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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

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

For the fiscal year ended December 31 , 2024

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 No. 001-37852

PROTAGONIST THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**98-0505495**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
7707 Gateway Boulevard, Suite 140 Newark , California 94560	
(Address of registrant's principal executive offices, including zip code)	**(510) 474-0170 (Registrant's telephone number, including area code)**

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

Title of each class	**Trading Symbol**	**Name of each exchange on which registered**
Common Stock, $0.00001 par value	**PTGX**	**The Nasdaq Stock Market LLC**

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

None

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

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

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

Large Accelerated Filer	☒	Accelerated Filer	☐
Non-Accelerated Filer	☐	Smaller Reporting Company	☐
		Emerging Growth Company	☐

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

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

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

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act of 1934). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was approximately $ 2.0 billion as of June 28, 2024, based upon the closing sale price on The Nasdaq Stock Market LLC reported on June 28, 2024. Excludes an aggregate of 630,843 shares of the registrant's common stock held by officers, directors and affiliated stockholders. For purposes of determining whether a stockholder was an affiliate of the registrant at June 28, 2024, the registrant assumed that a stockholder was an affiliate of the registrant if such stockholder (i) beneficially owned 10% or more of the registrant's common stock, as determined based on public filings and/or (ii) was an executive officer or director or was affiliated with an executive officer or director of the registrant. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

There were 61,384,289 shares of registrant's Common Stock, par value $0.00001 per share, outstanding as of February 19, 2025.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the registrant's definitive Proxy Statement for the registrant's 2025 Annual Meeting of Stockholders are incorporated by reference into Part III of this report. Such proxy statement will be filed with the Securities and Exchange Commission within 120 days after the end of the registrant's fiscal year ended December 31, 2024.

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

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PART I

This Annual Report on Form 10-K contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of historical fact, including statements concerning our plans, objectives, goals, strategies, future events, future revenues or performance, financing needs, expectations, plans or intentions relating to clinical development, product candidates, the regulatory approval process, products and markets, and business trends and other information referred to under the sections entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," are forward-looking statements. These statements are subject to substantial known and unknown risks, uncertainties and other factors that may cause our actual results, outcomes, performance or achievements, or the timing of such results, outcomes, performance or achievements, to be materially different from any results, outcomes, performances or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "anticipates," "assumes," "believes," "commitments," "could," "estimates," "expects," "forecasts," "intends," "may," "plans," "potential," "predicts," "projects," "should," "targets," "will," "would," "seeks" and similar expressions intended to identify forward-looking statements. Forward-looking statements reflect our current views with respect to future events, are based on assumptions, and are subject to risks, uncertainties and other important factors, including, among other things, the potential for our programs; the timing, initiation, progress and expected results of our clinical trials and research and development programs, including enrollment, data, costs and regulatory submissions; our cash runway; our ability to advance product candidates into, and successfully complete, non-clinical studies and clinical trials; the potential for eventual regulatory approval and commercialization of our product candidates; the commercialization of our product candidates, if approved; our ability and the potential to successfully manufacture and supply our product candidates for clinical trials and for commercial use, if approved; the pricing, coverage, and reimbursement of our product candidates, if approved; our potential receipt of milestone payments and royalties under our collaboration agreements; future operating results; our ability to generate sales, income or cash flow; our estimates regarding expenses, capital requirements, and needs for additional financing and our ability to obtain additional capital; our ability to retain the continued service of our key executives and to identify, hire, and retain additional qualified professionals, the impact of any future outbreaks of disease, epidemics and pandemics; ongoing military conflicts, including between Ukraine and Russia and in the Middle East; rising tensions between China and Taiwan; developments relating to our competitors and our industry, including competing product candidates and therapies; inflationary pressure and the availability of credit. Forward-looking statements involve risks, uncertainties and assumptions that are beyond our ability to control or predict, including those risks, uncertainties and assumptions discussed in Part I, Item 1A, of this Annual Report on Form 10-K. These statements are based on information available to us as of the date of this Annual Report and, while we believe such information provides a reasonable basis for these statements, the information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. Given these risks, uncertainties and other important factors, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our estimates and assumptions only as of the date of this Annual Report. Except as required by law, we assume no obligation to update any forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in any forward-looking statements, whether as a result of new information, future developments, changes in assumptions or otherwise. We caution investors that our business and financial performance are subject to substantial risks and uncertainties. "Protagonist," the Protagonist logo and other trademarks, service marks and trade names of Protagonist are registered and unregistered marks of Protagonist Therapeutics, Inc. in the United States and other jurisdictions.

Summary of Risk Factors

Below is a summary of the principal factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks and uncertainties that we face. Additional discussion of the risks and uncertainties summarized in this risk factor summary, and other risks and uncertainties that we face, can be found below under the heading Item 1A, "Risk Factors" and should be carefully considered, together with other information in this Annual Report on Form 10-K and our other filings with the SEC, before making an investment decision regarding our common stock.

- We have no approved products and no historical commercial revenue, which makes it difficult to assess our future prospects and financial results.
- We are heavily dependent on the success of our product candidates in clinical development.
- Clinical development is a lengthy and expensive process with an uncertain outcome, and failure can occur at any stage of clinical development.
- Our product candidates may cause undesirable side effects or have other properties adversely impacting safety that delay or prevent their regulatory approval, restrict their approved labeling, or otherwise limit their commercial opportunity, including being required by an independent data monitoring committee or regulatory authorities to delay or halt or clinical trials, or if such side effects or adverse events are sufficiently severe or prevalent, to suspend or cease altogether further development of our product candidates.
- We have incurred a cumulative net loss since our inception and anticipate that we may incur significant losses in the future.
- We have never generated any revenue from product sales and may never be profitable.
- Unstable market and macroeconomic conditions including elevated and sustained inflation and changes in trade policies, including tariffs or other trade restrictions or the threat of such actions, may have serious adverse consequences on our business, financial condition and stock price.
- We may require additional funding.
- Raising additional capital may cause dilution to our existing stockholders.
- We rely on J&J Innovative Medicines ("JNJ") to continue the development of product candidates subject to our license and collaboration with JNJ, and to successfully commercialize any resulting products, and we rely on Takeda Pharmaceuticals USA, Inc. ("Takeda") to successfully commercialize any products resulting from our collaboration agreement with Takeda.
- Our existing or future collaborations with third parties may not be successful.
- We rely on third parties to conduct our pre-clinical studies and clinical trials and are subject to risks associated with their businesses and performance of their obligations to us.
- We rely on third-party contract manufacturers to manufacture our drug substance and clinical drug product.
- If we are ultimately unable to obtain regulatory approval for our product candidates in the United States or other jurisdictions, our business will be substantially harmed.

- If our partners do not satisfy their obligations under our agreements with them, or if they terminate our partnerships with them, we may not be able to develop or successfully commercialize our partnered product candidates successfully.
- We face significant competition from other biotechnology and pharmaceutical companies.
- We may face risks to our business arising from outbreaks of disease, epidemics and pandemics, including risks to our ongoing and planned clinical trials and pre-clinical and discovery research.
- Unstable market and economic conditions, including elevated and sustained inflation, may have serious adverse consequences on our business, financial condition and stock price.
- Our success depends on our ability to attract, retain and motivate qualified executives and other personnel.
- We may experience difficulties in managing the growth of our organization.
- We are subject to risks associated with information technology systems or breaches of data security.
- Any misconduct by our employees, independent contractors, principal investigators, consultants and vendors could have a material adverse effect on our business.
- Our headquarters is located near known earthquake fault zones.
- If we are unable to obtain or protect intellectual property rights related to our product candidates and technologies, we may not be able to compete effectively in our markets.
- We may be involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time consuming and ultimately unsuccessful.
- Patents covering our product candidates could be found invalid or unenforceable.
- Third-party claims of intellectual property infringement may prevent or delay our drug discovery and development efforts.
- Our stock price has been and will likely continue to be volatile and may decline, regardless of our operating performance.

Item 1. Business

OVERVIEW

We are a discovery through late-stage development biopharmaceutical company focused on peptide therapeutics. Our clinical programs fall into two broad categories of diseases: (i) hematology and blood disorders, and (ii) inflammatory and immunomodulatory ("I&I") diseases. Two novel peptides derived from our proprietary discovery technology platform, rusfertide and icotrokinra (formerly known as JNJ-2113), are currently in advanced Phase 3 clinical development, with New Drug Application ("NDA") submissions to the U.S. Food and Drug Administration ("FDA") potentially in 2025.

Rusfertide, an injectable mimetic of the natural hormone hepcidin, is currently in Phase 3 development for treatment of the rare blood disorder polycythemia vera ("PV"). Rusfertide is being co-developed and will be co-commercialized with Takeda Pharmaceuticals, Inc. ("Takeda") and the Company remains primarily responsible for development through NDA filing. Icotrokinra is a first-in-class investigational targeted oral peptide that selectively blocks the Interleukin-23 receptor ("IL-23R") and is licensed to J&J Innovative Medicines ("JNJ"), formerly Janssen Biotech, Inc. Following icotrokinra's joint discovery by us and JNJ scientists pursuant to our IL-23R collaboration, we were primarily responsible for the development of icotrokinra through Phase 1, with JNJ assuming responsibility for development in Phase 2 and beyond.

We also have a number of pre-clinical stage oral drug discovery programs to address clinically and commercially validated targets, including IL-17 oral peptide antagonist PN-881, an oral metabolic/obesity peptide program, and an oral hepcidin mimetic/ferroportin blocker program.

2024 Key Highlights

Worldwide License and Collaboration Agreement for Rusfertide with Takeda

- On January 31, 2024, we and Takeda announced a worldwide license and collaboration agreement for rusfertide. We received an upfront cash payment of $300.0 million in April 2024, and we are eligible to receive up to $330.0 million in development, regulatory, and sales milestones, for a potential deal value of up to $630.0 million, as well as an equal share of profits and losses in the U.S. and royalties on net sales outside the U.S.

- Under the terms of the agreement, we have the right to opt-out of the 50:50 profit share. In that event, we would be eligible to receive additional cash payments of up to $400.0 million and enhanced milestones of up to $975.0 million, as well as royalties on worldwide net sales. Takeda would maintain full ex-U.S. rights under either scenario.

Two articles published in the New England Journal of Medicine ("NEJM") in February 2024

- On February 7, 2024, the icotrokinra Phase 2b FRONTIER 1 trial results in adults living with moderate-to-severe plaque psoriasis were published in the NEJM.

- On February 21, 2024, the complete Phase 2 REVIVE trial results for rusfertide, including efficacy and safety data, were published in the NEJM.

Addition to S&P SmallCap 600 Index

We joined the S&P SmallCap 600 Index on July 3, 2024.

Positive Phase 3 topline results from Phase 3 ICONIC studies of icotrokinra in plaque psoriasis

- On November 18, 2024, we announced that in the ICONIC-LEAD study, once-daily icotrokinra showed significant skin clearance versus placebo in adults and adolescents with moderate to severe plaque psoriasis. At week 16, nearly two-thirds (64.7%) of patients treated with icotrokinra achieved Investigator's Global Assessment ("IGA") scores of 0 or 1 (clear or almost clear skin), and 49.6% achieved PASI 90 (90% improvement in skin lesions as measured by the Psoriasis Area and Severity Index ("PASI")), compared to 8.3% and 4.4% on placebo, respectively.

- Further increases in response rates continued to be observed at week 24, with 74.1% of patients treated with icotrokinra achieving IGA scores of 0 or 1, and 64.9% achieving PASI 90. Safety data was found to be consistent with the Phase 2 FRONTIER 1 and 2 studies. A similar proportion of patients experienced adverse events between icotrokinra and placebo, with 49.3% and 49.1% of participants, respectively, experiencing a treatment-emergent adverse event ("TEAE") at week 16.

- In addition, positive topline results from the Phase 3 ICONIC-TOTAL study showed that once-daily icotrokinra met the primary endpoint of IGA of 0 or 1 at week 16 compared to placebo.

Nomination of PN-881, a potential best-in-class oral peptide IL-17 antagonist development candidate; additional discovery programs announced

- On November 21, 2024, we announced the nomination of PN-881 following extensive preclinical studies, including oral stability, potency, tissue distribution, and pharmacokinetics measurements, and evaluation in immunologic pharmacodynamics and preclinical efficacy models. PN-881 showed in vitro blockade of IL-17 AA homodimer, FF homodimer and AF heterodimer. It showed approximately 100-fold greater potency than secukinumab, and similar potency to the most potent approved antibody drugs and nanobody therapeutics currently in development.

- We expect to nominate an oral development candidate in the hepcidin mechanism-based hematology program in the fourth quarter of 2025, and an oral peptide-based development candidate in the metabolic/obesity program in the second quarter of 2025.

Achievement of an amended $165.0 million milestone

- Under the terms of the icotrokinra license and collaboration agreement with J&J, as amended in November 2024, we earned $165.0 million in milestone payments during the fourth quarter of 2024.

- The $165.0 million payment was received in January 2025, and we remain eligible for up to $630.0 million in future development and sales milestone payments, and tiered royalties of 6-10% on worldwide net sales. The 10% royalty tier applies to net worldwide sales of $4 billion or more.

Significantly enhanced cash resources

We ended fiscal 2024 with cash, cash equivalents and marketable securities of approximately $559.2 million, a significant increase from cash, cash equivalents and marketable securities of approximately $341.6 million as of December 31, 2023.

Figure 1: Our Product Pipeline

Rusfertide

Rusfertide is currently in Phase 3 development for the treatment of PV. VERIFY (ClinicalTrials.gov identifier NCT05210790) is a global double-blind, placebo-controlled Phase 3 clinical trial of rusfertide in PV for approximately 250 patients. The trial evaluates the efficacy, symptom burden and safety of once-weekly, subcutaneously self-administered rusfertide in patients with uncontrolled hematocrit who are phlebotomy dependent despite standard of care treatment. The trial enrolled patients across North and South America, Europe, Asia and Australia. We expect to announce top-line data for the trial's 32-week primary efficacy endpoint in March 2025, potentially leading to an NDA filing in the fourth quarter of 2025.

Our rusfertide Phase 2 clinical trials include the following:

- REVIVE (NCT04057040) – A Phase 2 proof of concept ("POC") trial, was initiated in the fourth quarter of 2019. We completed enrollment of patients in the first quarter of 2022 and 70 patients were enrolled through the end of the randomized withdrawal portion of the trial, which was completed during the first quarter of 2023 and is continuing in an ongoing open-label extension ("OLE");
- THRIVE (NCT06033586) – A Phase 2 long-term OLE for REVIVE patients on years three through five of treatment; and
- PACIFIC (NCT04767802) – Another Phase 2 trial for rusfertide for patients diagnosed with PV and with routinely elevated hematocrit levels (>48%), was initiated during the first quarter of 2021, and the 52-week trial was completed during the second quarter of 2023.

Final results from the REVIVE trial presented at the American Society of Hematology ("ASH") 2024 Annual Meeting in December 2024 showed that 54% of patients with PV experienced more than 2.5 years of durable hematocrit control (<45%), decreased phlebotomy use, long-term tolerability and improvements in patient-reported outcomes.

In January 2024, we entered into a worldwide license and collaboration agreement for rusfertide with Takeda (the "Takeda Collaboration Agreement"). We are primarily responsible for the development of rusfertide through a potential

NDA filing. Under the terms of the agreement, we received a one-time, non-refundable upfront payment of $300.0 million in April 2024, and we are eligible to receive additional worldwide development, regulatory and commercial milestone payments for rusfertide of up to $330.0 million, inclusive of the following potential upcoming milestones:

- $25.0 million upon successful achievement of the primary endpoint in the Phase 3 VERIFY trial for rusfertide in PV; and
- $50.0 million upon FDA approval of an NDA for rusfertide in PV (or $75.0 million if we exercise our full right to opt-out of the 50:50 U.S. profit and loss sharing arrangement).

We are also eligible to receive tiered royalties from 10% to 17% on ex-U.S. net sales of rusfertide and other specified second-generation injectable hepcidin memetic compounds (the "Licensed Products"). We and Takeda will also share equally in profits and losses (50% to us and 50% to Takeda) of the Licensed Products in the United States, if approved. See Note 3 to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K for further details related to the agreement, including our right to opt-out of the 50:50 U.S. profit and loss sharing arrangement.

Icotrokinra

Our IL-23R antagonist compound icotrokinra, licensed to J&J, is an orally delivered drug that is designed to block biological pathways currently targeted by marketed injectable antibody drugs. Our orally stable peptide approach may offer a targeted therapeutic approach for gastrointestinal and systemic compartments as needed. We believe that, compared to antibody drugs, icotrokinra has the potential to provide clinical improvement in an oral medication with increased convenience and compliance and the opportunity for the earlier introduction of targeted oral therapy.

JNJ has initiated the following icotrokinra trials:

- ICONIC-LEAD (NCT06095115) – A 684-patient randomized, controlled Phase 3 trial to evaluate the safety and efficacy of icotrokinra compared with placebo in participants with moderate-to-severe plaque psoriasis, with PASI-90 and IGA scores of 0 (clear) or 1 (almost clear) as co-primary endpoints;
- ICONIC-TOTAL (NCT06095102) – A 311-patient randomized, controlled Phase 3 trial to evaluate the efficacy and safety of icotrokinra compared with placebo for the treatment of plaque psoriasis in participants with at least moderate severity affecting special areas (scalp, genital, and/or palms of the hands and soles of the feet) with overall IGA scores of 0 or 1 as the primary endpoint;
- ICONIC-ADVANCE 1 (NCT06143878) – A 774-patient randomized, controlled Phase 3 trial to evaluate the effectiveness of icotrokinra in participants with moderate-to-severe plaque psoriasis compared to placebo and Sotyktu® ("deucravacitinib"). The trial's primary co-endpoints are PASI-90 and IGA scores of 0 or 1;
- ICONIC-ADVANCE 2 (NCT06220604) – A 731-patient Phase 3 trial similarly designed to ICONIC ADVANCE 1 in participants with moderate-to-severe plaque psoriasis;
- Pustular/Erythrodermic Psoriasis (NCT06295692) – A 19-patient open label Phase 3 trial to evaluate the effectiveness of icotrokinra in participants with pustular or erythrodermic psoriasis;
- ICONIC-PsA 2 (NCT06807424) – A 750-patient randomized, controlled Phase 3 trial to evaluate the efficacy and safety of icotrokinra compared with placebo in biologic-experienced patients with active psoriatic arthritis ("PsA"); and
- ANTHEM-UC (NCT06049017) – A 252-patient randomized, controlled Phase 2b trial to evaluate the safety and effectiveness of icotrokinra compared with placebo in participants with moderate-to-severely active ulcerative colitis ("UC").

