial research and collaboration term, plus potential extensions. The amounts allocated to the performance obligation for participation on each of the committees will be recognized on a straight-line basis over the anticipated performance period over the entirety of the arrangement with Servier. The amounts allocated to the four performance obligations for the material rights to acquire development and commercial licenses for the Co-Development Collaboration Products are granted in the future will be recognized over time upon delivery of each of the licenses through marketing approval. The amounts allocated to the four performance obligations for the material rights to acquire development and commercial licenses for the Servier Developed Collaboration Products are granted in the future will be recognized upon delivery of each of the licenses. As of December 31, 2021, there was $10.4 million of aggregate transaction price allocated to remaining performance obligations.

Additionally, the Company evaluated payments required to be made between both parties as a result of the shared development costs of the Initial Lead and Collaboration Products. The Company will classify payments made as a reduction of revenue and will classify payments received as revenue, in the period they are earned.

Under the Servier Agreements the Company is eligible to receive various research, development, commercial, and sales milestones. There is uncertainty that the events to obtain the research and development milestones will be achieved given the

nature of clinical development and the stage of the Company's technology. The Company has thus determined that all research and development milestones will be constrained until it is deemed probable that a significant revenue reversal will not occur.

In September 2019, Servier notified the Company of its decision to discontinue co-development of PRS-332, a PD-1-LAG-3 bispecific that served as the initial development program under the Pieris-Servier alliance, for strategic reasons. The Company does not presently intend to continue development of PRS-332 but retains full rights to advance the development and commercialization of the product on a world-wide basis in the future.

In February 2020, the research term was extended for 12 months. The Company updated the transaction price for the extension for revenue recognition purposes and allocated it ratably over all unsatisfied performance obligations. As part of the expiration of the initial research term, the option to expand the collaboration beyond the initial five committed programs also expired. In March 2020, Servier notified the Company of its decision to discontinue co-development of two earlier preclinical stage programs for strategic reasons based upon an extensive portfolio review. The notification required a 60-day period to complete remaining obligations on the programs; however, the Company determined that the material rights to acquire development and commercial licenses for one Co-Development Collaboration Product and for one Servier Developed Collaboration Products lapsed in March 2020 and recognized $7.1 million of previously deferred revenue associated with these material rights during 2020. The discontinuation of the two earlier preclinical stage programs decreased the future potential milestone payments the Company could achieve. The parties continue to advance the development of two preclinical programs: PRS-344/S095012, a 4-1BB/PD-L1 bispecific designed as a co-development program, and PRS-352, which addresses undisclosed targets and for which Servier has worldwide rights.

In February 2021, the research term was extended for another 12 months.

As of December 31, 2021, there is $5.8 million and $4.6 million of current and non-current deferred revenue, respectively, related to the Servier Agreements.

The Company incurred costs to obtain the contract with Servier. Upon adoption of ASC 606, the Company capitalized $0.5 million of third-party service fees in accordance with ASC 340. As of December 31, 2021, the remaining balance of the asset recognized from costs to obtain the Servier contract is $0.1 million. Amortization during the twelve months ended December 31, 2021 was de minimis. Amortization during the twelve months ended December 31, 2020 was $0.1 million.

Contract Balances

The Company receives payments from its collaboration partners based on payments established in each contract. Upfront payments and fees are recorded as deferred revenue upon receipt or when due until such time as the Company satisfies its performance obligations under each arrangement. A contract asset is a conditional right to consideration in exchange for goods or services that the Company has transferred to a customer. Amounts are recorded as accounts receivable when the Company's right is unconditional.

There were $31.6 million of additions to deferred revenue during the twelve months ended December 31, 2021 and reductions to deferred revenue were $11.0 million for the twelve months ended December 31, 2021.

4. Collaboration agreements

In August 2020, the Company entered into a Clinical Trial Collaboration and Supply Agreement, or the Lilly Agreement, with Eli Lilly and Company, or Lilly, pursuant to which the Company and Lilly will collaborate on a phase 2 clinical study, or the Study, to determine the safety and efficacy of the Company's cinrebafusp alfa in combination with the standard of care regimen for the second-line treatment of advanced or metastatic gastric cancer, ramucirumab (CYRAMZA®) and paclitaxel for the second-line treatment of HER2+ gastric cancer.

Under the terms of the non-exclusive Lilly Agreement, the Company will sponsor the Study and Lilly will supply the Company with ramucirumab as well as provide input on certain clinical and regulatory aspects of the Study in exchange for jointly owning clinical data and inventions relating to the combination regimen that may arise from the Study. Any material changes to the protocol for the Study, and any changes relating to ramucirumab, will require Lilly's prior written consent, which shall not be unreasonably withheld, conditioned or delayed.

The Lilly Agreement will expire upon completion of the parties' contractual obligations. The Lilly Agreement may also be terminated (a) by either party for an uncured material breach by the other party upon 60 days' notice, subject to a reasonable extension if such material breach requires more than 60 days to cure; (b) by either party in the event that the Study unreasonably affects patient safety, provided that the terminating party promptly notifies the other party and the other party is

given the opportunity to propose modifications to the Study to address the safety issues; (c) by either party, following15 days' written notice, if regulatory action is taken preventing the terminating party from providing its compound or if the terminating party decides to discontinue development of its compound; (d) by either party, immediately upon written notice to the other party for breach by the other party of its material obligations under certain sections of the Lilly Agreement, or breach of certain of the other party's representations and warranties; and (e) by Lilly in the event of certain safety concerns related to the use of ramucirumab in the Study.