In the fourth quarter of 2024, we announced positive topline results for the ICONIC-LEAD and ICONIC-TOTAL Phase 3 trials. In the ICONIC-LEAD trial, once daily icotrokinra showed significant skin clearance versus placebo in adults and adolescents with moderate to-severe plaque psoriasis. At week 16, nearly two-thirds (64.7%) of patients

treated with icotrokinra achieved IGA scores of 0 or 1 and 49.6% achieved PASI-90, compared to 8.3% and 4.4% on placebo, respectively. In addition, topline results from the Phase 3 ICONIC-TOTAL trial showed that once daily icotrokinra met the primary endpoint of IGA scores of 0 or 1 at week 16 as compared to placebo. Comprehensive results from both ICONIC-LEAD and ICONIC-TOTAL are expected to be presented at upcoming medical congresses and shared with health authorities in planned submissions.

Topline results for the ANTHEM trial are expected in the first quarter of 2025. Topline results for the ICONIC-ADVANCE 1, ICONIC-ADVANCE 2, and pustular/erythrodermic psoriasis trials are expected in the second quarter of 2025.

On July 27, 2021, we entered into an Amended and Restated License and Collaboration Agreement with JNJ, which amended and restated the License and Collaboration Agreement, effective July 13, 2017, by and between the Company and JNJ, as amended by the first amendment, effective May 7, 2019 (together, the "JNJ License and Collaboration Agreement") for the development and commercialization of icotrokinra. During the fourth quarter of 2023, we earned a $50.0 million milestone payment in connection with the dosing of the third patient in the ICONIC-TOTAL Phase 3 clinical trial of icotrokinra in patients with moderate-to-severe psoriasis and a $10.0 million milestone payment upon the dosing of the third patient in the ANTHEM Phase 2b trial in patients with moderately-to-severely active UC. The JNJ License and Collaboration Agreement was further amended in November 2024 to:

- increase the milestone payment for a Phase 3 clinical trial of any licensed product for any indication meeting its primary endpoint by $50.0 million, from $115.0 million to $165.0 million;
- eliminate the $35.0 million milestone payment previously due for the acceptance of an NDA filing by the FDA for a licensed product for any indication; and
- eliminate the $15.0 million milestone payment previously due for the dosing of the third patient in the first Phase 3 clinical trial of a licensed product for a second indication.

We earned the $165.0 million milestone payment described above during the fourth quarter of 2024. We have earned a total of $337.5 million in nonrefundable payments from JNJ from 2017 through December 31, 2024. We are eligible to receive up to $630.0 million in future development and sales milestone payments, inclusive of the following potential upcoming milestones:

- $50.0 million milestone upon approval of an NDA for icotrokinra in any indication;
- $25.0 million milestone upon the acceptance of an NDA filing by the FDA for icotrokinra in a second indication; and
- $45.0 million milestone upon the approval of an NDA for icotrokinra in a second indication.

We also remain eligible to receive upward tiering royalties on net product sales at percentages ranging from 6% percent to 10% percent, with 10% percent applicable for net sales over $4.0 billion. See Note 3 to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information.

PN-881

In the fourth quarter of 2024, we announced the selection of PN-881, a potential best-in-class oral peptide IL-17 antagonist, as a development candidate for the treatment of immune-mediated skin diseases. PN-881 targets three IL-17 dimers (IL-17 AA, AF and FF), which may offer potential treatment options for hidradenitis suppurativa ("HS"), spondyloarthritis, plaque psoriasis and psoriatic arthritis ("PsA"). Investigational New Drug ("IND"), or foreign equivalent, enabling studies are ongoing, and we expect to initiate a PN-881 Phase 1 study in the fourth quarter of 2025.

Discovery Platform

Our clinical and pre-clinical assets are all derived from our proprietary discovery platform. Our platform enables us to engineer novel, structurally constrained peptides that are designed to retain key advantages of both orally delivered small molecules and injectable antibody drugs while overcoming many of their limitations as therapeutic agents.

Importantly, constrained peptides can be designed to potentially alleviate the fundamental instability inherent in traditional peptides to allow different delivery forms, such as oral, subcutaneous, intravenous, and rectal. Our discovery pipeline has strategically focused on (i) hematology and blood disorders, (ii) I&I diseases and (iii) metabolic diseases, including obesity.

We have a pre-clinical stage program to identify an orally administered hepcidin mimetic/ferroportin blocker, which we believe to be complementary to the injectable rusfertide for offering the best treatment options for PV and other potential erythropoietic and iron imbalance disorders, and we expect to nominate a development candidate in the fourth quarter of 2025. We also have an oral peptide-based metabolic/obesity program and expect to nominate a development candidate in the second quarter of 2025.

RUSFERTIDE: AN INJECTABLE HEPCIDIN MIMETIC

Rusfertide, an injectable hepcidin mimetic, was discovered through our peptide technology platform. Hepcidin is a natural hormone that regulates iron metabolism. We are developing rusfertide for the treatment of PV.

Polycythemia Vera

PV is a rare myeloproliferative neoplasm that is typically associated with a Janus Kinase ("JAK") 2 mutation. PV is primarily characterized by the overproduction of red blood cells ("RBCs"), which contributes to an elevated risk of cardiovascular and thrombotic events, such as heart attack and stroke. PV is also associated with a risk of disease progression to myelofibrosis or leukemia. According to National Comprehensive Cancer Network ("NCCN") guidelines, age and thrombosis history determine a patient's risk classification as either low-risk or high-risk. Regardless of risk, treatment guidelines for PV consistently emphasize the importance of controlling the patient's hematocrit (RBCs as a percentage of whole blood) below 45% to reduce thrombotic risk.

Early-stage patients are typically treated with low dose aspirin and therapeutic phlebotomy. Hydroxyurea may also be used alone or in combination with phlebotomy. At later stages, patients may receive interferons, marketed as Besremi® or Pegasys®, or ruxolitinib, a JAK inhibitor marketed as Jakafi®. Cytoreductive therapies such as hydroxyurea, interferons and ruxolitinib impact all cell lines and can have challenging side effect profiles associated with their cytoreductive mechanisms. We believe there are substantial PV patient groups that could benefit from a new non-cytoreductive therapeutic option which specifically targets RBCs. Although NCCN guidelines state that hematocrit levels should be maintained below 45% to reduce thrombotic risk, analysis of a large medical claims database indicated that 78% of treated PV patients did not maintain hematocrit control below 45%. These findings showed that current therapies do not offer adequate hematocrit control, highlighting a significant unmet need in the United States alone where patients may have an elevated risk of cardiovascular and thrombotic events.

There are approximately 155,000 diagnosed (approximately 78,000 treated) patients living in the United States, with a similar number in Europe, representing an estimated market opportunity of approximately $1.0 billion to $2.0 billion. Patients are typically diagnosed between the ages of 50 and 70, and median survival is approximately 14 years. Approximately 55% of treated PV patients receive frequent phlebotomy and high doses of hydroxyurea, which can cause undue burden to the patient. Additionally, approximately 16% of patients experience a thrombotic event while receiving treatment(s) for PV. We believe rusfertide can potentially benefit a broad spectrum of patients across the continuum of care, either as monotherapy or in combination with other cytoreductive therapies.

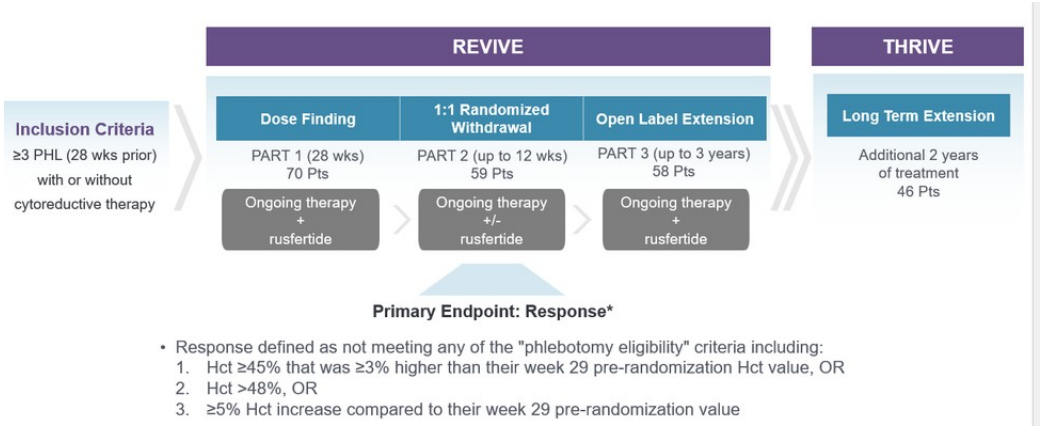
We believe that rusfertide has the potential to provide a substantial benefit to patients by offering a treatment focused on managing hematocrit in a consistent and predictable manner, dramatically decreasing the need for phlebotomy. Rusfertide is a non-cytoreductive mimetic of the natural hormone hepcidin, the master regulator of iron homeostasis in the body. Since high RBC production consumes iron stores, PV can cause iron deficiency, which is often exacerbated by phlebotomy. Rusfertide has a unique iron regulatory mechanism, which data from our Phase 2 REVIVE trial suggests allows for persistent control of hematocrit without causing iron deficiency. Rusfertide acts by redistributing iron away from the bone marrow, where iron is essential for RBC production, thereby limiting excess RBC production while still providing sufficient iron levels to support other normal cellular and organ functions.

Cancers are common in PV patients. A retrospective analysis presented at the ASH 2023 Annual Meeting in December 2023 on the incidence of cancers in PV patients not treated with rusfertide demonstrated the heightened underlying cancer risk in this population, particularly among those treated with hydroxyurea. Additionally, the majority of patients with prior TEAEs, who are at highest risk of developing a TEAE, did not experience recurrent TEAEs while on rusfertide. The mechanisms contributing to the increased risk of cancers in PV patients are not well understood. However, the subset of PV patients treated with hydroxyurea in this study of real-world claims data had nearly twice the rate of cancers compared to phlebotomy-only treated patients.

Clinical Development of Rusfertide in PV

In the fourth quarter of 2019, we initiated REVIVE, a Phase 2 trial of rusfertide in PV designed to evaluate safety and preliminary efficacy in patients requiring phlebotomy ("PHL"). The REVIVE trial was expected to enroll approximately 60 patients and consisted of a 16-week open-label dose finding stage every 4 weeks from 10 mg to 80 mg and a 12-week maintenance period at doses which generate desired hematocrit levels, followed by a 12-week randomized and blinded withdrawal stage. The endpoints of this clinical POC trial include measurement of blood parameters (hematocrit and hemoglobin levels), reductions or delay in phlebotomy requirements, and improvements in quality-of-life symptoms. We initiated THRIVE, a Phase 2 long-term extension trial, to monitor long-term safety and benefits of rusfertide for REVIVE patients on years three through five of treatment.

Figure 2. REVIVE and THRIVE: Rusfertide Phase 2 PV Trial Design



Preliminary results showed that the vast majority of patients treated with rusfertide in the REVIVE clinical trial were able to eliminate therapeutic phlebotomies and maintain a target hematocrit level of less than 45 percent. Treatment with rusfertide was also shown to reverse iron deficiency, an important side effect of regular therapeutic phlebotomies as a treatment for PV. Preliminary results indicated that rusfertide therapy resulted in rapid, sustained and durable hematocrit control without clinically meaningful changes in white blood cell and platelet counts. Rusfertide demonstrated similar efficacy in all categories of patients, independent of the PV patient risk category or concurrent therapy with hydroxyurea, interferon or ruxolitinib.

In March 2023, we announced positive topline results from the blinded, placebo-controlled, randomized withdrawal portion of the REVIVE trial. Subjects receiving rusfertide achieved statistically significant improvements versus placebo in the trial's primary endpoint. The double-blind, placebo-controlled, 12-week randomized withdrawal portion was included as Part 2 of the REVIVE trial to evaluate rusfertide in PV patients with frequent phlebotomy requirements. In the REVIVE trial, subjects were initially enrolled in the 28-week open label dose-titration and efficacy evaluation Part 1 of the trial, followed by 1:1 randomization of 53 subjects to placebo versus rusfertide therapy for a subsequent duration of 12 weeks. More subjects receiving rusfertide during the blinded randomized withdrawal portion

of the REVIVE trial were responders compared with placebo (69.2% versus 18.5%, p=0.0003). A trial subject was defined as a responder if the subject completed 12 weeks of double-blind treatment while maintaining hematocrit control without phlebotomy eligibility and without phlebotomy. During the 12 weeks of the blinded, randomized withdrawal, 92.3% of subjects on rusfertide (24 out of 26) were not phlebotomized.

In addition, in subjects with moderate or severe Myeloproliferative Neoplasm-Symptom Assessment Form ("MPN-SAF") symptom scores at baseline, the change from baseline was statistically significant in fatigue, problems with concentration, inactivity and itching during the 28-week open label Part 1 of the trial. Meaningful comparison of symptoms assessments in Part 2 are not possible since a majority of subjects randomized to placebo discontinued prior to the 12-week assessment of MPN-SAF symptoms.

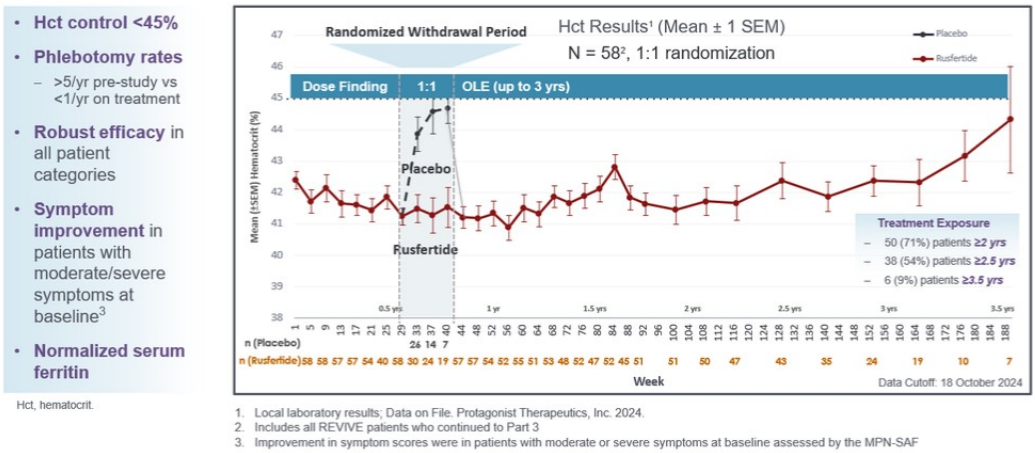
Rusfertide continued to be generally well tolerated in the REVIVE trial, with localized ISRs comprising the majority of reported adverse events. No new safety signals were observed in safety data disclosed in connection with the Part 2 efficacy results, relative to the safety data from the REVIVE trial presented at the December 2022 ASH Annual Meeting, which indicated that 84% of TEAEs were Grade 2 or below. 16% of patients experienced Grade 3 TEAEs and there were no Grade 4 TEAEs.

In December 2023, we presented two-year follow up data from patients in the Phase 2 REVIVE trial who continued into the OLE at the ASH 2023 Annual Meeting. The Phase 2 trial consisted of three parts including 70 patients in the dose-finding Part 1 (28 weeks), 59 patients in the placebo-controlled, randomized withdrawal Part 2 (13 weeks), and 58 patients in the OLE (52 weeks). At the end of Part 2, 69% (18/26) of rusfertide patients achieved hematocrit control and remained phlebotomy free at 12 weeks, compared to only 19% (5 out of 27) on placebo (p=0.0003). Among the 58 patients that continued into the OLE, as of October 17, 2023 (data cut-off date for the ASH presentation), 57 had been treated for over one year and 37 had been treated for over two years. The median follow-up was 2.1 years and data were provided out to 2.5 years in 21 patients.

Results showed that rusfertide, when used in patients previously treated with phlebotomy with or without cytoreductive therapy through two years, resulted in durable hematocrit control, decreased phlebotomy use, long-term tolerability, and no new safety signals in patients with PV. An analysis of the PACIFIC Phase 2 trial was also presented which showed that rusfertide improved markers of iron deficiency in patients with PV. In addition, data was presented regarding the prevalence of thromboembolic events and secondary cancers in PV patients not treated with rusfertide.

In February 2024, the full Phase 2 REVIVE trial results, including efficacy and safety data, were published in the NEJM. Updated long-term results from the REVIVE trial presented at the European Hematology Association Congress in June 2024 continued to show a durable positive effect on PV symptomology and other benefits, including iron deficiency as well as an encouraging safety profile.