The Company concluded that the Lilly Agreement is within the scope of ASC 808, which defines collaborative arrangements and addresses the presentation of the transactions between the two parties in the income statement and related disclosures. However, ASC 808 does not provide guidance on the recognition of consideration exchanged or accounting for the obligations that may arise between the parties. The Company has concluded that ASC 730, Research and Development, should be applied by analogy. There is no financial statement impact for the Lilly Agreement as the value of the drug supply received from Lilly is offset against the drug supply cost.

5. Grant Income

One of the Company's proprietary respiratory assets is PRS-220, an oral inhaled Anticalin protein targeting connective tissue growth factor, or CTGF, and it is being developed as a local treatment for idiopathic pulmonary fibrosis. In June 2021, the Company received a €14.2 million (approximately $17.0 million) grant from the Bavarian Ministry of Economic Affairs, Regional Development and Energy (the Bavarian Grant) supporting research and development for post-acute sequelae of SARS-CoV-2 infection (PASC) pulmonary fibrosis, or PASC-PF, also known as post-COVID-19 syndrome pulmonary fibrosis, or "long COVID".

The Bavarian Grant provides partial reimbursement for qualifying research and development activities on PRS-220, including drug manufacturing costs, activities and costs to support an IND filing, and phase 1 clinical trials costs. The Bavarian Grant provides reimbursement of qualifying costs incurred through August 2023, which follows the expected development timeline of this program. Qualifying costs incurred may exceed the annual grant funding thresholds. If the Company receives any proceeds from the sale of or licensing income from PRS-220, the funds available for reimbursement will be reduced proportionally if they are obtained prior to August 2023. The Company is required to communicate such proceeds in each case with the request to draw-down the funds.

6. Cash, Cash Equivalents and Investments

As of December 31, 2021 and 2020, cash equivalents were $56.9 million and $64.0 million, respectively, and are comprised of money market accounts, all of which are Level 1 investments. The Company did not hold any Level 2 or 3 investments as of December 31, 2021 and 2020 and did not have any transfers of investments between levels during the years ended December 31, 2021 and 2020.

The Company did not have any realized gains or losses for the year ended December 31, 2021. The Company had $0.6 million of realized losses for the year ended December 31, 2020.

7. Property and Equipment, Net

Property and equipment are summarized as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Leasehold improvements	$ 13,130	$ 14,159
Laboratory equipment	11,354	11,188
Office furniture and equipment	1,959	2,120
Computer equipment	396	394
Property and equipment at cost	26,839	27,861
Accumulated depreciation	(7,717)	(5,815)
Property and equipment, net	$ 19,122	$ 22,046

Depreciation expense was $2.4 million and $2.1 million for the years ended December 31, 2021 and 2020, respectively. There were no other changes in accumulated depreciation other than the foreign currency impact.

8. Accrued Expenses

Accrued expenses and other current liabilities consisted of the following (in thousands):

	Years Ended December 31,	
	2021	2020
Research and development fees	$ 5,682	$ 2,001
Compensation expense	3,581	2,759
Accrued accounts payable	2,980	1,220
Collaboration cost-sharing obligation	1,610	16
Accrued license obligations	1,541	358
Lease liabilities	1,049	1,030
Other current liabilities	393	347
Total	$ 16,836	$ 7,731

9. Income Taxes

The Company reported a loss before income taxes consisting of the following (in thousands):

	Years Ended December 31,	
	2021	2020
Domestic	$ (11,312)	$ (12,134)
Foreign	(34,426)	(24,932)
Loss before income taxes	$ (45,738)	$ (37,066)

The components of the provision for income taxes are as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Current:		
Federal	$ —	$ —
State	—	—
Foreign	—	164
Total current	—	164
Deferred:		
Federal	—	—
State	—	—
Foreign	—	—
Total deferred	—	—
Provision for income taxes	$ —	$ 164

The reconciliation of the federal statutory rate to the Company's effective tax rate is as follows:

	2021	2020
Federal income tax rate	21.0 %	21.0 %
Foreign rate differential	5.6	1.9
State tax, net of federal benefit	1.2	1.9
US tax on foreign income	—	—
Share-based awards compensation	(3.5)	(3.8)
Permanent items	(0.2)	(2.4)
Provision to return	3.3	—
Other	—	(0.4)
Change in valuation allowance	(27.4)	(18.7)
Effective income tax rate	— %	(0.5)%

The components of deferred tax assets and liabilities related to net tax effects of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income taxes purposes were as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	$ 49,280	$ 39,175
Share-based awards compensation	2,739	2,913
Accrued expenses	323	230
Depreciation and other	384	297
Unrealized foreign currency	256	771
Lease liability	4,022	4,582
Total deferred tax assets	57,004	47,968
Deferred tax liabilities:		
Right-of-use asset	(3,729)	(4,235)
Accrued expenses	(68)	—
Total deferred tax liabilities	(3,797)	(4,235)
Less: valuation allowance:	(53,207)	(43,733)
Net deferred tax asset	$ —	$ —

The Company operates in multiple jurisdictions. Accordingly, the Company files U.S. federal and state income tax returns as well as returns in multiple foreign jurisdictions. In assessing the realizability of deferred tax assets, management considers whether it is more likely than not that some portion or all deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible. Management considers the scheduled reversal of deferred tax liabilities, projected future taxable income, and tax-planning strategies in making this assessment. Management believes it is more likely than not that the results of future operations will not generate sufficient taxable income in the United States or in its foreign jurisdictions to realize the full benefits of its deferred tax assets. As of December 31, 2021, the Company continues to maintain a full valuation allowance against all net deferred tax assets.

The cumulative amount of earnings of our foreign subsidiaries are expected to be permanently invested in the foreign subsidiaries. Deferred taxes have not been provided on the excess of book basis over tax basis, or the excess tax basis over book basis in the shares of our foreign subsidiaries because these basis differences are not expected to reverse in the foreseeable future and are essentially permanent in duration. Our intention is to reinvest the earnings of the foreign subsidiaries indefinitely.

The increase in the valuation allowance of deferred tax assets of $9.5 million was primarily a result of the operating losses generated in current tax year.

As of December 31, 2021, the Company had net operating loss carryforwards for U.S. federal income tax purposes of $13.1 million and net operating loss carryforwards for state income tax purposes of $37.4 million. Federal tax loss carryforwards that were created prior to December 31, 2017 expire through 2037 and federal losses created after that date do not expire. State loss carryforwards expire starting in 2035. Pursuant to Section 382 of the Internal Revenue Code, and similar state tax law, certain substantial changes in the Company's ownership may result in a limitation on the amount of net operating loss and tax credit carryforwards that may be used in future years. Utilization of the net operating loss and tax credit carryforwards may be subject to an annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of net operating loss and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company completed a Section 382 study through December 31, 2020. Based on the study, the Company underwent an ownership change for Section 382 purposes which occurred in February 2018. As a result of the ownership change, the Company's net operating loss and tax credit carryforwards as of the ownership change dates are subject to limitation under Section 382; however, these limitations are not expected to result in any of the impacted net operating loss and tax credit carryforwards to expire unutilized. Any net operating losses or tax credits generated after the February 2018 change are not subject to this annual limitation. However, subsequent ownership changes, as defined by Section 382, may potentially further limit the amount of net operating loss and tax credit carryforwards that could be utilized to offset future taxable income and tax. The Company is currently open to examination under the statute of limitations by the Internal Revenue Service and state jurisdictions for the tax years ended

2016 through the current year. Carryforward tax attributes generated in years past may still be adjusted upon future examination if they have or will be used in a future period. The Company is currently under examination in Germany for 2014 through 2017; however, the Company is not under examination by the Internal Revenue Service or any other jurisdictions for any tax years.

As of December 31, 2021, the Company had German corporate income tax and trade tax net operating loss carryforwards of approximately $154.8 million and $153.9 million respectively. Under current German laws, tax loss carryforwards may only be used to offset any relevant later assessment period (calendar year) of $1.2 million plus 60% of the exceeding taxable income and trade profit of such period and do not expire. In addition, certain transactions, including transfers of shares or interest in the loss holding entity, may result in the partial or total forfeiture of tax losses existing at that date. Partial or total forfeiture of tax losses may further occur in corporate reorganizations of the loss holding entity.

The Company accounts for uncertain tax positions pursuant to ASC 740,*Income Taxes*, which prescribes a recognition threshold and measurement process for financial statement recognition of uncertain tax positions taken or expected to be taken in a tax return. If the tax position meets this threshold, the benefit to be recognized is measured at the largest amount of benefit that is more likely than not (determined by cumulative probability) of being realized upon ultimate settlement with the taxing authority. The Company recorded an uncertain tax position related to a prior year position, that if successfully challenged by tax authorities could result in the loss of certain tax attributes. The balance of uncertain tax positions will remain until such time that settlement is reached with the relevant tax authorities or should the statute of limitations expire. The Company recognizes interest and penalties, if any, related to uncertain tax positions in income tax expense. No interest and penalties related to uncertain tax positions were accrued at December 31, 2021 and December 31, 2020.

The following table sets forth a reconciliation of the beginning and ending amounts of unrecognized tax benefits, excluding the impact of interest and penalties, for the years ended December 31, 2021 (in thousands):

Unrecognized tax benefits at December 31, 2020	$	6,135
Currency translation adjustment		(470)
Unrecognized tax benefits at December 31, 2021	$	5,665

The Company does not expect unrecognized tax benefits to change significantly over the next 12 months. The full amount of unrecognized tax benefits would impact the effective rate, subject to valuation allowance considerations, if recognized.

10. Stockholders' equity

The Company had 300,000,000 shares authorized and 72,222,661 and 56,002,815 shares of common stock issued and outstanding as of December 31, 2021 and December 31, 2020, respectively, with a par value of $0.001 per share.

The Company had 10,000,000 shares authorized and 15,617 shares of preferred stock issued and outstanding as of December 31, 2021. The Company had 10,000,000 shares authorized and 14,429 shares of preferred stock issued and outstanding as of December 31, 2020. Preferred stock has a par value of $0.001 per share, and consists of the following tranches:

- Series A Convertible, 85 and 2,907 shares issued and outstanding at December 31, 2021 and December 31, 2020, respectively.
- Series B Convertible, 4,026 and 5,000 shares issued and outstanding at December 31, 2021 and December 31, 2020, respectively.
- Series C Convertible, 3,506 and 3,522 shares issued and outstanding at December 31, 2021 and December 31, 2020, respectively.
- Series D Convertible, 3,000 shares issued and outstanding at both December 31, 2021 and December 31, 2020.
- Series E Convertible, 5,000 and zero shares issued and outstanding at December 31, 2021 and December 31, 2020, respectively.

Common Stock

Each share of the Company's common stock is entitled toone vote and all shares rank equally as to voting and other matters. Dividends may be declared and paid on the common stock from funds legally available therefor, if, as and when determined by the Board of Directors.