Figure 3. REVIVE: Clinical Efficacy of Rusfertide in REVIVE Trial
Data as of October 18, 2024



In November 2024, final data from the REVIVE trial was presented at the ASH 2024 Annual Meeting (Figure 3). As of October 18, 2024 (the data cut-off date for presentation at ASH), 50 (71%), 38 (54%), and 17 (24%) patients received rusfertide for ≥2, ≥2.5, or ≥3 years, respectively. Of the 58 patients who entered the REVIVE Part 3 OLE, the median duration of therapy was 131.4 weeks (2.5 years). As of October 18, 2024, 46, or over 80%, of patients have rolled over to the THRIVE trial and are eligible to receive up to two additional years of rusfertide treatment. Trial results showed that rusfertide, when added to therapeutic phlebotomy with or without cytoreductive therapy, achieved long term durable control of hematocrit below the 45% threshold for over three years.

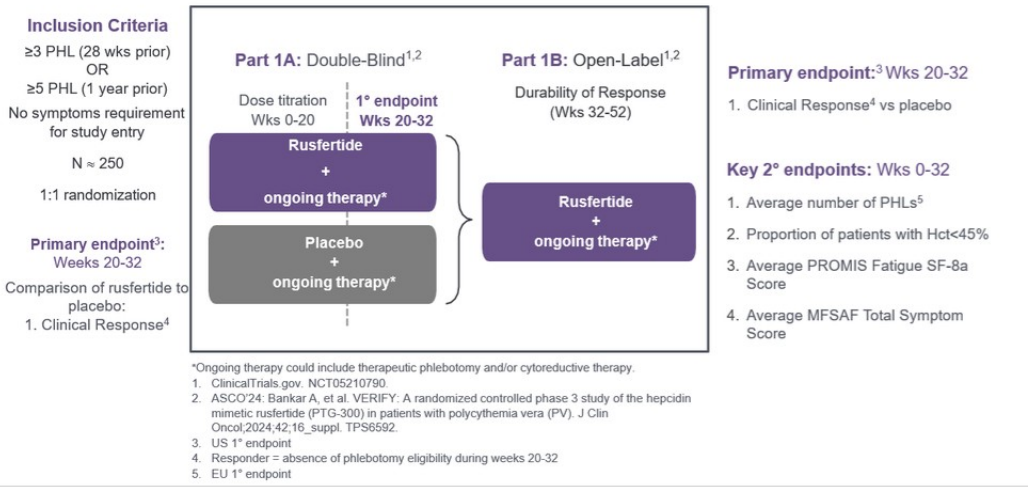
Prior to enrollment, the estimated mean phlebotomy rate ("EPHL") in patients who enrolled in the trial was >5 per year. In Part 1, the EPHL was <1 per year in patients who received rusfertide (N=70). In Part 2 (randomized withdrawal phase), the EPHL was <1 per year and approximately 6.1 per year in the rusfertide and placebo groups, respectively. For patients who continued to Part 3 (Week 42+), the EPHL remained at <1 per year. Patients showed increased mean corpuscular volume and continued improvement and normalization of serum ferritin levels. Platelet levels increased following initiation of rusfertide therapy and stabilized over time and mean leukocyte counts remained stable throughout the trial.

The MPN-SAF was used to assess mean change from baseline in the individual symptom score in patients with moderate (score of 4-6 out of 10) or severe (score of 7-10 out of 10) symptoms at baseline. In patients who had moderate or severe symptoms at baseline (score of ≥4 out of 10), there were significant improvements from baseline in fatigue, early satiety, abdominal discomfort, inactivity, problems with concentration, night sweats, and itching at the end of Part 3.

Overall, 18 (26%) patients experienced serious adverse events ("SAEs"); most SAEs were unrelated and likely associated with the underlying disease. One patient developed acute myeloid leukemia after treatment discontinuation. After more than 150 patient-years of rusfertide exposure, malignancies were reported in 11 patients (nine patients had skin malignancies); all of these patients had prior risk factors that may have contributed to development of these malignancies. There was no obvious correlation between increased exposure to rusfertide and the malignancies reported. Seven thrombotic events (six arterial and one venous) occurred in six patients who all had high-risk PV. No thrombotic events have been reported in patients with low-risk PV as of October 18, 2024.

These results indicate that rusfertide continued to demonstrate a positive clinical impact in the treatment of PV patients. With more than three years of data showing strong and continued improvements in hematocrit as well as encouraging evidence of symptoms improvement, we believe rusfertide continues to show its potential as a first-in-class erythrocytosis-focused treatment option for patients with PV.

Figure 4. VERIFY: Rusfertide Phase 3 PV Trial Design



We initiated VERIFY, a global double-blind, placebo-controlled Phase 3 clinical trial of rusfertide in PV for approximately 250 patients, in the first quarter of 2022 (Figure 4). We expect to announce top-line data for the trial's 32-week primary efficacy endpoint in the first quarter of 2025, potentially leading to an NDA filing in the fourth quarter of 2025.

We currently have the following designations for rusfertide in PV:

- The FDA granted orphan drug designation for rusfertide for the treatment of PV in June 2020;
- The European Medicines Agency ("EMA") granted orphan drug designation for rusfertide for the treatment of PV in October 2020; and
- The FDA granted fast track designation for rusfertide for the treatment of PV in December 2020.

Rodent Carcinogenicity Studies

Rat carcinogenicity study. In the fourth quarter of 2024, we received the draft audited pathology report from our two-year study evaluating the carcinogenicity potential of rusfertide when administered once weekly. The draft report concluded that there were no carcinogenicity-related findings associated with rusfertide. We expect to receive the final audited report during the first quarter of 2025 which will then be submitted to the FDA.

RasH2 mouse carcinogenicity study. In 2021, we completed a 26-week rasH2 transgenic mouse carcinogenicity study related to rusfertide. In the rasH2 study, there were rusfertide related findings associated with benign squamous cell papilloma and malignant squamous cell carcinoma. Our rusfertide clinical trials were placed on a brief clinical hold from mid-September to early October 2021 following our receipt of the results of the RasH2 mouse study.

Takeda Collaboration Agreement

In January 2024, we entered into a worldwide license and collaboration agreement for the development and commercialization of rusfertide with Takeda. See Part II, Item 7. “Management’s Discussion and Analysis – Overview” and Note 3 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for additional information.

OVERVIEW OF DISEASES DRIVEN BY IL-23 AND IL-17 PATHWAYS

IL-23 is a member of the Interleukin 12 (“IL-12”) family of cytokines with pro-inflammatory and immune stimulatory properties. Cytokines are cell signaling proteins that are released by cells and affect the behavior of other cells. Binding of the IL-23 ligand to the IL-23R receptor leads to an expression of pro-inflammatory cytokines involved in the local tissue autocrine cascade that is an important pathway of many inflammatory diseases, including psoriasis, PsA and inflammatory bowel disease (“IBD”). The injectable antibody drug Stelara® (marketed for psoriasis, PsA, UC and CD) is a p40 antagonist antibody that inhibits both the IL-23 and IL-12 pathways. Next-generation antibody drugs, such as Tremfya® and Skyrizi®, target the p19 subunit of the IL-23 ligand and are specific inhibitors of the IL-23 pathway, which is believed to be the critical driver of local tissue pathology. Tremfya® is approved in psoriasis, PsA and UC and has completed successful Phase 3 clinical trials in CD. Skyrizi® is approved in psoriasis, PsA, UC and CD. The anti-IL-23 antibody Omvoh® (mirikizumab) has been approved in UC and CD, and the anti-IL-23 antibody Ilumya® trial (tildrakizumab) has been approved in psoriasis.

IL-23 is a pro-inflammatory cytokine with immune stimulatory properties. Binding of the IL-17 ligand to the IL-17R receptor leads to an expression of pro-inflammatory cytokines involved in the local tissue autocrine cascade that is an important pathway of many inflammatory diseases, including psoriasis, PsA, spondyloarthropathies, and HS). The injectable antibody drugs Cosentyx® and Taltz® (marketed for psoriasis, PsA, ankylosing spondylitis (“AS”) and non-radiographic axial spondyloarthropathies (“nr-axSpA”), with Cosentyx® also marketed for HS, and pediatric enthesitis-related arthritis) are IL-17A antagonist antibodies that inhibit the IL-17 pathway. The injectable antibody drug Bimzelx® blocks both IL-17A and IL-17F, thereby more completely blocking the IL-17 pathway by blocking its three dimeric forms – IL-17AA, -AF, and -FF. Bimzelx® is approved in psoriasis, PsA, AS, nr-axSpA, and HS. The injectable antibody Saliq® is an antibody that blocks the IL-17 receptor A, thereby blocking the IL-17 pathway, and is approved in psoriasis.

Psoriasis

Psoriasis is a chronic inflammatory disease of the skin that affects 130 million people worldwide and over 8 million in the United States, translating to 2-3% of the adult population. Psoriasis is associated with several comorbid conditions including cardiovascular disease and obesity, and 30% of psoriasis patients develop arthritic complications. Psoriasis is also associated with significantly decreased quality of life for patients.

Plaque psoriasis is the most common form of psoriasis, which is recognized as the most prevalent immune-mediated inflammatory disease, involving skin and joints and associated with abnormalities of other systems. Several factors, such as surface area covered and symptom burden, impact whether one’s psoriasis is considered mild, moderate, or severe. Typically, 3-10% of affected body surface area is considered moderate psoriasis, and more than 10% is considered severe psoriasis. Global market sales for psoriasis therapies in 2023 were $24.9 billion, with U.S. market sales of $18.4 billion. The global market forecast for 2033 anticipates sales of $32.0 billion, with U.S. market sales of $23.8 billion. Identification of the IL-23/IL-17 axis as the key pathway driving psoriatic inflammation has led to the development of more effective and safer systemic therapies that inhibit IL-17 (e.g., Taltz®, Cosentyx®, Bimzelx®, Saliq®) and IL-23 (e.g., Tremfya®, Skyrizi®, Ilumya®). These biologics have revolutionized the treatment of moderate-to-severe psoriasis, with superior efficacy and safety compared to conventional oral therapies (e.g., methotrexate, cyclosporin), and first-generation biologics (e.g., anti-TNFs, Stelara®). The anti-IL-17 class is ineffective in IBD, surprisingly showing overall worsening of disease in Phase 2 trials, which is reflected in the product labels. There is still an unmet need for new therapies. Only 25% of biologic eligible moderate-to-severe psoriasis patients are treated with a biologic. The parenteral route of administration for these advanced biologics poses a patient level barrier to entry. Two

oral medicines have been approved in moderate-to-severe psoriasis. Otezla® was approved in 2014. It is the least effective of all drugs approved since 2004 but is used widely because of a perceived positive safety profile. In 2022, the first TYK2 inhibitor, Sotyktu®, was approved. A second TYK2 inhibitor, TAK-279 is in Phase 3 trials for moderate-to-severe plaque psoriasis. We believe there is still significant need for safe and effective oral therapies in moderate-to-severe psoriasis.

Psoriatic Arthritis

PsA is an inflammatory disease of the peripheral and axial joints that complicates psoriasis in up to 30% of patients. Among the over 8 million patients in the United States with psoriasis in 2024, it is estimated that approximately 1 million patients have PsA. Many patients with active PsA may have mild psoriasis and many patients with severe psoriasis may have only mild PsA symptoms. PsA is associated with several chronic conditions. PsA may present even before skin symptoms in 10% to 15% of patients. Cardiovascular comorbidities have a higher prevalence in PsA than psoriasis and can impact lifespan and quality of life. Several new targeted therapies have been approved for use in PsA, with additional therapies in development. These advances have improved outcomes, including reductions in musculoskeletal symptoms, skin manifestations and radiographic joint damage. Many of the same drugs approved in psoriasis are also approved in PsA. One notable exception is that the JAK inhibitors, Xeljanz® and Rinvoq®, are approved in PsA without the respective label in psoriasis.

Hidradenitis Suppurativa

HS is a chronic, debilitating, inflammatory follicular skin disease with recurring painful flare-ups that affected approximately 2.9 million people in the U.S. and 6.3 million worldwide in 2024. HS can progress and worsen over time, with tunnels forming under the skin between abscesses, which can lead to scarring. HS symptoms typically affect intertriginous areas of the skin, such as the breasts, buttocks, groin, inner thighs, and under the arms. The suppuration is often accompanied by a foul smell, and the psychosocial burden, including isolation, can be severe. HS is associated with frequent, long-term sick leave, often having a substantial socio-economic impact. Global market sales for HS therapies in 2024 were $1.5 billion, with U.S. market sales of $1.2 billion. The global market forecast for 2034 anticipates sales of $6.5 billion, with U.S. market sales of $5.4 billion. Treatment for HS depends on the severity of the disease and traditionally included skin care, topical medications, antibiotics, acitretin, hormonal medications, and, in severe cases, surgical removal of the affected skin. Several new targeted therapies have more recently been approved, including an injectable antibody drug Humira®, which binds to tumor necrosis factor alpha (“TNFα”), as well as the anti-IL-17 drugs Cosentyx® and Bimzelx®. Though these advances have improved outcomes, there remains significant unmet need for new therapies.

Axial Spondyloarthritis

Axial spondyloarthritis (“axSpA”) is a systemic disease leading to arthritis affecting the spine and the sacroiliac joint that affected approximately 2.9 million people in the U.S. and 4.7 million patients worldwide in 2024. AxSpA has a strong genetic predisposition most commonly associated with HLA-B27. Over time, the disease may progress from nr-axSpA, which is associated with damage that may not be visible in X-rays but may be seen on magnetic resonance images, to AS, also known as radiographic axSpA, with damage to the sacroiliac joints and spine visible on X-rays. Severe disease can lead to fusion of the vertebrae, a condition referred to as bamboo spine. Men are more likely to accrue radiographic joint damage, whereas women tend to experience comparatively worse quality of life and disease activity. The disease can occur at any age but typically begins between ages 20 and 40. AS is more common in men than in women. However, nr-axSpA may be just as common in women as in men. It is less common among African Americans than people of other racial backgrounds. Global market sales for axSpA therapies in 2024 were $7.5 million, with U.S. market sales of $6.0 million. The global market forecast for 2034 anticipates sales of $10.7 million, with U.S. market sales of $8.7 million. Therapeutic options for patients with axSpA have expanded significantly over the past two decades. Patients who have failed non-steroidal anti-inflammatory drugs have multiple therapeutic options, including TNFα inhibitors (Enbrel®, Humira®, Remicade®, Simponi®, Cimzia®), IL-17 (Cosentyx®, Taltz®, Bimzelx®) and JAK inhibitors (Xeljanz®, Rinvoq®).

Inflammatory Bowel Disease ("IBD")

IBD is a group of chronic autoimmune and inflammatory conditions of the colon and small intestine, consisting primarily of UC and CD. In UC, inflammation may be limited to part of the colon or extend through its entirety. UC is primarily characterized by ulceration of the intestinal surface, accompanied by rectal bleeding and frequent, urgent bowel movements. CD occurs anywhere along the GI tract, commonly affecting the small intestine and the proximal large intestine. CD complications may include strictures and fistula, which penetrate all layers of the intestine. UC is usually diagnosed earlier than CD due to bleeding symptoms. Patients with CD may initially present with abdominal pain, fatigue and anorexia, which can be misdiagnosed. Both diseases' peak diagnosis years are in young adulthood and are found about equally in both males and females. Management is lifelong and affects school attendance, graduation rates, childbearing and work productivity. IBD prevalence is increasing worldwide and is correlated with the adoption of western diets and lifestyle, as well as genetic factors (5-20% of affected patients have a first degree relative with the disease).

According to the Crohn's & Colitis Foundation, IBD is diagnosed in over 0.7% of Americans, resulting in a population of approximately 2.4 million patients in the United States. In 2023, global sales for UC therapies were approximately $7.8 billion, and the market is expected to grow to $13.2 billion by 2030. In 2023, global sales for CD therapies were estimated to be $15.2 billion, with anticipated growth to $18.1 billion by 2030.

For many years, tumor necrosis factor-alpha ("TNF-α") antibody drugs were the primary treatment for moderate-to-severe IBD. Humira® and Remicade® are injectable and infused, respectively. Approximately one third of IBD patients do not respond to TNF-α antibody drugs and approximately another 30% to 40% become refractory within the first year of treatment. Additionally, TNF-α antibody drugs may predispose patients to an increased risk of serious infection and the development of anti-drug antibodies, which over time can cause loss of drug response. More recently, antibody products focused on potentially safer mechanisms of action have been gaining market share. One such product is Takeda's Entyvio®, which targets the α4β7 integrin pathway. Takeda reported 2023 sales of Entyvio® of approximately $5.2 billion. Similarly, Johnson & Johnson's Stelara®, which targets the IL-12 and IL-23 pathways, has gained significant traction. Johnson & Johnson global sales of Stelara® (approved for psoriasis, PsA, moderate-to-severe CD and UC) were $10.4 billion in 2024. Three anti-IL-23 mAbs have been evaluated in IBD. Skyrizi® and Omvoh® are approved in UC and CD, and Tremfya® is approved in UC and recently completed successful Phase 3 clinical trials in CD. The pan-JAK inhibitor Xeljanz® is approved in UC and the more selective JAK1/3 inhibitor Rinvoq® was approved in 2022 for UC and CD. The S1P1 modulator class of oral small molecules has also demonstrated efficacy in IBD, with Zeposia® approved in UC (but not CD) in 2021, and etrasimod approved in UC in 2023. The S1P1 class is associated with immunosuppression, cardiac, pulmonary and ocular toxicities.