Preferred Stock

The Company has issued multiple series (Series A through E) of preferred stock to certain entities affiliated with Biotechnology Value Fund, L.P., or BVF. In each case, each share Preferred Stock is convertible into 1,000 shares of the Company's common stock (subject to adjustment as provided in the Certificate of Designation for each series) at any time at the option of the holder, provided that the holder is prohibited from converting the Preferred Stock into shares of the Company's common stock if, as a result of such conversion, the holder, together with its affiliates, would own more than 9.99% of the total number of shares of Common Stock then issued and outstanding, or the Beneficial Ownership Limitation. The holder may reset the Beneficial Ownership Limitation to a higher or lower number, not to exceed 19.99% of the total number of common shares issued and outstanding immediately after giving effect to a conversion, upon providing written notice to the Company. Any such notice providing for an increase to the Beneficial Ownership Limitation will be effective 61 days after delivery to the Company.

Series A, Series B, Series C, Series D and Series E Preferred Stock rank senior to the Company's common stock; senior to any class or series of capital stock of the Company created after the designation of and specifically ranking by its terms as junior to the five series of Preferred Stock; in parity with each other and with any class or series of capital stock of the Company created after the designation of and specifically ranking by its terms as in parity with the existing five series of Preferred Stock; and junior to any class or series of capital stock of the Company created after the designation of and specifically ranking by its terms as senior to the existing five series of Preferred Stock. In the event of the Company's liquidation, dissolution or winding up, subject to the rights of holders of, holders are entitled to receive a payment equal to $0.001 per share of Preferred Stock pursuant to the rights and preferences discussed above, plus an additional amount equal to any dividends declared but unpaid on such shares. However, if the assets of the Company are insufficient to comply with the preceding sentence, then all remaining assets of the Company shall be distributed ratably to holders of the shares of the existing five series of Preferred Stock.

For each series of Preferred Stock, the Company designated the requisite number of shares of its authorized and unissued preferred stock as a specific series of Preferred Stock and filed a Certificate of Designation with the Nevada Secretary of State.

Shares of Preferred Stock generally have no voting rights, except as required by law and except that the consent of holders of a majority of the then outstanding Preferred Stock is required to amend the terms of the Certificate of Designation for each respective series of Preferred Stock. Holders of Preferred Stock are entitled to receive any dividends payable to holders of the Company's common stock subject to the rights and preferences discussed above, in each case, as to distributions of assets upon the Company's liquidation, dissolution or winding up whether voluntarily or involuntarily and/or the right to receive dividends.

Series A Preferred Stock

In June 2016, the Company entered into a securities purchase agreement for a private placement of the Company's securities with a select group of institutional investors, or the 2016 PIPE. The 2016 PIPE sale transaction, by the Company, consisted of 8,188,804 units at a price of $2.015 per unit for gross proceeds, to the Company, of approximately $16.5 million. After deducting for placement agent fees and offering expenses, the aggregate net proceeds from the private placement was approximately $15.3 million. In connection with the 2016 PIPE, the Company issued 3,225,804 shares of common stock and 4,963 shares of Series A Preferred Stock to the 2016 PIPE investors.

Series B Preferred Stock

On January 30, 2019, the Company and certain entities affiliated with Biotechnology Value Fund, L.P., or BVF entered into an exchange agreement pursuant to which BVF agreed to exchange an aggregate of 5,000,000 shares of the Company's common stock owned by BVF for an aggregate of 5,000 shares of Series B Preferred Stock.

Series C and 2019 Private Placement

In November 2019, the Company entered into a securities purchase agreement for a private placement, or the Purchase Agreement with a select group of institutional investors, including lead investor BVF as well as existing and new investors, or Investors. The private placement consisted of 9,014,960 units, at a price of $3.55 per unit, or the Financing, for gross proceeds of approximately $32.0 million, and net proceeds to the Company of approximately $31.0 million. Each unit consists of (i) one share of the Company's common stock, or Common Shares, or 0.001 shares of non-voting Series C convertible preferred stock, or Series C Preferred Shares, and together with the Common Shares, or Shares, and (ii) one immediately-exercisable warrant to purchase one share of the Company's common stock with an exercise price of $7.10, or Exercise Price.

If (i) the initial public disclosure of the phase 2a Study of PRS-060/AZD1402 that includes the "p" value achieved for the primary endpoint of such study reveals top-line data on the primary efficacy endpoint in the phase 2a Study with a "p" value below 0.05 (i.e., $p < 0.05$) in at least one dose level; and (ii) the 10-day volume weighted average stock price commencing on the trading day immediately after the initial public disclosure is at least three percent more than the Exercise Price, ((i) and (ii), collectively, the "Performance Condition"), then the warrants will be exercisable for a period of 60 days from the date of the

initial data disclosure and may only be exercised for cash. Otherwise, the warrants will be exercisable for a period of five years from the date of issuance, or Exercise Date. If the Performance Condition has not been met and the last reported sale price of the Company's common stock immediately prior to the Expiration Date was greater than the Exercise Price, then the warrants shall be automatically deemed exercised on a cashless basis on the Expiration Date.

Upon issuance, each Series C Preferred Share included an embedded beneficial conversion feature as the market price of the Company's Common Stock on the date of issuance of the Series C convertible preferred stock was $3.43 per share. As a result, the Company recorded the intrinsic value of the beneficial conversion feature of $2.8 million as a discount on the Series C convertible preferred stock at issuance. As the Series C Preferred Shares are immediately convertible upon issuance and do not include a stated redemption date, the discount was immediately accreted as a deemed dividend.

Series D Preferred Stock Conversion

On March 31, 2020, the Company and certain entities affiliated with BVF entered into an exchange agreement pursuant to which, on April 1, 2020, BVF exchanged an aggregate of 3,000,000 shares of the Company's common stock owned by BVF for an aggregate of 3,000 shares of Series D Preferred Stock.

Series E Preferred Stock Conversion

On May 20, 2021, the Company and certain entities affiliated with BVF entered into an exchange agreement pursuant to which, BVF exchanged an aggregate of 5,000,000 shares of the Company's common stock owned by BVF for an aggregate of 5,000 shares of Series E Preferred Stock.

Open Market Sales Agreement

In August 2019, the Company entered into a sales agreement with Jefferies LLC pursuant to which the Company may offer and sell shares of its common stock, from time to time, up to an aggregate gross sales proceeds of $50.0 million (the 2019 ATM Program). In August 2021, the Company established a second ATM offering program, or the 2021 ATM Program, under the existing sales agreement with Jefferies LLC, pursuant to which the Company may offer and sell shares of its common stock, par value $0.001 per share, from time to time, up to an aggregate amount of gross sales proceeds of $50.0 million. The 2021 ATM Program is offered under a shelf registration statement on Form S-3 that was filed with and declared effective by the SEC in August 2021.

For the year ended December 31, 2021, the Company sold 8.2 million shares for gross proceeds of $39.7 million under both ATM programs at an average stock price of $4.85. For the year ended December 31, 2020, the Company sold 3.6 million shares at a price of $2.80 per share resulting in gross proceeds of $10.0 million under the 2019 ATM Program only, which expired in August 2021.

11. Net Loss per Share

Basic net loss per share is calculated by dividing net income (loss) by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock and if-converted methods. For purposes of the diluted net loss per share calculation, preferred stock, stock options, and warrants are considered to be common stock equivalents but have been excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented.

For the years ended December 31, 2021 and 2020, and as calculated using the treasury stock method, approximately 36.8 million and 37.0 million of weighted average shares, respectively, were excluded from the calculation of diluted weighted average shares outstanding as their effect was antidilutive.

12. Stock and Employee Benefit Plans

Employee, Director and Consultant Equity Incentive Plans

At the Annual Shareholder Meeting, held on June 23, 2020, the shareholders approved the 2020 Employee, Director and Consultant Equity Incentive Plan, or the 2020 Plan. The 2020 Plan originally permitted the Company to issue up to 3,500,000 shares of common stock pursuant to awards granted under the 2020 Plan. Upon approval of the 2020 Plan, the

2019 Employee, Director and Consultant Equity Incentive Plan, or the 2019 Plan, was terminated; all unissued options were canceled and no additional awards will be made thereunder. All outstanding awards under the 2019 Plan will remain in effect and any awards forfeited from the outstanding awards will be allocated back into the 2020 Plan. The 2020 Plan, similar to the 2019 Plan, provided for the grant of stock options, restricted and unrestricted stock awards, and other stock-based awards to employees of the Company, non-employee directors of the Company, and certain other consultants performing services for the Company as designated by either the Board of Directors or the compensation committee of the Board of Directors. At the 2021 Annual Meeting of Stockholders, held on June 25, 2021, the Company's stockholders approved the first amendment to the 2020 Plan to add 2,250,000 shares for issuance under the 2020 Plan, which increased the total permitted for issuance under the 2020 Plan to 5,750,000.

There were approximately 1,579,678 shares remaining and available for grant under the 2019 Plan that terminated pursuant to the approval of the 2020 Plan. The 2020 Plan permits the Company to issue up to 5,750,000 shares reserved for issuance pursuant to the 2020 Plan and any additional shares which may be issued if awards outstanding under the Registrant's 2014, 2016, 2018 and 2019 Plans are canceled or expire.

The Company's stock options have a maximum term of 10 years from the date of grant. Stock options granted may be either incentive stock options or nonqualified stock options and the exercise price of stock options must be at least equal to the fair market value of the common stock on the date of grant. The Company's general policy is to issue common shares upon the exercise of stock options.

The Company estimates the fair value of each stock award on the grant date using the Black-Scholes option-pricing model based on the following assumptions:

	Years Ended December 31,	
	2021	2020
Risk free interest rate	0.46% - 1.20%	0.33% - 1.53%
Expected term (in years)	5.31 - 5.73	5 - 5.73
Dividend yield	—	—
Expected volatility	75.0% - 81.7%	70.0% - 75.8%

The weighted-average fair value of the 3,182,696 and 2,311,481 options granted during the years ended December 31, 2021 and 2020 was $2.04 and $1.92, respectively. As of December 31, 2021, there were 3,282,399 shares available for future grant under the 2020 Plan.

The following table summarizes stock option activity for employees and non-employees:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life	Aggregate Intrinsic Value (in thousands)
Outstanding, December 31, 2020	9,591,123	$ 3.44		$ 2,303
Granted	2,822,696	3.05		—
Exercised	482,115	2.14		1,106
Canceled	379,991	4.96		102
Outstanding, December 31, 2021	11,551,713	$ 3.34	6.71 years	$ 11,402
Vested or expected to vest, December 31, 2021	11,551,713	$ 3.34	6.71 years	$ 11,402
Exercisable, December 31, 2021	7,376,177	$ 3.45	5.52 years	$ 7,964

Periodically, the Company grants inducement options, which are awards outside of approved stock option plans, and which are material awards to the executive officers or other personnel entering senior leadership roles with the Company. The terms of inducement option awards were substantially the same as those issued under our 2020 Plan. These awards are excluded from the table above. The following table summarizes stock option activity for these inducement options (in thousands):