The development of new, potent and targeted orally delivered therapies for IBD may offer safer and more effective treatment options, alone or in combination, for moderate-to-severe IBD patients. In addition, many clinicians continue to advocate for earlier introduction of targeted therapeutics in mild-to-moderate IBD to prevent disease progression and irreversible gastrointestinal damage. Given that the most effective agents in IBD induce remission in no more than 30% of patients, there has been much recent interest in combination therapies to break through this "therapeutic ceiling." In 2022, JNJ reported results of the VEGA study, the first randomized double bind clinical trial to assess the combination of an anti-TNF (Simponi®) with an anti-IL-23 (Tremfya®) in moderate-to-severe UC. In the Phase 2a POC trial, investigators found 83.1% of patients in the treatment group achieved a clinical response and 36.6% of patients treated with the combination therapy achieved clinical remission. The high rates of clinical response and remission are both higher than the response and remission rates of patients treated with guselkumab alone (74.6%; 21.1%) and golimumab alone (61.1%; 22.2%). Hence, we believe the IL-23 inhibition mechanism is a potentially paradigm shifting combination strategy to improve remission rates in UC.

ICOTROKINRA: AN ORAL IL-23 RECEPTOR ANTAGONIST

JNJ License and Collaboration Agreement

We have a worldwide license and collaboration agreement with JNJ to research, develop and co-detail IL-23R antagonist compounds for all indications, including IBD. See Part II, Item 7. "Management's Discussion and Analysis –

Overview" and Note 3 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for additional information. JNJ is an experienced innovator in therapeutics targeting the IL-23 pathway. Stelara® is a monoclonal antibody targeting IL-12 and IL-23 through their common p40 subunit is approved in psoriasis, PsA, CD and UC. Stelara® generated $10.4 billion in sales in 2024. Tremfya® is a specific IL-23 monoclonal antibody. It is approved in psoriasis and PsA and has completed successful Phase 3 trials in UC and CD. Tremfya® generated $3.7 billion in sales in 2024. We believe that in both psoriasis and IBD, there is an urgent need for safe and effective oral therapies. It is notable that Stelara® lost patent exclusivity in 2023 with biosimilar competition expected.

Icotrokinra, an orally delivered IL-23R specific antagonist for the potential treatment of psoriasis, PsA and IBD indications, was discovered through our peptide technology platform. IL-23, a member of the IL-12 family of pro-inflammatory cytokines, is a protein that regulates inflammatory and immune function and plays a key role in the development of IBD. By blocking IL-23R, we believe icotrokinra may improve disease symptoms while potentially minimizing the risk of systemic side effects. During the fourth quarter of 2021, a decision was made by JNJ to advance development of icotrokinra. For icotrokinra, JNJ is primarily responsible for the conduct of all further development, and we were primarily responsible for the discovery, IND-enabling studies and the initial Phase 1 study.

Clinical Development of Icotrokinra

In February 2022, JNJ initiated FRONTIER 1, a 255-patient Phase 2b clinical trial of icotrokinra in moderate-to-severe plaque psoriasis, which was completed in December 2022. FRONTIER 1 was a randomized, multicenter, double-blind, placebo-controlled trial that evaluated three once-daily dosages and two twice-daily dosages of icotrokinra taken orally. The primary endpoint of the trial was the proportion of patients achieving PASI-75 at 16 weeks. In July 2023, we announced updated positive topline results from the trial, which were presented by JNJ at the World Congress of Dermatology in Singapore. Icotrokinra achieved the trial's primary and secondary efficacy endpoints. A statistically significant greater proportion of patients who received icotrokinra achieved PASI-75 responses as well as PASI-90 and PASI-100 responses compared to placebo at week 16 in all five of the trial's treatment groups. A clear dose response was observed across an eight-fold dose range. Treatment was well tolerated, with no meaningful difference in frequency of adverse events across treatment groups versus placebo.

At JNJ's Enterprise Business Review in December 2023, JNJ highlighted icotrokinra as a potential first- and best-in-class targeted oral IL-23 peptide antagonist with potential across multiple indications, including plaque psoriasis, PsA and inflammatory bowel disease, with potential peak year sales projected at greater than $5.0 billion. JNJ IL-23 monoclonal antibody drugs Stelara and Tremfya generated approximately $14.1 billion in revenues in 2024.

In February 2024, the icotrokinra Phase 2b FRONTIER 1 trial results in adults living with moderate-to-severe plaque psoriasis were published in the NEJM. In March 2024, data presented at the American Academy of Dermatology 2024 Annual Meeting showed that, in the Phase 2b FRONTIER 2 trial, icotrokinra maintained high rates of skin clearance through 52 weeks in adults with moderate-to-severe plaque psoriasis. In August 2024, positive pre-clinical and clinical pharmacokinetic, pharmacodynamic and safety data for icotrokinra was published in the journal, Scientific Reports. Three Company-sponsored poster presentations and one Company-sponsored oral presentation were delivered at the 2024 European Academy of Dermatology and Venereology Congress in September 2024.

JNJ initiated six additional icotrokinra trials in psoriasis and one in UC, as discussed above. All of the trials in the ICONIC program use the 200 mg q.d. immediate release formulation of icotrokinra from the FRONTIER 1 trial.

In November 2024, we announced positive topline results from ICONIC-LEAD and ICONIC-TOTAL Phase 3 trials of icotrokinra in individuals 12 years of age and older with moderate to severe plaque psoriasis. In the ICONIC-LEAD trial, once-daily icotrokinra showed significant skin clearance versus placebo in adults and adolescents with moderate to severe plaque psoriasis. At week 16, nearly two-thirds (64.7%) of patients treated with icotrokinra achieved IGA scores of 0/1, and 49.6% achieved PASI 90, compared to 8.3% and 4.4% on placebo, respectively. Further increases in response rates continued to be observed at week 24, with 74.1% of patients treated with icotrokinra achieving IGA scores of 0/1, and 64.9% achieving PASI 90. Safety data was found to be consistent with the Phase 2 FRONTIER 1 and 2 trials. A similar proportion of patients experienced adverse events between icotrokinra and placebo, with 49.3% and

49.1% of participants experiencing a TEAE at week 16. In addition, positive topline results from the Phase 3 ICONIC-TOTAL trial showed once-daily icotrokinra met the primary endpoint of IGA of 0/1 at week 16 compared to placebo.

We believe these positive Phase 3 results confirm the efficacy and safety trends that were observed with the previous Phase 2 FRONTIER 1 and 2 studies, highlighting icotrokinra's potential as a best-in-class oral agent providing a combination of significant skin clearance with demonstrated tolerability in a once-daily pill for treating plaque psoriasis. We believe these results also continue to validate our innovative peptide technology platform and its effectiveness in creating highly differentiated new chemical entities to address unmet needs in various disease areas. Comprehensive results from both ICONIC-LEAD and ICONIC-TOTAL are being prepared for presentation at upcoming medical congresses and we expect these to be shared with health authorities in planned submissions.

PN-881: AN ORAL IL-17 RECEPTOR ANTAGONIST

In the fourth quarter of 2024, we announced the selection of PN-881, a potential best-in-class oral peptide IL-17 antagonist, as a development candidate for the treatment of immune-mediated skin diseases. PN-881 has been evaluated in extensive preclinical studies, including oral stability, potency, tissue distribution, and pharmacokinetics measurements, and evaluation in immunologic pharmacodynamics and preclinical efficacy models.

Figure 5. PN-881 Potently Inhibits IL-17A and IL-17F

PN-881 vs Competitors	HT-1080 (nM)[1]					
	IL-17AA		IL-17AF		IL-17FF	
	IC_{50}	IC_{90}	IC_{50}	IC_{90}	IC_{50}	IC_{90}
Oral agents						
PN-881	**0.13**	**0.56**	**27**	**55**	**14**	**76**
DC-806[2] (or close analogue)	228	3323	ND	ND	Inactive	Inactive
Injectable agents						
Cosentyx®	11	118	151	604	Inactive	Inactive
Taltz®	0.12	0.35	ND[3]	ND[3]	Inactive	Inactive
Bimzelx®	0.17	0.32	19	26	13	16

1. Similar results observed in human dermal neonatal fibroblasts (HDFn) after stimulation with IL-17AA, IL-17AF, or IL-17FF
2. Compound #166 from DICE patent: US 2020/0247785 A1. DC-806 development discontinued & replaced with DC-111
3. ND = Not determined

PN-881 has demonstrated in vitro blockade of IL-17 AA homodimer, FF homodimer and AF heterodimer. In assays using the HT-1080 human fibrosarcoma cell line stimulated with a combination of IL-17 and TNF-a produce IL-6, blocking IL-17 was shown to inhibit IL-6 production. In this assay, PN-881 inhibited 50% of IL-6 production (the IC50) at a concentration of 120 picomoles ("pM") and showed an IC 90, or 90% inhibition, at 560 pM. This potency was approximately 100-fold greater than the potency of secukinumab, and similar potency to the most potent approved antibody drugs and nanobody therapeutics in development (Figure 5). In multiple preclinical studies with oral dosing, PN-881 showed effective blockade in vivo of IL-17 in serum and skin and achieved pre-clinical proof-of-concept in a skin inflammation rodent disease model.

IND-enabling, or foreign equivalent, studies of PN-881 are ongoing or planned, including 7-day and 3-month toxicology studies. Planned clinical studies include a Phase 1 single ascending dose ("SAD") and multiple ascending dose ("MAD") study expected to begin in the fourth quarter of 2025. Results of the Phase 1 trial are expected to inform the design and dosing in a subsequent dose-ranging psoriasis trial. Rapid expansion into other IL-17 mediated diseases, including PsA, HS and axSpA, is expected to be based on results observed in psoriasis studies.

We believe an IL-17 antagonist peptide like PN-881, with best-in-class potential as an oral targeted therapy, may offer an attractive therapeutic option for patients with broad opportunity for multiple indications in addition to psoriasis. We expect to initiate a PN-881 first-in-human Phase 1 study in fourth quarter of 2025.

PN-943

PN-943 is a wholly owned investigational orally delivered gut-restricted alpha 4 beta 7 specific integrin antagonist for IBD. We completed a Phase 2 trial of PN-943 in patients with moderate-to-severe UC in early 2023. We do not intend to dedicate further internal resources to clinical development or contract manufacturing activities for our PN-943 clinical program.

OUR PEPTIDE TECHNOLOGY PLATFORM

Our proprietary technology platform is purposefully built to exploit the advantages of constrained peptides, which are much smaller than antibody-based drugs and may be delivered orally but are big enough to bind and block the difficult targets that antibodies bind and modulate. The platform has been successfully applied to a diverse set of biological targets that has led to several pre-clinical and clinical stage peptide-based new chemical entities, including our clinical stage product candidates, for a variety of clinical indications. Our platform is comprised of a series of tools and methods, including a combination of molecular design, phage display, stability assays, medicinal chemistry, surrogate biomarkers, formulations, *in vitro* biochemical, cell and tissue-based assays, and *in vivo* pharmacology and pharmacokinetic approaches. We apply this platform to the discovery and development of constrained peptides as new drug candidates.

The platform is used to develop potential drug candidates (agonists and antagonists): (i) using the structure of a target, when available, (ii) *de novo* when no target structure exists, or (iii) from publicly disclosed peptide starting points. In a structure-based approach, our proprietary molecular design software and structural database of several thousand constrained peptides, termed Vectrix™, are screened to identify suitable scaffolds. The scaffolds identified form the basis of designing and constructing the first set of phage or chemical libraries. The initial hits are identified by either panning or screening such libraries, respectively. When structural information is unavailable for a target, hits are identified by panning a set of 34 proprietary cluster-based phage libraries consisting of millions of constrained peptides. Once the hits are identified, they are optimized using a set of peptide, peptide mimetic and medicinal chemistry techniques that include the incorporation of new or manipulation of existing cyclization-constraints, as well as natural or unnatural amino acids and chemical conjugation or acylation techniques. These techniques are applied to optimize potency, selectivity, stability, exposure and ultimately efficacy. For rusfertide, hit discovery and optimization relied exclusively on medicinal and computational chemistry, with no phage display, to develop potent and selective injectable candidates with enhanced stability and exposure in blood. For injectable products, stability in blood is determined using *in vitro* assay techniques to identify chemical and biological sites of degradation, which are then optimized while still maintaining potency and selectivity. Conjugation strategies are used to optimize the exposure of the injected peptide. For icotrokinra, phage display is tightly coupled to medicinal chemistry, structural biology and oral stability techniques to develop potent, selective and orally delivered molecules. Oral stability is profiled in a series of *in vitro* and *ex vivo* assays that portray the chemical and metabolic barriers a peptide will encounter as it transits the GI and systemic compartments as needed. These metabolically labile spots in the peptides are optimized using medicinal chemistry-based approaches to engineer oral stability while maintaining selectivity and potency. Various *in vivo* pharmacology tools are then used to quantify peptide exposure in relevant GI and systemic compartments. This data can be used to optimize required exposure over the required time frame to achieve *in vivo* efficacy. This is complemented by formulation technologies to enhance GI and systemic exposure by exploiting the intrinsic stability of our oral peptides. Finally, various biomarkers are also developed to correlate exposure with efficacy to guide candidate selection, dose selection and provide preliminary POC of target engagement in clinical trials.

Discovery and Pre-clinical Activities

We believe we have built a versatile, well-validated and unique discovery platform. For example, this peptide technology platform has been used to develop product candidates for diverse target classes including G-protein-coupled receptors, ion channels, transporters, cytokines and their receptors for a variety of therapeutic areas. In the future we may tackle other I&I, metabolic and blood disorders and expand our technology platform to provide potential opportunities to pursue a wider variety of diseases that may include oral, topical and systemic approaches. We also intend to progress our platform to achieve systemic bioavailability and activity with oral peptides, macrocycles and peptidomimetics, thereby enabling us to address systemic diseases. Examples of this approach are the discovery and development of icotrokinra, our IL-23R antagonist in collaboration with JNJ, and PN-881, our recently announced IL-17 peptide antagonist product candidate, as described above.

Competition

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. While we believe that our product candidates, technology, knowledge and experience provide us with certain competitive advantages, we face competition from established and emerging pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions, among others.

Rusfertide

Ruxolitinib, marketed as Jakafi®, was approved in 2014 for the treatment of adults with PV who have inadequate response to or are intolerant to hydroxyurea. Approximately 5,300 PV patients are treated with Jakafi® each year. Besremi®, a ropeginterferon alfa-2b product indicated for the treatment of adults with PV, was approved with a black box warning in November 2021.

We are aware of other investigational compounds under clinical development for treatment of PV, including short interfering RNA approaches aimed at modulating or increasing endogenous hepcidin levels.

Icotrokinra

In psoriasis and PsA, competition will come from companies with approved injectable agents in the IL-17 and IL-12/23 pathway, including Cosentyx®, Taltz®, Siliq®, Tremfya®, and Skyrizi®. Bimekizumab (anti-IL-17A and F, UCB) has completed a positive Phase 3 program in psoriasis. Otezla® (Amgen) was the first oral agent approved in both psoriasis and PsA. The oral JAK inhibitors Xeljanz® (Pfizer) and Rinvoq® are approved in PsA. Several oral small molecules that inhibit the Janus kinase TYK2 are advancing in development. The Bristol Myers Squibb (“BMS”) TYK2 inhibitor, Sotyktu®, was approved for psoriasis in 2022. Second generation allosteric TYK2 inhibitors from Nimbus Therapeutics (recently in-licensed by Takeda) are moving into Phase 3 development, and a molecule from Ventyx Biosciences has initiated Phase 2 development. Several small molecules that inhibit IL-17 have completed Phase 1 development.

In IBD, competition will come from companies with injectable agents in the anti-integrin class (Entyvio®, Takeda, approved) and the anti-IL-12/23 class that may be approved in the next several years, including JNJ’s Stelara® (approved in UC and CD), Abbvie’s risankizumab (Skyrizi®) (UC and CD Phase 3), JNJ’s guselkumab (Tremfya®) (UC and CD); and Eli Lilly’s mirikizumab (Omvoh®) (UC and CD).

In addition, orally delivered agents with novel mechanisms of action that are approved for or in development and may be approved for UC and/or CD prior to or shortly after the launch of our product candidates can have significant impact in the competitive environment, including:

- JAK inhibitors: The pan-JAK tofacitinib (Xeljanz®) is approved in UC. The next-generation selective JAK1/3 inhibitors, including Abbvie’s upadacitinib (Rinvoq®), were approved in UC and CD in 2022. Pfizer’s selective JAK1/TEC inhibitor ritlecitinib is in Phase 2 development for UC and CD;

- S1P1 receptor modulators: BMS's ozanimod (Zeposia®) and Pfizer's etrasimod (Velsipity®) are approved in UC. Etrasimod is being studied in CD, though ozanimod was not found to show efficacy in CD; and

- Eli Lilly is developing MORF-057, an oral small molecule targeting α4β7, which is progressing in Phase 2 development in UC and CD. Other oral small molecules targeting α4β7 from Gilead and Ensho Therapeutics are in early clinical development. Many other agents are in early-stage development in IBD, including injectable anti-TLIA antibodies by Pfizer and Merck, and Teva and Sanofi which have recently presented positive Phase 2 results in IBD.

PN-881

In competitive areas, we believe there is a strong need for a differentiated oral approach. The injectable mAbs Cosentyx and Taltz targeting IL-17 AA and AF are approved in psoriasis, PsA, and SpA. Cosentyx was also recently the first IL-17 inhibitor approved in HS. Siliq, a mAb to the IL-17 receptor, is approved in psoriasis only and carries a black box warning for suicidal ideations. Bimzelx is a mAb that targets IL-17 AA, AF and FF. It is approved in psoriasis, PsA, HS, SS and nr-axSpA. Sonelokimab (MoonLake) is an injectable nanobody with IL-17 AA, AF and FF activity and has demonstrated POC in Phase 2 in psoriasis, PsA, and HS. There are several oral IL-17 small molecules in clinical development with the most advanced, DC-853 (Lilly via acquisition of DICE Therapeutics) in a Phase 2b trial in psoriasis. JNJ and Sanofi are also developing small molecules.