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life	Aggregate Intrinsic Value (in thousands)
Outstanding, December 31, 2020	420,313	$ 5.00		$ —
Granted	360,000	$ 3.48		$ —
Canceled or Expired	120,313	$ 5.87		$ —
Outstanding, December 31, 2021	660,000	$ 4.01	8.71 years	$ 108
Vested or expected to vest, December 31, 2021	660,000	$ 4.01	8.71 years	$ 108
Exercisable, December 31, 2021	168,750	$ 4.65	7.66 years	$ —

Employee Stock Purchase Plans

The 2018 ESPP provides eligible employees with the opportunity, through regular payroll deductions, to purchase shares of the Company's common stock at 85% of the lower closing market price of the common stock at the beginning date or ending date of each purchase period. The plan includes two six-month purchase periods per year beginning in both June and December. The Company has reserved 500,000 shares of common stock for the administration of the 2018 ESPP. Total shares purchased under the plan were 64,257 and 69,544 for the years ended December 31, 2021 and 2020, respectively. The fair value of shares expected to be purchased under the 2018 ESPP was determined using the Black-Scholes model with the following assumptions:

	Years Ended December 31,	
	2021	2020
Risk free interest rate	0.04% - 0.10%	0.10% - 0.18%
Expected term (in years)	0.5 years	0.5 years
Dividend yield	—	—
Expected volatility	60.46% - 131.21%	74.36% - 120.89%

Total Stock-based Compensation Expense

Total stock-based compensation expense is recorded in operating expenses based upon the functional responsibilities of the individuals holding the respective options as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Research and development	$ 2,274	$ 2,394
General and administrative	2,941	2,696
Total stock-based compensation	$ 5,215	$ 5,090

As of December 31, 2021, the total unrecognized compensation cost related to all non-vested awards was $8.1 million of which $1.2 million are for inducement options. The Company expects to recognize the compensation cost over a remaining weighted-average period of 2.64 years.

13. License Agreement

TUM License

The Company and the Technical University of Munich, or TUM, initiated discussions in the second quarter of 2018 to clarify, expand and restructure the research and licensing agreement with TUM, the TUM License, including the parties' obligations under the TUM License. The TUM License assigns or exclusively licenses to the Company certain intellectual property related to the Company's Anticalin platform technology. The parties' discussions relate to revised commercial terms and to re-initiating additional collaborations between faculty at TUM and Pieris. While an amended and restated license agreement has not yet been completed, the Company intends to enter into such an amendment. These discussions may also lead to an increase in the Company's collaborative research activities with TUM.

14. Leases

The Company currently leases office space in Boston, Massachusetts. In August 2015, the Company entered into a sublease to lease approximately 3,950 square feet. The sublease originally expired on February 27, 2022 or such earlier date pursuant to the termination provisions of the sublease. In July 2021, the Company extended the lease for this office space for an additional 10 months through December 31, 2022.

In October 2018, Pieris GmbH entered into a lease for office and laboratory space located in Hallbergmoos, Germany, or the Hallbergmoos Lease. Pieris GmbH moved its operations, formerly conducted in Freising, Germany, to the Hallbergmoos facility in February 2020.

Under the Hallbergmoos Lease, Pieris GmbH rents approximately 105,000 square feet, of which approximately 96,400 square feet were delivered by the lessor in February 2020 and approximately 8,600 square feet were delivered by the lessor by May 2020. An additional approximately 22,300 square feet is expected to be delivered by the lessor by October 2024. Pieris GmbH has a first right of refusal to lease an additional approximate 13,400 square feet.

The Hallbergmoos Lease provides for an initial rental term of 12.5 years which commenced in February 2020 when the leased property was delivered to Pieris GmbH. Pieris GmbH also has an option to extend the Hallbergmoos Lease for two additional 60-month periods. The Company is not reasonably certain to exercise the option to extend the lease expiration beyond its current expiration date. Pieris GmbH may sublease space within the leased property with lessor's consent, which may not be unreasonably withheld.

Monthly base rent for the initial 105,000 square feet of the leased property, including parking spaces, will total approximately $0.2 million per month, which amount shall be adjusted starting on the second anniversary of the commencement date by an amount equal to the German consumer price index. In addition to the base rent, Pieris GmbH is also responsible for certain administrative and operational costs in accordance with the Hallbergmoos Lease. Pieris GmbH provided a security deposit of $0.8 million at upon signing the lease agreement. The Company will serve as a guarantor for the Hallbergmoos Lease.

The Hallbergmoos Lease included $11.5 million of tenant improvements allowance for normal tenant improvements, for which construction began in March 2019. The Company capitalized the leasehold incentives which are included in Property and equipment, net on the Consolidated Balance Sheet and are amortized on a straight-line basis over the shorter of the useful life or the remaining lease term.

The Company also leased approximately 19,000 square feet of office and laboratory space in Freising, Germany under four agreements, the Freising Leases, including three leases for space on three floors of the same building and a letter agreement for additional conference room space within the building. The Freising Leases all terminated on March 31, 2020.

The following table summarizes operating lease costs included in operating expenses (in thousands):

	Years Ended December 31,	
	2021	2020
Operating lease costs	$ 1,483	$ 1,509
Variable lease costs (1)	739	708
Total lease cost	$ 2,222	$ 2,217

(1) Variable lease costs include certain additional charges for operating costs, including insurance, maintenance, taxes, utilities, and other costs incurred, which are billed based on both usage and as a percentage of the Company's share of total square footage.

The following table summarizes the weighted-average remaining lease term and discount rate:

	As of December 31,	
	2021	2020
Weighted-average remaining lease term (years)	10.4	11.4
Weighted-average discount rate	10.5 %	10.5 %

Cash paid for amounts included in the measurement of the lease liabilities were $2.6 million and $2.2 million for the twelve months ended December 31, 2021 and 2020, respectively.

As of December 31, 2021, the maturities of the Company's operating lease liabilities and future minimum lease payments were as follows (in thousands):

	Total
2022	$ 2,474
2023	2,235
2024	2,235
2025	2,235
2026	2,235
Thereafter	12,482
Total undiscounted lease payments	23,896
Less: present value adjustment	(9,006)
Present value of lease liabilities	14,890

EXHIBIT 10.39

PIERIS PHARMACEUTICALS, INC.

AMENDED AND RESTATED NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

The Board of Directors of Pieris Pharmaceuticals, Inc. (the "Company") has approved the following Amended and Restated Non-Employee Director Compensation Policy (this "Policy") which establishes compensation to be paid to non-employee directors of the Company, effective as of December 7, 2021 ("Effective Time"), to provide an inducement to obtain and retain the services of qualified persons to serve as members of the Company's Board of Directors.

Applicable Persons

This Policy shall apply to each director of the Company who is not an employee of the Company or any Affiliate (each, a "Non-Employee Director"). "Affiliate" shall mean an entity which is a direct or indirect parent or subsidiary of the Company, as determined pursuant to Section 424 of the Internal Revenue Code of 1986, as amended.

Stock Option Grants

All stock option amounts set forth herein shall be subject to automatic adjustment in the event of any stock split or other recapitalization affecting the Company's common stock, par value $0.001 per share (the "Common Stock").

Annual Stock Option Grants

Each calendar year, (i) each Non-Employee Director shall be automatically granted a non-qualified stock option to purchase 40,000 shares of Common Stock under the Stock Plan on the date of the annual meeting of the Board of Directors coincident with or immediately following the Company's annual meeting of stockholders (the "Annual Stockholders Meeting"), and (ii) the Chairperson shall be automatically granted an additional non-qualified stock option to purchase 5,000 shares of Common Stock under the Stock Plan (together, the "Annual Director Awards"). To the extent that the Non-Employee Director or Chairperson, as applicable, has served in that position for less than one year, then the Annual Director Award shall be pro-rated with respect to such Non-Employee Director or Chairperson.

Initial Stock Option Grant for Newly Appointed or Elected Directors and Chairperson

Each new Non-Employee Director shall be automatically granted a non-qualified stock option to purchase 80,000 shares of Common Stock under the Stock Plan at the first regularly scheduled meeting of the Board of Directors on or after his or her initial appointment or election to the Board of Directors (the "Initial Director Award").

Terms for All Option Grants

Unless otherwise specified in this Policy or by the Board of Directors or the Compensation Committee at the time of grant, all options granted under this Policy shall: (i) vest, in the case of (A) the Annual Director Awards, at the end of the "Directors' Compensation Year", which shall be defined as the approximately one-year period beginning on the date of each regular Annual Stockholders Meeting and ending on the date of the next regular Annual Stockholders Meeting, subject to the Non-Employee Director's continued service on the Board of Directors through the applicable Directors' Compensation Year and (B) the Initial Director Award, as to thirty-three percent (33%) of the shares underlying the Initial Director Award on the first anniversary of the date of the Non-Employee Director's initial appointment or election as Director on the Board of Directors (the "Initial Vesting Date"), with the remaining sixty-seven percent (67%) of the shares underlying the Initial Director Award vesting in eight (8) equal quarterly installments at the end of each full calendar quarter following the Initial Vesting Date, subject to the Non-Employee Director's continued service on the Board of Directors on the vesting date; (ii) have an exercise price equal to the fair market value of the Common Stock on the grant date, as determined in the Stock Plan; (iii) terminate ten years after the grant date; and (iv) contain such other terms and conditions as set forth in the form of option agreement approved by the Board of Directors or the Compensation Committee prior to the grant date.

Annual Fees

Each Non-Employee serving on the Board of Directors and the Audit Committee, Compensation Committee, Nominating and Corporate Governance Committee, and/or Science and Technology Committee, as applicable, shall be entitled to the following annual amounts (the "Annual Fees"):

Board of Directors or Committee of Board of Directors	**Annual Retainer Amount for Member**	**Annual Retainer Amount for Chair**
Board of Directors	$35,000	$30,000*
Audit Committee	$7,500	$15,000**
Science and Technology Committee	$5,000	$10,000**
Compensation Committee	$5,000	$10,000**
Nominating and Corporate Governance Committee	$4,000	$8,000**

* The annual retainer amount for the Chair of the Board of Directors is in addition to the annual retainer amount for a Member of the Board of Directors.
** Annual retainer amounts for the Chair of Committees of the Board of Directors are in lieu of the annual retainer amount for a Member of the applicable Committee of the Board of Directors.

Except as otherwise set forth in this Policy, all Annual Fees shall be paid for the period from January 1 through December 31 of each year. Such Annual Fees shall be paid in cash or a grant of an option to purchase Common Stock under the Stock Plan, at the election of each Non-Employee Director, as follows:

- cash in the amount of each Non-Employee Director's Annual Fees; or

- an option to purchase such number of shares of Common Stock as is equal to the full dollar amount of each Non-Employee Director's Annual Fees (as calculated below under "Calculation of Shares and Grant Terms").