Material Agreements

Takeda Collaboration Agreement

In January 2024, we entered into the Takeda Collaboration Agreement. See Part II, Item 7, "Management's Discussion and Analysis – Overview" and Note 3 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for additional information.

JNJ License and Collaboration Agreement

On July 27, 2021, we entered into an Amended and Restated License and Collaboration Agreement (the "JNJ License and Collaboration Agreement") with JNJ, which amended and restated the License and Collaboration Agreement, effective July 13, 2017, by and between us and JNJ (the "Original Agreement"), as amended by the first amendment, effective May 7, 2019 (the "First Amendment"). The JNJ License and Collaboration Agreement, which relates to the development, manufacture and commercialization of oral IL-23 receptor antagonist drug candidates and enables JNJ to develop collaboration compounds for multiple indications, was further amended in November 2024. See Part II, Item 7, "Management's Discussion and Analysis – Overview" and Note 3 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for additional information.

Research Collaboration and License Agreement with Zealand Pharma A/S

In June 2012, we entered into a Research Collaboration and License Agreement (the "Zealand Agreement") with Zealand Pharma A/S ("Zealand") to identify, optimize and develop novel disulfide-rich peptides to discover a hepcidin mimetic. We amended this agreement on February 28, 2014, at which point we assumed responsibility for the development program. See Part II, Item 7. "Management's Discussion and Analysis – Contractual Obligations and Other Commitments" and Note 7 and Note 9 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for additional information.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to the development of our business, including seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets relating to our proprietary technology platform and on know-how, and continuing technological innovation to develop, strengthen, and maintain our

proprietary position in the field of peptide-based therapeutics that may be important for the development of our business. We will also take advantage of regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions where available.

Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same. For more information, please see Item 1A, “Risk Factors—Risks Related to Our Intellectual Property.”

We own or co-own 30 issued U.S. patents, over 68 granted ex-U.S. patents, and numerous U.S. and ex-U.S. patent applications related to our clinical assets. We possess substantial know-how and trade secrets relating to the discovery, development and commercialization of peptide based therapeutic products. Our proprietary intellectual property, including patent and non-patent intellectual property, is generally directed to, for example, peptide-based therapeutic compounds and compositions, methods of using these peptide-based therapeutic compounds and compositions to treat or prevent disease, methods of manufacturing peptide-based therapeutic compounds and compositions, and other proprietary technologies and processes related to our lead product development candidates. Specific patents and patent applications are directed to compositions of α*4*β7 integrin peptides, IL-23R antagonist peptides, IL-17 antagonist peptides and hepcidin mimetics peptides, as well as methods of synthesizing and using these peptides to treat disorders. Applications are currently pending in the United States and other major jurisdictions, including Australia, Canada, China, Japan, and Europe. We expect our patents and patent applications, if issued, and if the appropriate maintenance, renewal, annuity, or other governmental fees are paid, to expire from October 2033 to December 2044 (excluding possible patent term extensions).

Our objective is to continue to expand our portfolio of patents and patent applications in order to protect our clinical assets and related peptide-based drug technologies.

We also license patents and patent applications directed to processes and methods related to our technology platform. These patents have issued in the United States and other major jurisdictions, including Australia and Europe. Some licensed patents are expired. Material aspects of our technology platform are protected by trade secrets and confidentiality agreements.

In addition to the above, we have established expertise and development capabilities focused in the areas of pre-clinical research and development, manufacturing and manufacturing process scale-up, quality control, quality assurance, regulatory affairs and clinical trial design and implementation. We believe that our focus and expertise will help us develop products based on our proprietary intellectual property.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing the non-provisional application. In the United States, a patent’s term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in granting a patent or may be shortened if a patent is terminally disclaimed over an earlier-filed patent.

The term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration of a U.S. patent as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Moreover, a patent can only be extended

once, and thus, if a single patent is applicable to multiple products, it can only be extended based on one product. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. When possible, we expect to apply for patent term extensions for patents covering our product candidates and their methods of use.

Trade Secrets

We rely on trade secrets to protect certain aspects of our technology, particularly in relation to our technology platform. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. For more information, please see Item 1A, “Risk Factors—Risks Related to Our Intellectual Property.”

Manufacturing

We contract with third parties for the manufacturing of our product candidates for pre-clinical studies and clinical trials and eventually for commercial supplies and intend to continue to do so in the future. We do not own or operate any manufacturing facilities and we have no plans to build any owned clinical or commercial scale manufacturing capabilities. We believe that the use of contract manufacturing organizations (“CMOs”) eliminates the need for us to directly invest in manufacturing facilities, equipment and additional staff. We have established a global supply chain for raw material, active pharmaceutical ingredients (“API”), drug product manufacturing and distribution. We work with contract manufacturers in the United States, Europe and Asia. Although we rely on contract manufacturers, our personnel and consultants have extensive manufacturing and quality control experience overseeing CMOs. We regularly consider second source or back-up manufacturers for both API and drug product manufacturing. To date, our third-party manufacturers have met the manufacturing requirements for our product candidates. We expect third-party manufacturers to be capable of providing supplies needed for our product candidates to meet anticipated full-scale commercial demands, and we have selected CMOs that can manufacture our product candidates for our ongoing and planned clinical trials as well as commercial supplies. We currently engage CMOs on a “fee for services” basis for our current development and clinical supplies.

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs, such as those we are developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of our product candidates.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act and its implementing regulations. The process of obtaining regulatory approvals and the compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA’s refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

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

- completion of pre-clinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practices ("GLP") regulations;
- submission to the FDA of an IND application, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board ("IRB") at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice ("GCP") requirements to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA (or Biologics License Application ("BLA") for a biologic product);
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices ("cGMP") requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of an FDA inspection of one or more clinical trial sites to assure compliance with GCP requirements and the clinical protocol; and
- FDA review and approval of the NDA.

Pre-clinical Studies

Pre-clinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. These pre-clinical studies must comply with GLP. An IND sponsor must submit the results of the pre-clinical tests, together with manufacturing information, analytical data and any available clinical data or literature to the FDA as part of an IND. Some pre-clinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on a clinical hold. In such 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 Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements. GCP requirements mandate that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND (or equivalent international submission). In addition, an IRB or ethics committee must review and approve the plan for any clinical trial at all institutions participating in the clinical trial before it commences at that site. Information about certain clinical trials must be submitted within specific time frames to the National Institutes of Health for public dissemination on www.clinicaltrials.gov.

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

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and is tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, and to preliminarily evaluate the efficacy of the investigational drug product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- Phase 3: The drug is administered to an expanded patient population to establish the overall risk-benefit profile of the product, and to provide adequate labeling information (labeling) for the safe and efficacious administration for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Furthermore, 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 are being exposed to an unacceptable health risk. Similarly, an IRB or ethics committee can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Marketing Approval

Following successful completion of the required clinical testing and the results of the pre-clinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other information, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to an application user fee. Under the Prescription Drug User Fee Act ("PDUFA") guidelines, the FDA has a target of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to the FDA.

In addition, under the Pediatric Research Equity Act of 2003, certain NDAs or supplements to an NDA must contain data that is adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements.

The FDA also may require submission of a risk evaluation and mitigation strategy ("REMS") plan to ensure that the benefits of the drug outweigh its risks. REMS plans typically 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 conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the requested 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 a substantive review. The FDA reviews an NDA to determine whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by

the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter or a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or pre-clinical testing for the FDA to reconsider the application. Even after submission of this additional information, the FDA may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product. It may also require that contraindications, warnings or precautions be included in the product labeling or require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval. In addition, the FDA may mandate 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. This 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 studies or surveillance programs. After approval, some types of alterations, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Fast Track Designation

The FDA has various programs, such as fast track designation. These programs are intended to expedite or simplify the process for the development and FDA review of drugs for the treatment of serious or life-threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients faster. The sponsor of a new drug may request fast track designation concurrent with, or after, the filing of the IND. 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. A product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety. Fast track designation provides additional opportunities for interaction with the FDA's review team and may allow for rolling review of NDA components before the completed application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. However, the FDA's time goal for reviewing an application does not begin until the last section of the NDA is submitted. The FDA may decide to rescind the fast track designation if it determines that the qualifying criteria no longer apply.

Orphan Designation

The FDA may grant orphan designation to drugs or biologics intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States. The FDA may also grant the designation if the disease affects more than 200,000 individuals in the United States, and there is no reasonable expectation that the cost of developing and marketing the product for this type of disease or condition will be recovered from sales in the United States. Orphan designation must be requested before submitting an NDA or BLA. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Drugs or

biologics with orphan designation are not subject to a PDUFA fee upon the submission of an NDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

In the United States, orphan designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan exclusivity, which means the FDA may not approve any other application to market the same product for the same indication for a period of seven years, except in limited circumstances. Such circumstances include a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer with orphan exclusivity is unable to assure sufficient quantities of the approved orphan designated product. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity.

There is some uncertainty with respect to the FDA's interpretation of the scope of orphan drug exclusivity. Historically, exclusivity was specific to the orphan indication for which the drug or biologic was approved. As a result, the scope of exclusivity was interpreted as preventing approval of a competing product. However, in 2021, the federal court in Catalyst Pharmaceuticals, Inc. v. Becerra, suggested that orphan drug exclusivity covers the full scope of the orphan-designated "disease or condition" regardless of whether a drug obtained approval for a narrower use.

Breakthrough Therapy Designation

A sponsor can request designation of a drug candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug 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 designated as breakthrough therapies are also eligible for accelerated approval and priority review. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. The FDA may decide to rescind the breakthrough designation if it determines that the qualifying criteria no longer apply.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA. These regulations include requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to FDA review and approval. There also are continuing, annual program user fee requirements for any marketed products.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies. They are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval 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 side effects of unanticipated severity or frequency, problems 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 studies or clinical trials to assess new safety risks, or imposition of distribution or other restrictions under a REMS program. Other potential consequences include:

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

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved prescribing information. The FDA and other agencies 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.

Coverage and Reimbursement

Sales of our product candidates, if approved, will depend, in part, on the extent to which the cost of such products will be covered and adequately reimbursed by third-party payors, such as government healthcare programs, commercial insurance and managed health care organizations. These third-party payors are increasingly limiting coverage and reducing reimbursements for medical products and services by challenging the prices and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

There is no uniform policy requirement for coverage and reimbursement for drug products among third-party payors in the United States. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. Coverage determination can be a time-consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained or applied consistently. Even if reimbursement is provided, market acceptance of our products may be adversely affected if the amount of payment for our products proves to be unprofitable for health care providers or less profitable than alternative treatments, or due to administrative burdens.

In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payor to not cover our product candidates could reduce physician usage of our products candidates, once approved, and have a material adverse effect on our sales.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively referred to as the ACA, enacted in March 2010, has had and is expected to continue to have a

significant impact on the health care industry. The ACA imposes a significant annual fee on certain companies that manufacture or import branded prescription drug products. The ACA also increased the Medicaid rebate rate and expanded the rebate program to include Medicaid managed care organizations. It also contains substantial new provisions intended to broaden access to health insurance, reduce the growth of health care spending, enhance remedies against health care fraud and abuse, add new transparency requirements for the health care industry, impose new taxes and fees on pharmaceutical manufacturers, and impose additional health policy reforms, any or all of which may affect our business.

There have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, President Trump signed several Executive Orders and other directives designed to delay the implementation of certain ACA requirements or otherwise circumvent some of the health insurance mandates. Concurrently, Congress considered legislation to repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the ACA have been enacted. The Tax Cuts and Jobs Act of 2017, or the Tax Act, included a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on some individuals who do not maintain qualifying health coverage for all or part of a year. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated “Cadillac” tax on high-cost employer-sponsored health coverage and the medical device tax, and also eliminated the health insurance tax. The Bipartisan Budget Act of 2018 amends the ACA to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole,” and increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in the Medicare Part D program. The Inflation Reduction Act (“IRA”), enacted August 16, 2022, aims to control prescription drug prices in the upcoming years. The IRA will allow the Centers for Medicare & Medicaid Services (“CMS”) to cap out-of-pocket costs in 2025 and to negotiate prescription drug prices in 2026 for the first time. Additionally, the IRA provides a new “inflation rebate” covering Medicare patients beginning in 2023 to prevent rapid and arbitrary price increases in prescription drugs. These and any other legislation or healthcare reform measures of the Biden administration may impact the ACA and our business. There may also be further challenges to the ACA, and new laws may also result in additional reductions in Medicare and other health care funding.

Further, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. This scrutiny has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration implemented drug pricing reform through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that attempt to implement several of the administration’s proposals The FDA also released a final rule, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, the U.S. Department of Health and Human Services (“HHS”) finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule was delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers.

Federal and state legislatures have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare therapies.

It is uncertain whether and how future legislation, whether domestic or foreign, could affect prospects for our product candidates or what actions payors for health care treatment and services may take in response to such health care reform proposals or legislation. Adoption of price controls and other cost-containment measures, and adoption of more

restrictive policies in jurisdictions with existing controls and measures reforms may prevent or limit our ability to generate revenue, attain profitability or commercialize our product candidates.

Other Health Care Laws and Compliance Requirements

We will also be subject to health care regulation and enforcement by the federal and state government and foreign governments in which we will conduct our business once our products are approved. The laws that may affect our ability to operate include the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic health care transactions and protects the security and privacy of protected health information; the criminal health care fraud statutes under HIPAA also prohibit persons and entities from knowingly and willfully executing a scheme to defraud any health care benefit program, including private payors, or 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 health care benefits, items or services; the Anti-Kickback Statute, which prohibits persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal health care programs such as the Medicare and Medicaid programs; federal false claims laws and civil monetary penalties laws that prohibit any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid; and the Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the CMS information related to payments and other transfers of value made to various healthcare professionals including physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, certified nurse-midwives and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members. Beginning on January 1, 2023, California Assembly Bill 1278 requires California physicians and surgeons to notify patients of the Open Payments database established under the federal Physician Payments Sunshine Act.

The majority of states also have statutes or regulations similar to the federal anti-kickback and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. We may be subject to state laws governing the privacy and security of health information in certain circumstances, such as California's Confidentiality of Medical Information Act and Washington's My Health My Data Act, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. In addition, we may be subject to reporting requirements under state transparency laws, as well as state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government that otherwise restricts certain payments that may be made to health care providers and entities. In addition, certain states and local jurisdictions require the registration of pharmaceutical sales representatives.

Even when HIPAA and state health information privacy laws do not apply, according to the FTC and state Attorneys General, violating consumers' privacy rights or failing to take appropriate steps to keep consumers' personal information secure may constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act and state consumer protection laws.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exceptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If we are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including significant administrative, civil and criminal penalties, damages, fines, imprisonment, disgorgement, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, exclusion of products from reimbursement under U.S. federal or state health care programs, and the curtailment or restructuring of our operations.

Government Regulation Outside of the United States

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing clinical studies and any commercial sales and distribution of our products.

Drug and Biologic Development Process in the European Union ("EU")

All clinical trials included in applications for marketing authorization for human medicines in the EU must be carried out in accordance with EU regulations. This means that such clinical trials must comply with EU clinical trial legislation, as well as ethical principles equivalent to those set out in the EU and in Iceland, Norway and Liechtenstein (together, the European Economic Area, or "EEA"), including adhering to international good clinical practice and the Declaration of Helsinki. The conduct of clinical trials in the EU is governed by the EU Clinical Trials Regulation (EU) No. 536/2014 ("CTR") which entered into force on January 31, 2022.

Under the CTR, a sponsor may submit a single application for approval of a clinical trial through a centralized EU clinical trials portal. One national regulatory authority (the reporting EU Member State proposed by the applicant) will take the lead in validating and evaluating the application consult and coordinate with the other concerned Member States. If an application is rejected, it may be amended and resubmitted through the EU clinical trials portal. If an approval is issued, the sponsor may start the clinical trial in all concerned Member States. However, a concerned EU Member State may in limited circumstances declare an "opt-out" from an approval and prevent the clinical trial from being conducted in such Member State. The CTR also aims to streamline and simplify the rules on safety reporting and introduces enhanced transparency requirements such as mandatory submission of a summary of the clinical trial results to the EU Database ("CTIS"). Since January 31, 2023, submission of initial clinical trial applications via CTIS is mandatory, and by January 31, 2025, all ongoing trials approved under the former Clinical Trials Directive will need to comply with the CTR and have to be transitioned to CTIS.

National laws, regulations, and the applicable GCP and Good Laboratory Practice standards must also be respected during the conduct of the trials, including the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use ("ICH") guidelines on GCP and the ethical principles that have their origin in the Declaration of Helsinki.

Drug Marketing Authorization

In the EEA, after completion of all required clinical testing, pharmaceutical products may only be placed on the market after obtaining a Marketing Authorization ("MA"). To obtain an MA of a drug under EU regulatory systems, an applicant can submit a Marketing Authorization Application ("MAA") through, amongst others, a centralized or decentralized procedure.

The centralized procedure provides for the grant of a single MA that is issued by the European Commission ("EC") following the scientific assessment of the application by the EMA that is valid for all EU Member States as well as in the three additional EEA Member States. The centralized procedure is compulsory for specific medicinal products, including for medicines developed by means of certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (gene therapy, somatic cell therapy or tissue engineered medicines), and medicinal products with a new active substance indicated for the treatment of certain diseases (HIV/AIDS, cancer, neurodegenerative disorders, diabetes, autoimmune and viral diseases). For medicinal products containing a new active substance not yet authorized in the EEA before May 20, 2004 and indicated for the treatment of other diseases, medicinal products that constitute significant therapeutic, scientific or technical innovations or for which the grant of an MA through the centralized procedure would be in the interest of public health at EU level, an applicant may voluntarily submit an application for an MA through the centralized procedure.

Under the centralized procedure, the Committee for Medicinal Products for Human Use ("CHMP"), established at the EMA, is responsible for conducting the initial assessment of a drug. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing MA. Under the centralized procedure, the timeframe for the evaluation of an MAA by the CHMP is, in principle, 210 days

from receipt of a valid MAA. However, this timeline excludes clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP, so the overall process typically takes a year or more, unless the application is eligible for an accelerated assessment. Accelerated evaluation 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. Upon request, the CHMP can reduce the time frame to 150 days if the applicant provides sufficient justification for an accelerated assessment. The CHMP will provide a positive opinion regarding the application only if it meets certain quality, safety and efficacy requirements. This opinion is then transmitted to the EC, which has the ultimate authority for granting an MA within 67 days after receipt of the CHMP opinion.

Medicines that fall outside the mandatory scope of the centralized procedure have three routes to authorization: (i) they can be authorized under the centralized procedure if they concern a significant therapeutic, scientific or technical innovation, or if their authorization would be in the interest of public health; (ii) they can be authorized under a decentralized procedure where an applicant applies for simultaneous authorization in more than one EU Member State; or (iii) they can be authorized in an EU Member State in accordance with that state's national procedures and then be authorized in other EU countries by a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization (mutual recognition procedure).

The decentralized procedure permits companies to file identical MA applications for a medicinal product to the competent authorities in various EU Member States simultaneously if such medicinal product has not received marketing approval in any EU Member State before. This procedure is available for pharmaceutical products not falling within the mandatory scope of the centralized procedure. The competent authority of a single EU Member State, known as the reference EU Member State, is appointed to review the application and provide an assessment report. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference EU Member State and concerned EU Member States. The reference EU Member State prepares a draft assessment report and drafts of the related materials within 120 days after receipt of a valid application. Subsequently, each concerned EU Member State must decide whether to approve the assessment report and related materials. If an EU Member State cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the EC, whose decision is binding for all EU Member States.

All new MAAs must include a Risk Management Plan ("RMP"), describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available. An updated RMP must be submitted: (i) at the request of EMA or a national competent authority, or (ii) whenever the risk-management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit-risk profile or as a result of an important pharmacovigilance or risk-minimization milestone being reached. The regulatory authorities may also impose specific obligations as a condition of the MA. Since October 20, 2023, all RMPs for centrally authorized products are published by the EMA, subject only to limited redactions.

MAs have an initial duration of five years. After these five years, the authorization may subsequently be renewed on the basis of a reevaluation of the risk-benefit balance. Once renewed, the MA is valid for an unlimited period unless the EC or the national competent authority decides on justified grounds relating to pharmacovigilance to proceed with only one additional five-year renewal. Applications for renewal must be made to the EMA at least nine months before the five-year period expires.

European Data Protection Laws

The collection and use of personal health data and other personal data in the EU is governed by the provisions of the European General Data Protection Regulation (EU) 2016/679 ("GDPR") and related data protection laws in individual EU Member States. The GDPR imposes strict requirements on the processing of personal data, including the legal basis for the processing, the information that has to be provided to individuals before their data is processed,

personal data breaches which may have to be notified to national data protection authorities and data subjects, the measures to be taken when engaging processors, and the technical and organization measures to ensure the security and confidentiality of the personal data. EU Member States may also have additional requirements for health, genetic, and biometric data through their national legislation. The GDPR also imposes restrictions on the transfer of personal data to countries outside of the EU that do not provide an adequate level of data protection. To enable such transfers, appropriate safeguards, such as standard contractual clauses ("SCCs") must be in place. When relying on SCCs, data exporters are also required to conduct a transfer risk assessment to verify if anything in the law and/or practices of the third country may impinge on the effectiveness of the SCCs in the context of the transfer at stake and, if so, to identify and adopt supplementary measures that are necessary to bring the level of protection of the data transferred to the EU standard of essential equivalence. Where no supplementary measure is suitable, the data exporter should avoid, suspend or terminate the transfer. Alternatively, such transfers can be based on an adequacy decision by the EU commission. Regarding transfers to the US, the EU commission issued an adequacy decision for transfers to companies that are certified under the new EU-US Data Privacy Framework, which entered into force on June 10, 2023.

Failure to comply with the requirements of the GDPR and the related national data protection laws of the EU Member States may result in significant monetary fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater, other administrative penalties and a number of criminal offenses for organizations and, in certain cases, their directors and officers, as well as civil liability claims from individuals whose personal data was processed.

Sustainability, Corporate Responsibility and Human Capital Disclosures

Governance and Leadership

Our Board of Directors ("Board") plays a pivotal role in overseeing our strategic direction, risk management related to sustainability and corporate responsibility matters and our overall governance framework. Our Board composition reflects a wide range of backgrounds, skills and experiences. Our executive leadership team is responsible for driving our performance and guiding our long-term growth initiatives. We believe in fostering a culture of integrity, ethical decision making, and responsible corporate citizenship.

Business Ethics

We are committed to creating an environment where we are able to excel in our business while maintaining high standards of business conduct and ethics. Our Code of Business Conduct and Ethics ("Code of Conduct") reflects the business practices and principles of behavior that supports this commitment, including our policies on bribery, corruption, conflicts of interest, insider trading, and our whistleblower program. We expect all of our directors, officers, and employees to read, understand, and comply with the Code of Conduct and its application to the performance of his or her business responsibilities.

Environmental Commitment

We are committed to protecting the environment and attempt to mitigate any negative impact of our operations, promoting reuse and recycling and conserving resources, where feasible. We have safety protocols in place for handling biohazardous waste in our operations, including in our clinical trials, and we use third-party vendors for biohazardous waste and chemical disposal.

Social Responsibility

We are committed to providing patients with access to our investigational therapies, to the extent appropriate at the development stage. We are currently focused on our clinical programs and getting our therapies through the approval process and approved as rapidly as possible provided they are shown to be safe and effective. We provide access to our investigational therapies through our clinical trials, including in some cases long-term extensions of those trials that provide access to our therapies for up to several years. We also support educational efforts related to therapeutic areas in focus for our company, and life sciences education more broadly. In addition to financial support of continuing

education, we are active sponsors, mentors, and hosts for students seeking to broaden their understanding of life sciences in the interest of advancing human health.

Human Capital

We recognize that our success is driven by the knowledge, skills and dedication of our employees. Our human capital is fundamental to our ability to innovate and develop life-changing peptide drug therapies. We invest in our employees by seeking to foster a supportive and inclusive workplace. We offer competitive compensation and benefits and provide opportunities for professional growth and development.

As of December 31, 2024, our total global workforce consisted of 126 full-time equivalent employees, 98 of whom were in research and development. The remaining 28 employees worked in finance, legal, business development, human resources, information technology ("IT") and administrative support. 117 of our full-time equivalent employees are located in the United States and 9 are located in Australia. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Attracting, developing and retaining talented employees to support the growth of our business is an integral part of our human capital strategy and critical to our long-term success. We have robust recruitment and retention processes in place that are designed to attract and retain individuals who possess the necessary expertise, innovative drive and commitment to contribute to our mission. We offer competitive compensation packages, including performance-based incentives, equity awards, and robust benefits, including 401(k) plan matching contributions and an employee stock purchase plan for U.S. employees. The principal purpose of our equity incentive and annual bonus programs is to attract, retain and motivate personnel through the granting of stock-based compensation awards and cash-based performance bonus awards. As a biopharmaceutical company, we recognize the importance of access to high quality healthcare and as such we currently cover 100% of our U.S. employees' monthly healthcare premiums. For the year ended December 31, 2024, our employee turnover rate was approximately 11%.

We have a performance development review process in which managers provide regular feedback to assist with the development of our employees, including the use of individual plans to assist with career development. We also invest in the growth and development of our employees through various training and development programs that help build and strengthen our employees' leadership and professional skills. This reflects the quality and readiness of our people to take on new roles, as well as our intentional focus on growing and developing careers, as well as promoting from within.

Safeguarding the health and safety of our employees is a top priority. We are committed to providing a safe working environment for all of our employees. Our cross-functional safety committee meets regularly to discuss policies and protocols, strategic planning, business continuity and other matters. We invest in initiatives aimed at promoting employee well-being. To support our employees personally and professionally, we have Employee Assistance Programs to address employee challenges and needs. We value feedback from our employees and use it to improve our workplace policies and practices.

Corporate and Other Information

Our website address is www.protagonist-inc.com. References to our website address do not constitute incorporation by reference of the information contained on the website, and the information contained on the website is not part of this document.

We make available, free of charge on our corporate website, copies of our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, Proxy Statements, and all amendments to these reports, as soon as reasonably practicable after such material is electronically filed with or furnished to the SEC pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended ("Exchange Act").

Item 1A. Risk Factors

In evaluating our business, you should carefully consider the following discussion of material risks, events and uncertainties that make an investment in us speculative or risky in addition to the other information included in this Annual Report. A manifestation of any of the following risks and uncertainties could, in circumstances we may or may not be able to accurately predict, materially and adversely affect our business and operations, growth, reputation, prospects, operating and financial results, financial condition, cash flows, liquidity and stock price. Some of the factors, events and contingencies discussed below may have occurred in the past, but the disclosures below are not representations as to whether or not the factors, events or contingencies have occurred in the past and instead reflect our beliefs and opinions as to the factors, events, or contingencies that could materially and adversely affect us in the future. The risks and uncertainties described below are not the only ones we face. Our operations could also be affected by factors, events or uncertainties that are not presently known to us or that we currently do not consider to present significant risks to our business. Therefore, you should not consider the following risks to be a complete statement of all the potential risks or uncertainties that we face.

Risks Related to Clinical Development

We are a biopharmaceutical company with no approved products and no historical commercial revenue, which makes it difficult to assess our future prospects and financial results.

We are a biopharmaceutical company with a somewhat limited operating history as a publicly traded company. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of uncertainty. Our operations to date have been limited to developing our technology, undertaking pre-clinical studies and clinical trials of our pipeline candidates and conducting research to identify additional product candidates. We have not yet successfully developed an approved product or generated revenue from product sales or successfully conducted a pivotal registration trial for one of our product candidates. Consequently, the ability to accurately assess our future operating results or business prospects is significantly more limited than if we had a longer operating history or approved products on the market.

We expect that our financial condition and operating results will fluctuate significantly from period to period due to a variety of factors, many of which are beyond our control, including the success of our programs, decisions by regulatory bodies, actions taken by competitors or current or future licensees or collaborative partners, market and macroeconomic conditions and other factors identified in these risk factors. Accordingly, the likelihood of our success must be evaluated in light of many potential challenges and variables associated with a clinical-stage biopharmaceutical company, many of which are outside of our control, and past results, including operating or financial results, should not be relied on as an indication of future results.

We are heavily dependent on the success of our product candidates in clinical development, and if any of these products fail to receive regulatory approval or are not successfully commercialized, our business would be adversely affected.

We currently have no product candidates that are approved for commercial sale, and we may never develop a marketable product. We expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to our current product candidates and the development of other product candidates. We cannot be certain that our product candidates will receive regulatory approval or, if approved, be successfully commercialized. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of our product candidates will be subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries. In addition, even if approved, our pricing and reimbursement will be subject to further review and discussions with payors. We are not permitted to market any product candidate in the United States until after approval of an NDA from the FDA, or in any foreign countries until approval by corresponding regulatory authorities. We will need to successfully conduct and complete large, extensive clinical trials in the target patient populations to support a potential application for regulatory approval by the FDA or corresponding regulatory authorities. Those trials, such as our ongoing VERIFY Phase 3 trial evaluating rusfertide for the treatment of PV or subsequent late-stage product candidates, may not demonstrate the safety and efficacy of our product candidates to support a marketing approval in the United States or other jurisdictions.

Our product candidates require additional clinical development, regulatory approval and secure sources of commercial manufacturing supply prior to commercialization. We cannot assure you that our clinical trials for our product candidates will be initiated or completed in a timely manner or successfully, or at all. Further we cannot be certain that we plan to advance any other product candidates into clinical trials. Moreover, any delay or setback in the development of any product candidate would be expected to adversely affect our business and cause our stock price to fall. For example, our stock price dropped significantly in September 2021 following the announcement of a full clinical hold imposed by the FDA on our rusfertide clinical studies. Our stock price also dropped significantly in April 2022 following the announcement of our voluntary withdrawal of Breakthrough Therapy Designation for rusfertide and the announcement of topline data from our Phase 2 clinical trial evaluating PN-943 in UC.

Clinical development is a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results. Clinical failure can occur at any stage of clinical development.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical development process. The results of pre-clinical studies and early clinical trials of our product candidates and studies and trials of other products may not be predictive of the results of later-stage clinical trials. Any hypothesis formed from pre-clinical or early clinical observations for any of our product candidates may prove to be incorrect, and the data generated in animal models or observed in limited patient populations may be of limited value and may not be applicable in clinical trials conducted under the controlled conditions required by applicable regulatory requirements.

In addition to our planned pre-clinical studies and clinical trials, we will be required to complete one or more large scale, well-controlled clinical trials to demonstrate substantial evidence of efficacy and safety for each product candidate we intend to commercialize. Further, given the patient populations for which we are developing therapeutics, we expect to have to evaluate long-term exposure to establish the safety of our therapeutics in a chronic-dose setting. We have not yet completed a Phase 3 clinical trial or submitted an NDA. As a result, we have no corporate history or track record of successfully completing these phases of the development cycle. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through pre-clinical studies and initial clinical trials. Clinical trial failures may result from a multitude of factors including, but not limited to, flaws in trial design, dose selection, placebo effect, patient enrollment criteria and failure to demonstrate favorable safety and/or efficacy traits of the product candidate. Based upon negative or inconclusive results, we may decide, or regulators may require us, to conduct additional clinical trials or pre-clinical studies.

We may experience delays in ongoing clinical trials, and we do not know whether planned clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. For example, we initially experienced slower than expected patient enrollment in VERIFY, a global Phase 3 clinical trial of rusfertide in PV. Clinical trials can be delayed for a variety of reasons, including if a clinical trial is modified, suspended or terminated by us. For example, in keeping with our organizational prioritization of rusfertide in PV, plans to initiate trials of rusfertide in other indications have been paused. Clinical trials can also be delayed by the institutional review boards or ethics committees of the institutions in which such clinical trials are being conducted, by a Data Safety Monitoring Board, for such trial or by the FDA or other regulatory authorities. Such authorities may impose a modification, suspension or termination due to a number of factors.

For example, our rusfertide clinical studies were subject to a three-week clinical hold by the FDA beginning in September 2021. The clinical hold was triggered by a non-clinical finding in a 26-week rasH2 transgenic mouse model indicating benign and malignant subcutaneous skin tumors. Also, in April 2022, the FDA indicated that it intended to rescind Breakthrough Therapy Designation for rusfertide in PV, and we voluntarily withdrew our request. For additional information, see the risk factor entitled “Our product candidates may cause undesirable side effects or have other properties adversely impacting safety that delay or prevent their regulatory approval, restrict their approved labeling, or otherwise limit their commercial opportunity” below.

In addition, there are a significant number of global clinical trials in hematologic disorders that are currently ongoing, especially in Phases 2 and 3, making it highly competitive and challenging to recruit subjects. Other companies targeting the same patient populations as our clinical trials for such medicines may make it more difficult for us to

complete enrollment in our clinical trials. Furthermore, any negative results we may report in clinical trials of our product candidate may make it difficult or impossible to recruit and retain patients in other ongoing or subsequent clinical trials of that same product candidate. Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both.

If we experience material delays in the completion of any clinical trial, the reduction in remaining patent term would harm the commercial prospects for that product candidate and our ability to generate product revenue from any of these product candidates will be delayed. Any of these occurrences may harm our business, financial condition and prospects significantly.

If we are unable to discover and develop new product candidates, our business will be adversely affected.

As part of our strategy, we seek to discover and develop new product candidates. Research programs to identify appropriate biological targets, pathways and product candidates require substantial scientific, technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates yet fail to yield product candidates for clinical development for many reasons.

Our proprietary peptide platform may not result in any products of commercial value.

We have developed a proprietary peptide technology platform to enable the identification, testing, design and development of new product candidates. Our peptide platform may not yield additional product candidates that enter clinical development and, ultimately, become commercially valuable. Although we expect to continue to enhance the capabilities of our platform by developing and integrating existing and new research technologies, our enhancement and development efforts may not succeed. As a result, we may not be able to advance our drug discovery capabilities as quickly as we expect or identify as many potential drug candidates as we desire.

Our product candidates may cause undesirable side effects or have other properties adversely impacting safety that delay or prevent their regulatory approval, restrict their approved labeling, or otherwise limit their commercial opportunity.

If undesirable side effects or adverse events are caused by our product candidates or by other companies' similar approved drugs or product candidates, then we may elect to, or be required by an independent data monitoring committee or regulatory authorities to, delay or halt our clinical trials. If such side effects or adverse events are sufficiently severe or prevalent, the FDA or comparable foreign regulatory authorities could order us to suspend or cease altogether further development of our product candidates. Even if our product candidates are approved, side effects or adverse events could result in significant delay in or denial of, regulatory approval, restrictive labeling, or potential product liability claims. Moreover, for our product candidates that are in development for indications for which injectable antibody drugs have been approved, clinical trials for those product candidates may need to show a risk/benefit profile that is competitive with those existing products in order to obtain regulatory approval or, if approved, a product label that is favorable for commercialization.

For example, in September 2021, our clinical studies for rusfertide were placed on a brief full clinical hold by the FDA following a non-clinical finding in a rasH2 transgenic mouse model indicating benign and malignant subcutaneous skin tumors. Any similar findings in human clinical trials may adversely impact regulatory approval, product labeling or commercialization of rusfertide.