Election

Each Non-Employee Director shall make an annual election on the form provided by the Company, indicating the combination of cash and/or Common Stock elected in the year prior to the payment, indicating his or her election for the following calendar year. If no election has been made prior to the first date of the calendar year, then the Non-Employee Director shall receive all Annual Fees in cash. Each newly elected or appointed Non-Employee Director shall make an election prior to the beginning of the next calendar quarter after his or her initial appointment or election.

Payments

Payments payable to Non-Employee Directors shall be paid quarterly in arrears promptly following the end of each calendar quarter, provided that (i) the amount of such payment shall be prorated for any portion of such quarter that such director was not serving on the Board or a committee or, in the case of the Annual Fees paid for service as a chairperson, as a chairperson, and (ii) no fee shall be payable in respect of any period prior to the date such director was elected to the Board or a committee or, in the case of the Annual Fees paid for service as a chairperson, as a chairperson.

Calculation of Shares and Grant Terms

If an option to purchase Common Stock is to be received as payment, the number of shares underlying such option shall equal the Black Scholes value of the options computed in accordance with FASB Topic 718 on the 25th day of the month following the end of each calendar quarter (the "Calculation Date") (rounded down to the nearest whole number so that no fractional shares shall be issued). The option shall be automatically and without any further action required by the Board of Directors issued as of the Calculation Date and shall be fully vested as of the date of grant.

Expenses

Upon presentation of documentation of such expenses reasonably satisfactory to the Company, each Non-Employee Director shall be reimbursed for his or her reasonable out-of-pocket business expenses incurred in connection with attending meetings of the Board of Directors and committees thereof or in connection with other business related to the Board of Directors.

Amendments

The Compensation Committee shall periodically review this Policy to assess whether any amendments in the type and amount of compensation provided herein should be made and shall make recommendations to the Board of Directors for its approval of any amendments to this Policy.

Exhibit 21.1

Subsidiaries

Entity	Jurisdiction of Organization
Pieris Pharmaceuticals GmbH	Germany
Pieris Australia Pty Limited	Australia
Pieris Pharmaceuticals Securities Corporation	Massachusetts

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statements (Form S-3 Nos. 333-212439 and 333-235350),
(2) Registration Statement (Form S-8 No. 333-204487) pertaining to the Pieris Pharmaceuticals, Inc. 2014 Employee, Director and Consultant Equity Incentive Plan,
(3) Registration Statement (Form S-8 No. 333-209308) pertaining to the Pieris Pharmaceuticals, Inc. 2014 Employee, Director and Consultant Equity Incentive Plan and Inducement Stock Option Award for Louis Matis, M.D.,
(4) Registration Statement (Form S-8 No. 333-213771) pertaining to the Pieris Pharmaceuticals, Inc. 2016 Employee, Director and Consultant Equity Incentive Plan,
(5) Registration Statement (Post-Effective Amendment to Form S-1 on Form S-3 No. 333-202123),
(6) Registration Statement (Form S-8 No. 333-221497) pertaining to Inducement Stock Option Awards for Claude Knopf, Allan Reine, M.D, and Ingmar Bruns, M.D., Ph.D,
(7) Registration Statement (Form S-8 No. 333-226733) pertaining to the Pieris Pharmaceuticals, Inc. 2018 Employee, Director and Consultant Equity Incentive Plan,
(8) Registration Statement (Form S-8 No. 333-226735) pertaining to the Pieris Pharmaceuticals, Inc. 2018 Employee Stock Purchase Plan,
(9) Registration Statement (Form S-8 No. 333-233194) pertaining to the Pieris Pharmaceuticals, Inc. 2019 Employee, Director and Consultant Equity Incentive Plan,
(10) Registration Statement (Form S-8 No. 333-234625) pertaining to the Non-Qualified Stock Option Agreement, dated August 30, 2019, and
(11) Registration Statement (Form S-8 No. 333-243735) pertaining to the Pieris Pharmaceuticals, Inc. 2020 Employee, Director and Consultant Equity Incentive Plan;

of our report dated March 1, 2022, with respect to the consolidated financial statements of Pieris Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) of Pieris Pharmaceuticals, Inc. for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 1, 2022

Exhibit 31.1

CERTIFICATIONS UNDER SECTION 302

I, Stephen S. Yoder, certify that:

1. I have reviewed this annual report on Form 10-K of Pieris Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 1, 2022

/s/ Stephen S. Yoder

Stephen S. Yoder

Title: Chief Executive Officer and President (principal executive officer)

Exhibit 31.2

CERTIFICATIONS UNDER SECTION 302

I, Thomas Bures, certify that:

1. I have reviewed this annual report on Form 10-K of Pieris Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 1, 2022

/s/ Thomas Bures

Thomas Bures

Title: Senior VP, Chief Financial Officer and Treasurer (principal financial officer)

Exhibit 32.1

CERTIFICATIONS UNDER SECTION 906

Pursuant to section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), the undersigned officer of Pieris Pharmaceuticals, Inc., a Nevada corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report for the year ended December 31, 2021 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 1, 2022

/s/ Stephen S. Yoder

Stephen S. Yoder

Title: Chief Executive Officer and President
(principal executive officer)

Exhibit 32.2

CERTIFICATIONS UNDER SECTION 906

Pursuant to section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), the undersigned officer of Pieris Pharmaceuticals, Inc., a Nevada corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report for the year ended December 31, 2021 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 1, 2022

/s/ Thomas Bures

Thomas Bures

Title: Senior VP, Chief Financial Officer and Treasurer
(principal financial officer)