We have focused our limited resources to pursue particular product candidates and indications, and consequently, we may fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we have historically focused on research programs and product candidates mainly on the development of rusfertide and the product candidates subject to our JNJ collaboration. We have an ongoing commitment to optimize and focus resources toward our rusfertide program in PV. In

addition, in keeping with our organizational prioritization of rusfertide in PV, plans to initiate trials of rusfertide in additional disease indications have been paused. As a result, we may forego or delay the pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration partnerships, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Risks Related to our Financial Position and Capital Requirements

We have incurred a cumulative net loss since our inception and anticipate that we may incur significant losses in the future. We have never generated any revenue from product sales and may never be profitable.

We have incurred a cumulative net operating loss since inception and may continue to incur operating losses in the future. As of December 31, 2024, we had an accumulated deficit of $340.5 million. We expect to continue to incur significant research, development and other expenses related to our ongoing operations and product development. As a result, we expect to continue to incur losses in the future as we continue our development of, and seek regulatory approvals for, our product candidates.

We do not anticipate generating revenue from sales of products for a number of years, if ever, and we have not yet successfully completed registrational or pivotal clinical trials for our product candidates. If any of our product candidates fail in clinical trials or do not gain regulatory approval or fail to achieve market acceptance, we may never become profitable. Revenue we generate from our collaborations with JNJ, Takeda, and any future collaboration arrangements may not be sufficient to sustain our operations. Failure to become and remain profitable may adversely affect the market price of our common stock and our ability to raise capital and continue operations.

We may require additional funding, which may not be available to us on acceptable terms, or at all.

Our operations have consumed substantial amounts of cash since inception. Developing pharmaceutical product candidates, including conducting pre-clinical studies and clinical trials, is expensive. We may require additional future capital in order to complete clinical development and, if we are successful, to commercialize any of our current product candidates. Further, in the event that the JNJ License and Collaboration Agreement or the Takeda Collaboration Agreement is terminated, we may not receive any additional fees or milestone payments under these agreements. Absent the funding support obtained under these agreements, our further development of the collaboration product candidates would require significant additional capital from us, or the establishment of alternative collaborations with third parties, which may not be possible.

As of December 31, 2024, we had cash, cash equivalents and marketable securities of $559.2 million. Based upon our current operating plan and expected expenditures we believe that our existing cash, cash equivalents, and marketable securities will be sufficient to fund our operations for at least the next 12 months. However, we may need to have access to additional funds in the future in order to complete clinical development or commercialize our product candidates to a point where our operations generate net cash inflows.

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

We have in the past and may in the future seek additional funding through a combination of equity offerings, including the use of the 2022 ATM Facility, debt financings, collaborations and/or licensing arrangements. Additional funding may not be available to us on acceptable terms, or at all. Our ability to raise additional capital may be adversely impacted by adverse economic conditions and market volatility, including as a result of public health crises; changes in trade policies, including tariffs or other trade restrictions or the threat of such actions; political instability, including the ongoing conflict between Russia and Ukraine and in the Middle East and rising tensions between China and Taiwan; and high interest rates. The incurrence of indebtedness and/or the issuance of certain equity securities could result in fixed

payment obligations and could also result in certain additional restrictive covenants, such as limitations on our ability to incur debt and/or issue additional equity, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. In addition, the issuance of additional equity securities by us, or the possibility of such issuance, may cause the market price of our common stock to decline. In the event that we enter into additional collaborations and/or licensing arrangements in order to raise capital, we may be required to accept unfavorable terms, including relinquishing or licensing to a third party on unfavorable terms our rights to our proprietary technology platform or product candidates. To the extent that we raise additional capital through the sale of equity securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. If we issue common stock or securities convertible into common stock, our common stockholders will experience additional dilution and, as a result, our stock price may decline.

Risks Related to our Reliance on Third Parties

If JNJ does not elect to continue the development of icotrokinra, or if Takeda does not elect to develop and commercialize rusfertide, our business and business prospects would be adversely affected.

Icotrokinra, the product candidate in development pursuant to our JNJ collaboration, and rusfertide, the product candidate in development pursuant to the Takeda Collaboration Agreement, may prove to have undesirable or unintended side effects or other characteristics adversely affecting its safety, efficacy or cost effectiveness that could prevent or limit its approval for marketing and successful commercial use, or that could delay or prevent the commencement and/or completion of clinical trials.

Under the terms of the JNJ License and Collaboration Agreement, JNJ may terminate the agreement for convenience and without cause on written notice of a certain period. In addition, prior to any termination of the agreement, JNJ will generally have control over the further clinical development of icotrokinra and any other licensed compounds. JNJ's decisions with respect to such development will affect the timing and availability of potential future payments under the agreement, if any. For example, during the fourth quarter of 2021, a decision was made by JNJ to stop further development of both PTG-200 and PN-232 in favor of icotrokinra.

Under the terms of the Takeda Collaboration Agreement, Takeda may terminate the agreement for convenience in its entirety or as to a major region by providing advance written notice following the earliest of (i) the receipt of Phase 3 data with respect to the VERIFY clinical trial, (ii) the third anniversary of the effective date of the agreement or (iii) the occurrence of certain specified adverse events related to the clinical development of rusfertide.

If the JNJ License and Collaboration Agreement or the Takeda Collaboration Agreement is terminated early, or if JNJ's or Takeda's development activities are terminated early or suspended for an extended period of time, or are otherwise unsuccessful, our business and business prospects would be materially and adversely affected.

We may have disagreements with JNJ during the term of the JNJ License and Collaboration Agreement or Takeda under the Takeda Collaboration Agreement, and if they are not settled amicably or in the favor of Protagonist, the result may harm our business.

We are subject to the risk of possible disagreements with JNJ regarding the development of icotrokinra or other matters under the JNJ License and Collaboration Agreement and Takeda regarding the development of rusfertide or other matters under the Takeda Collaboration Agreement, such as the interpretation of such agreement or ownership of proprietary rights. Also, because the period of collaborative development under the agreement has ended, JNJ has sole decision-making authority for product candidates resulting from the collaboration, which could lead to disputes with JNJ. Disagreements with JNJ or Takeda could lead to litigation or arbitration, which would be expensive and would be time-consuming for our management and employees.

Our current and future development and commercialization collaborations may not be successful.

Other than our collaboration with JNJ License and Collaboration Agreement and our collaboration with Takeda under the Takeda Collaboration Agreement, we have no active collaborations for any of our product candidates. Our collaborations with JNJ and Takeda and any future collaboration arrangements may not ultimately be successful, which could have a negative impact on our business, results of operations, financial condition and growth prospects. We do not maintain significant rights or control of future development and commercialization activities under our collaboration with JNJ, or in ex-U.S. territories under our collaboration with Takeda. This could lead to potential disputes in the future over the terms of the collaborations and the respective rights of the parties, and these risks and uncertainties could be present with respect to our potential future collaborations as well.

If our strategic collaborations do not result in the successful development and commercialization of product candidates or if one of our collaborators fails to fulfill its obligations under the collaboration agreement or terminates its agreement with us, we may not receive any future milestone, royalty or other payments under the applicable collaboration agreement. In addition, if a collaboration is terminated, it may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

We rely on third parties to conduct our pre-clinical studies and clinical trials. If these third parties do not successfully carry out their contractual obligations or do not meet regulatory requirements or expected deadlines, we may not be able to obtain timely regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third-party contract research organizations (“CROs”) to execute, monitor and manage clinical trials and collect data for our pre-clinical studies and clinical programs. We control only certain aspects of their activities. We and our CROs are required to comply with GCPs, which are regulations and guidelines promulgated by the FDA, the EMA and comparable foreign regulatory authorities for all of our product candidates in clinical development. If we or any of our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA or comparable foreign regulatory authorities may not accept the data or require us to perform additional clinical trials before considering our filing for regulatory approval or approving our marketing application. In addition, significant portions of the clinical studies for our product candidates are expected to be conducted outside of the United States, which will make it more difficult for us to monitor CROs and perform visits of our clinical trial sites and will force us to rely heavily on CROs for the proper and timely conduct of our clinical trials and compliance with applicable regulations, including GCPs.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. If CROs 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 clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly.

We face a variety of manufacturing risks and rely on third parties to manufacture our drug substance and clinical drug product and we intend to rely on third parties to produce commercial supplies of any approved product candidate.

We rely on contract manufacturers to manufacture and provide product for us that meets applicable regulatory requirements. We do not currently have, nor do we plan to develop, the infrastructure or capability internally to manufacture our drug supplies and we expect to continue to depend on contract manufacturers for the foreseeable future. As we proceed with the development and potential commercialization of our product candidates, we will need to increase the scale at which the drug is manufactured, which will require the development of new manufacturing processes to potentially reduce the cost of goods. We will rely on our internal process research and development efforts and those of contract manufacturers to develop the required manufacturing processes for cost-effective, large-scale

production. If we and our contract manufacturers are not successful in converting to commercial-scale manufacturing, then our product costs may not be competitive and the development and/or commercialization of our product candidates would be materially and adversely affected. Moreover, our contract manufacturers are the sole source of supply for our clinical product candidates. If we were to experience an unexpected loss of supply for any reason, whether as a result of manufacturing, supply or storage issues, natural disasters, geopolitical conflict, outbreaks of disease, epidemics and pandemics, or otherwise, we could experience delays, disruptions, suspensions or termination of our clinical trial and planned development program, or be required to restart or repeat, any ongoing clinical trials.

We also rely on our contract manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical trials. There are a limited number of suppliers for raw materials that our vendors use to manufacture our drugs and there may be a need to assess alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our product candidates for our clinical trials, and if approved, for commercial sale. Moreover, we currently do not have any agreements for the commercial production of these raw materials. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the clinical trial, any significant delay in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a contract manufacturer or other third-party manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates.

Risks Related to Regulatory Process and Other Legal Compliance Matters

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy and time consuming, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

Our business is substantially dependent on our ability to successfully develop, obtain regulatory approval for and then successfully commercialize our product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA, the EMA or any other foreign regulatory authority, and we may never receive such regulatory approval for any of our product candidates. The time required to obtain approval by the FDA and comparable foreign authorities is difficult to predict, typically takes many years following the commencement of clinical trials and depends upon numerous factors. Approval policies, regulations and the types and amount of clinical and manufacturing data necessary to gain approval may change during the course of clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that none of our existing product candidates or any product candidates we have in development or may seek to develop in the future will ever obtain regulatory approval.

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

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials, or our interpretation of the data submitted in support of regulatory approval;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication or that a product candidate's clinical and other benefits outweigh its safety risks;
- the results of clinical trials may fail to achieve the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- the data collected from pre-clinical studies and clinical trials of our product candidates may not be sufficient to support the submission of an NDA, supplemental NDA, or other regulatory submissions necessary to obtain regulatory approval;

- we or our contractors may not meet the GMP and other applicable requirements for manufacturing processes, procedures, documentation and facilities necessary for approval by the FDA or comparable foreign regulatory authorities; and

- changes to the approval policies or regulations of the FDA or comparable foreign regulatory authorities with respect to our product candidates may result in our clinical data becoming insufficient for approval.

In addition, even if we were to obtain regulatory approval, regulatory authorities may approve our product candidates for fewer or more limited indications than what we requested approval for or may include safety warnings or other restrictions that may negatively impact the commercial viability of our product candidates, including the potential for a favorable price or reimbursement at a level that we would otherwise intend to charge for our products. Likewise, regulatory authorities may grant approval contingent on the performance of costly post-marketing clinical trials or the conduct of an expensive risk-evaluation and mitigation system, which could significantly reduce the potential for commercial success or viability of our product candidates. Any of the foregoing possibilities could materially harm the prospects for our product candidates and business and operations.

We may fail to obtain additional orphan drug designations from the FDA and/or the EMA for our product candidates, as applicable, and even if we obtain such designations, we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

Our strategy includes filing for orphan drug designation where available for our product candidates. Rusfertide has received orphan drug designation for the treatment of patients with PV from the FDA and the EMA. Despite this designation, we may be unable to maintain the benefits associated with orphan drug status, including market exclusivity. We may not be the first to obtain regulatory approval of a product candidate for a given orphan-designated indication. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet patient needs. Further, even if we obtain orphan drug designation exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may receive and be approved for the same condition, and only the first applicant to receive approval for a given active ingredient will receive the benefits of marketing exclusivity. Even after an orphan-designated product is approved, the FDA can subsequently approve a later drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care.

Risks Related to Commercialization of our Product Candidates

We currently have no marketing and sales organization. To the extent any of our product candidates for which we maintain commercial rights is approved for marketing, if we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be able to effectively market and sell any products or generate product revenue.

We currently do not have a marketing or sales organization for the marketing, sales and distribution of pharmaceutical products, and have only a limited number of employees engaged in those activities. In order to commercialize or co-commercialize any of our product candidates that receive marketing approval, we will have to build adequate marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. We may not be successful in doing so. In the event of the successful development of any of our product candidates, we may elect to build a targeted specialty sales force which will be expensive and time-consuming. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. As we have done with Takeda with respect to rusfertide, we may choose to partner 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. In the case of the JNJ License and Collaboration Agreement or the Takeda Collaboration Agreement, we may elect to exercise our right to co-detail products, which would require us to establish a U.S. sales team. If we are not successful in

commercializing our product candidates, either on our own or through collaborations with one or more third parties, our future revenue will be materially and adversely impacted.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

Legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements. See Item 1. "Business – Government Regulation" for additional information.

Pharmaceutical and biological product marketing is subject to substantial regulation in the U.S. and EU, and any failure by us or our future commercial and collaborative partners to comply with applicable statutes or regulations can adversely affect our business.

Any marketing activities associated with our product candidates, if approved for commercialization, will be subject to numerous federal, state and equivalent foreign laws governing the marketing and promotion of pharmaceutical and biological products. The FDA and EMA regulates post-approval promotional labeling and advertising in the United States and EU, respectively, to ensure that they conform to statutory and regulatory requirements. In addition to FDA and EMA restrictions, the marketing of prescription drugs is subject to laws and regulations prohibiting fraud and abuse under government healthcare programs. Similarly, many states have similar statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, and, in some states, such statutes or regulations apply regardless of the payor. In addition, government authorities may also seek to hold us responsible for any failure of our future commercialization or collaborative partners to comply with applicable statutes or regulations. If we, or our commercial or collaborative partners, fail to comply with applicable FDA or EMA regulations or other laws or regulations relating to the marketing of our product candidates, if approved for commercialization, we could be subject to criminal prosecution, civil penalties, seizure of products, injunctions and exclusion of our product candidates from reimbursement under government programs, as well as other regulatory or investigatory actions against our future product candidates, our commercial or collaborative partners or us.

The healthcare system is under significant financial pressure to reduce costs, which could reduce payment and reimbursement rates for drugs.

Throughout the world and particularly in the United States, the healthcare system is under significant financial pressure to reduce costs. The price of pharmaceuticals has been a topic of considerable public discussion that could lead to price controls or other price-limiting strategies by payors that have the effect of lowering payment and reimbursement rates for drugs or otherwise making the commercialization of pharmaceuticals less profitable. Many federal and state legislatures have considered, and adopted, healthcare policies intended to curb rising healthcare costs, such as the Inflation Reduction Act of 2022. These cost-containment measures may include, among other measures: requirements for pharmaceutical companies to negotiate prescription drug prices with government healthcare programs; controls on government-funded reimbursement for drugs; new or increased requirements to pay prescription drug rebates to government healthcare programs, including if drug prices increase at a higher rate than inflation; controls on healthcare providers; challenges to or limits on the pricing of drugs, including pricing controls or limits or prohibitions on reimbursement for specific products through other means; requirements to try less expensive products or generics before a more expensive branded product; and public funding for cost effectiveness research, which may be used by government and private third-party payors to make coverage and payment decisions. Political, economic and regulatory

developments may further complicate developments in healthcare systems and pharmaceutical drug pricing. These developments could, for example, impact our potential licensing agreements as commercial and collaborative partners may also consider the impact of these pressures on their licensing strategies.

Any new laws or regulations that have the effect of imposing additional costs or regulatory burden on pharmaceutical manufacturers, or otherwise negatively affect the industry, could adversely affect our ability to successfully commercialize our product candidates. The implementation of any price controls, caps on prescription drugs or price transparency requirements could adversely affect our business, operating results and financial condition.

We currently conduct, and intend to continue to conduct, a substantial portion of the clinical trials for our product candidates outside of the United States. If approved, we may commercialize our product candidates abroad. We will thus be subject to the risks of doing business outside of the United States.

We currently conduct, and intend to continue to conduct, a substantial portion of our clinical trials outside of the United States and, if approved, we intend to also market our product candidates outside of the United States. We are thus subject to risks associated with doing business outside of the United States. Our business and financial results in the future could be adversely affected due to a variety of factors associated with conducting development and marketing of our product candidates, if approved, outside of the United States, including varying medical standards and practices, geopolitical risks, uncertainty around intellectual property protection, and regulatory risks, such as compliance with the Foreign Corrupt Practices Act. If we are unable to anticipate and address these risks properly, our business and financial results will be harmed.

We may fail or elect not to commercialize our product candidates, even if approved.

We cannot be sure that, if our clinical trials for any of our product candidates are successfully completed, we will be able to submit an NDA to the FDA or that any NDA we submit will be approved by the FDA in a timely manner, if at all. After completing clinical trials for a product candidate in humans, a drug dossier is prepared and submitted to the FDA as an NDA, and includes all pre-clinical studies and clinical trial data relevant to the safety and effectiveness of the product at the suggested dose and duration of use for the proposed indication as well as manufacturing information, in order to allow the FDA to review such drug dossier and to consider a product candidate for approval for commercialization in the United States. If we are unable to submit an NDA with respect to any of our current product candidates, if any NDA we submit is not approved by the FDA, or we elect not to file an NDA, or if we are unable to obtain any required state and local distribution licenses or similar authorizations, we will be unable to commercialize that product. The FDA can and does reject NDAs and require additional clinical trials, even when product candidates achieve favorable results in Phase 3 clinical trials. Also, we may be subject to pricing pressures from competitive products that could make it difficult or impossible for us to commercialize the product candidate successfully. If we fail to commercialize any of our product candidates, our business, financial condition, results of operations and prospects may be materially and adversely affected.

The commercial success of any current or future product candidate will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

We or our collaboration partners in any potential commercial launch of our product candidates may not be successful in achieving widespread patient or physician awareness or acceptance of such product candidate. Even though we expect that our product candidate will be priced responsibly, if approved, there is no guarantee that it or any other product that we bring to the market directly or through a strategic partner will gain market acceptance by physicians, patients, third-party payors and others in the medical community. The degree of market acceptance of any of our product candidates, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- the safety and efficacy of the product in clinical trials, and potential advantages over competing treatments;
- the publication of unfavorable safety or efficacy data concerning our product by third parties;

- the prevalence and severity of any side effects, including any limitations or warnings contained in a product's approved labeling;
- the clinical indications for which approval is granted;
- recognition and acceptance of our product candidates over our competitors' products;
- prevalence of the disease or condition for which the product is approved;
- the cost of treatment, particularly in relation to competing treatments;
- the willingness of the target patient population to try our therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- the extent to which the product is approved for inclusion on formularies of hospitals and managed care organizations;
- publicity concerning our products or competing products and treatments;
- the extent to which third-party payors provide coverage and adequate reimbursement for the product candidate, or any other product candidates we may pursue, if approved;
- our ability to maintain compliance with regulatory requirements; and
- labeling or naming imposed by FDA or other regulatory agencies.

Even if a product candidate we may develop in the future displays an equivalent or more favorable efficacy and safety profile in pre-clinical and clinical trials, market acceptance of the product candidate will not be fully known until after it is launched and may be negatively affected by a potential poor safety experience and the track record of other product candidates. Our efforts, or those of any strategic licensing or collaboration partner, to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources, may be under-resourced compared to large well-funded pharmaceutical entities and may never be successful. If ay product candidates we may develop in the future are approved but fail to achieve an adequate level of acceptance by physicians, patients, third-party payors and others in the medical community, we will not be able to generate sufficient revenue to become or remain profitable.

If the market opportunities for our approved product candidates, if any, are smaller than we expect, it could materially adversely affect our financial condition and results of operations.

If the market opportunity for our products, if approved, is smaller than we expect, we may never become or remain profitable nor generate sufficient revenue growth to sustain our business even if we obtain significant market share for them. The potentially addressable patient population for our products may be limited or may not be amenable to treatment with our products, and new patients may become increasingly difficult to identify or access, which would adversely affect our results of operations and our business.

Risks Related to our Business and Industry

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

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors worldwide, including major multinational pharmaceutical companies, biotechnology companies, specialty pharmaceutical and generic pharmaceutical companies as well as universities and other research institutions.

Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. As a result, these companies may obtain regulatory approval more rapidly than we are able and may be more effective in selling and marketing their products. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of newer technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, pharmaceutical products that are easier to develop, more effective or less costly than any product candidates that we are currently developing or that we may develop. If approved, our product candidates are expected to face competition from commercially available drugs as well as drugs that are in the development pipelines of our competitors.

Pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make our product candidates less competitive. In addition, any new product that competes with an approved product must demonstrate advantages in efficacy, convenience, tolerability or safety in order to overcome price competition and to be commercially successful. If our competitors succeed in obtaining FDA, EMA or other regulatory approval or discovering, developing and commercializing drugs before we do, there would be a material adverse impact on the future prospects for our product candidates and business. For example, in November 2021, the FDA approved a Biologics License Application for ropeginterferon alfa-2b for use in treatment for patients with PV in the absence of symptomatic splenomegaly from PharmaEssentia Corporation, the manufacturer of the novel pegylated interferon. We also face competition in certain instances from the existing standards of care, which may be significantly less expensive than our expected drug prices. For example, one widely used treatment for patients is phlebotomy and/or chelation therapy. While patients may not like therapies that involve frequent blood draws, these therapies are inexpensive and may present pricing challenges for us if our drug candidates are successfully developed and approved. See Item 1, “Business – Competition” for additional information.

Outbreaks of disease, epidemics and pandemics have and could continue to adversely impact our business, including our ongoing and planned clinical trials and pre-clinical and discovery research.

Our future results of operations and liquidity could be adversely impacted by direct and indirect impacts of epidemics and pandemics. We have and could in the future experience additional disruptions or increased expenses that may adversely impact our business, including delays or difficulties in enrolling patients in our ongoing clinical trials and our future clinical trials; delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff or maintaining ongoing operations at such sites; and delays in manufacturing and receiving the supplies, materials and services needed to conduct clinical trials and pre-clinical research.

A continued and prolonged public health crisis could have a material negative impact on our business, financial condition, and operating results.

Unstable market and macroeconomic conditions, including elevated and sustained inflation, may have serious adverse consequences on our business, financial condition and stock price.

As has been widely reported, we are currently operating in a period of macroeconomic uncertainty and capital markets disruption, which has been significantly impacted by domestic and global monetary and fiscal policy, trade regulations, including changes in trade policies, tariffs or other trade restrictions or the threat of such actions,

geopolitical instability, including ongoing military conflicts between Russia and Ukraine and in the Middle East, rising tensions between China and Taiwan, and high interest rates. In particular, the conflict in Ukraine has exacerbated market disruptions, including significant volatility in commodity prices, as well as supply chain interruptions, and has contributed to record inflation globally. The U.S. Federal Reserve and other central banks may be unable to contain inflation through more restrictive monetary policy and inflation may increase or continue for a prolonged period of time. Inflationary factors, such as increases in the cost of clinical supplies, interest rates, overhead costs and transportation costs may adversely affect our operating results. We continue to monitor these events and the potential impact on our business. Although we do not believe that inflation has had a material impact on our financial position or results of operations to date, our financial position or results of operations may be adversely affected in the future due to the macroeconomic factors discussed above, and such factors may lead to increases in the cost of manufacturing our product candidates and delays in initiating trials. In addition, global credit and financial markets have experienced extreme volatility and disruptions in the past several years and the foregoing factors have led to and may continue to cause diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, uncertainty about economic stability and increased inflation.

There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. A future recession or market correction or other significant geopolitical events could materially affect our business and the value of our common stock. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, or do not improve, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which could directly affect our ability to attain our operating goals.

We maintain our cash at financial institutions, often in balances that exceed federally insured limits. The failure of financial institutions could adversely affect our ability to pay our operational expenses or make other payments.

Our cash held in non-interest-bearing and interest-bearing accounts generally exceeds the Federal Deposit Insurance Corporation (the “FDIC”) insurance limits. If such banking institutions were to fail, we could lose all or a portion of those amounts held in excess of such insurance limitations. For example, the FDIC took control of Silicon Valley Bank on March 10, 2023. The Federal Reserve subsequently announced that account holders would be made whole. However, the FDIC may not make all account holders whole in the event of future bank failures. In addition, even if account holders are ultimately made whole with respect to a future bank failure, account holders’ access to their accounts and assets held in their accounts may be substantially delayed. Any material loss that we may experience in the future or inability for a material time period to access our cash and cash equivalents could have an adverse effect on our ability to pay our operational expenses or make other payments, which could adversely affect our business.

If we fail to comply with state and federal healthcare regulatory laws, we could face substantial penalties, damages, fines, disgorgement, integrity oversight and reporting obligations, exclusion from participation in governmental healthcare programs, and the curtailment of our operations, any of which could adversely affect our business, operations, and financial condition.

Healthcare providers, including physicians, and third-party payors will play a primary role in the recommendation and prescription of any future product candidates we may develop or any product candidates for which we obtain marketing approval. Our arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may affect the business or financial arrangements and relationships through which we would market, sell and distribute our products. Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients’ rights are and will be applicable to our business. The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute;

- the federal false claims laws, including the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA");
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and their implementing regulations, which also imposes obligations, including mandatory contractual terms, on HIPAA-covered entities, their business associates as well as their covered subcontractors with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal civil monetary penalties statute;
- the federal Physician Payments Sunshine Act; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws.

Further, the ACA, among other things, amended the intent requirements of the federal Anti-Kickback Statute and certain criminal statutes governing healthcare fraud. Any violations of these laws, or any action against us for violation of these laws, even if we successfully defend against it, could result in a material adverse effect on our reputation, business, results of operations and financial condition.

We have entered into consulting and scientific advisory board arrangements with physicians and other healthcare providers, including some who could influence the use of our product candidates, if approved. While we have worked to structure our arrangements to comply with applicable laws, because of the complex and far-reaching nature of these laws, regulatory agencies may view these transactions as prohibited arrangements that must be restructured or discontinued, or for which we could be subject to other significant penalties. We could be adversely affected if regulatory agencies interpret our financial relationships with providers who may influence the ordering of and use our product candidates, if approved, to be in violation of applicable laws.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. Federal and state enforcement bodies have continued to increase their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of significant investigations, prosecutions, convictions and settlements in the healthcare industry. Additionally, as a result of these investigations, healthcare providers and entities may have to agree to additional onerous compliance and reporting requirements as part of a consent decree or corporate integrity agreement. Any such investigation or settlement could significantly increase our costs or otherwise have an adverse effect on our business.

If our operations are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, integrity oversight and reporting obligations, exclusion from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If, and to the extent that, we or our collaboration partners are unable to comply with these regulations, our ability to earn potential royalties from sales of product candidates under our collaboration agreements would be materially and adversely impacted. If any of the physicians or other healthcare 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 significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. The imposition of any of these penalties or other commercial limitations could negatively impact our collaboration arrangements or cause our collaboration partners to terminate the related license and collaboration agreement, either of which would materially and adversely affect our business, financial condition and results of operations.

Our future success depends on our ability to retain our executive officers and to attract, retain and motivate qualified personnel. If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

We are highly dependent on our existing senior management team. The loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements would harm our research and development efforts, our collaboration efforts, as well as our business, financial condition and prospects. Our success also depends on our ability to continue to attract, retain and motivate highly skilled and experienced personnel with scientific, medical, regulatory, manufacturing, marketing, sales, general and administrative and management training and skills.

We may not be able to attract or retain qualified personnel in the future due to the intense competition for a limited number of qualified personnel among biopharmaceutical, biotechnology, pharmaceutical and other businesses. Many of the other biopharmaceutical and pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. Many are located in areas of the country with lower costs of living. Additionally, the United States has recently experienced historically high levels of inflation and an acute workforce shortage generally, which has created a hyper-competitive wage environment that may increase our operating costs. Any or all of these factors may limit our ability to continue to attract and retain high quality personnel, which could negatively affect our ability to successfully develop and commercialize product candidates and to grow our business and operations as currently contemplated.

We expect to expand the size of our organization in the future, and we may experience difficulties in managing this growth.

As of December 31, 2024, we had 126 full-time equivalent employees, including 98 full-time equivalent employees engaged in research and development. As our development and commercialization plans and strategies develop, we expect to need additional managerial, operational, scientific, sales, marketing, research, development, regulatory, manufacturing, financial and other resources. In addition, as our operations expand, we expect that we will need to manage relationships with strategic collaborators, CROs, contract manufacturers, suppliers, vendors and other third parties. Our future financial performance and our ability to develop and commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. We may not be successful in accomplishing these tasks in growing our company, and our failure to accomplish any of them could adversely affect our business and operations.

Significant disruptions of information technology systems or cybersecurity incidents could adversely affect our business.

Our business is increasingly dependent on critical, complex and interdependent information technology systems, including internet-based systems, to support business processes as well as internal and external communications. The size and complexity of our internal computer systems and those of our CROs, contract manufacturers, collaboration partners, and other third parties on which we rely may make them potentially vulnerable to breakdown, telecommunications and electrical failures, and malicious intrusion such as ransomware and computer viruses that may result in the impairment of key business processes. Our systems are potentially vulnerable to cybersecurity breaches, by employees or others, which may expose sensitive data to unauthorized persons. Such cybersecurity breaches or other cybersecurity incidents may allow hackers access to our pre-clinical compounds, strategies, discoveries, trade secrets and/or other confidential information. Additionally, sensitive data could be leaked, disclosed or revealed as a result of or in connection with our employees', personnel's, vendors' or partners' use of generative artificial intelligence technologies. Any disruption or cybersecurity incident, to the extent it was to result in the loss, destruction, unavailability, alteration or dissemination of, or damage to, our data or applications, or for it to be believed or reported that any of these occurred, could harm our reputation, compel us to comply with federal and/or state breach notification laws, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to liability under laws and regulations that protect personal data, resulting in increased costs or loss of revenue. The risk of a cybersecurity incident or other informational technology disruption, particularly through cyber-attacks, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from

around the world has increased. If we are unable to prevent such cybersecurity incidents or privacy violations or implement satisfactory remedial measures, our operations could be disrupted, and we may suffer loss of reputation, financial loss and other regulatory penalties.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We 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, and produce hazardous waste products. We generally contract with third parties for the disposal of these materials and waste. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Our employees, independent contractors, principal investigators, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk that our employees, independent contractors, principal investigators, consultants or vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (i) FDA laws and regulations or those of comparable foreign regulatory authorities, (ii) manufacturing standards, (iii) federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations established and enforced by comparable foreign regulatory authorities, or (iv) laws that require the true, complete and accurate reporting of financial information or data. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. 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.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims 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. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to stop development or, if approved, limit commercialization of our product candidates.

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 development or commercialization of our product candidates. We currently carry clinical trial liability insurance for our clinical trials. Although we maintain such insurance, 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 our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Our headquarters is located near known earthquake fault zones. The occurrence of an earthquake, fire or any other catastrophic event could disrupt our operations or the operations of third parties who provide vital support functions to us, which could have a material adverse effect on our business and financial condition.

We and some of the third-party service providers on which we depend for various support functions are vulnerable to damage from catastrophic events, such as power loss, natural disasters, extreme weather, terrorism, pandemics and similar unforeseen events beyond our control. Our corporate headquarters, including our laboratory facilities, are located in the San Francisco Bay Area, which in the past has experienced severe earthquakes and wildfires. We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects.

The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our product candidates could limit our ability to generate revenue.

The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford medications and therapies. Sales of any of our product candidates that receive marketing approval will depend substantially, both in the United States and internationally, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain adequate pricing that will allow us to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products as increasingly high barriers are being erected to the entry of new products into the healthcare markets. Coverage and reimbursement can differ significantly from payor to payor. It is difficult to predict what CMS will decide with respect to reimbursement for novel products such as ours since there is no body of established practices and precedents for these new products.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada and other countries may cause us to price our product candidates on less favorable terms than we currently anticipate. In many countries, particularly the countries of the European Union, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies. In general, the prices of products under such systems are substantially lower than in the United States. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

Risks Related to our Intellectual Property

If we are unable to obtain or protect intellectual property rights related to our product candidates and technologies, we may not be able to compete effectively in our markets.

We rely upon a combination of patent protection, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates and technologies. The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. We may or may not file or prosecute all necessary or desirable patent applications. The patent applications that we own or license may fail to result in issued patents in the United States or in other foreign countries, or they may fail to result in issued patents with claims that cover our product candidates or technologies in the United States or in other foreign countries. Any failure to

identify relevant prior art relating to a patent or patent applications can invalidate a patent or prevent a patent from issuing. Even if patents have been issued, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patent and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates and technologies, or prevent others from designing around our claims.

If the breadth or strength of protection provided by our patents is challenged, or if they fail to provide meaningful exclusivity for our product candidates, it could prevent us from asserting exclusivity over the covered product and allow generic competition. We cannot offer any assurances about which, if any, of our patent applications will issue, the breadth of any such issued patent, or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition or other challenge to our patents or patent applications could significantly diminish the commercial prospects of any products that we develop.

In addition, patents have a limited lifespan. In the United States and in many other countries, the natural expiration of a patent is generally 20 years after it is filed, and once any patents covering a product expire, generic competitors may enter the market. Our granted U.S. patent covering rusfertide expires in 2034 but is eligible for extension of up to five years for a portion of the time spent in development. Although the life of a patent can be increased based on certain delays caused by the U.S. Patent and Trademark Office, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. If we encounter delays in our clinical trials or in gaining regulatory approval, the period of time during which we could market any of our product candidates under patent protection, if approved, would be reduced.

We may not be able to protect our intellectual property rights throughout the world. Filing, prosecuting and defending patents on all of our product candidates throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States may be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights, including trade secrets, to the same extent as federal and state laws of the United States and many countries limit the enforceability of patents against third parties, including government agencies or government contractors.

Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing. Also, if our trade secrets are disclosed in a foreign jurisdiction, competitors worldwide could have access to our proprietary information and we may be without satisfactory recourse. Such disclosure could have a material adverse effect on our business.

We also rely on trade secret protection and confidentiality agreements to protect proprietary scientific, business and technical information and know-how that is not or may not be patentable or that we elect not to patent. For example, we primarily rely on trade secrets and confidentiality agreements to protect our peptide therapeutics technology platform. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. If we are unable to protect the confidentiality of our trade secrets and proprietary know-how or if competitors independently develop viable competing products, our business and competitive position may be harmed.

Although we require all of our employees to assign their inventions to us, and endeavor to execute confidentiality agreements with all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how and other confidential information related to such technology, we cannot be certain that we have executed such agreements with all third parties who may have helped to develop our intellectual property or who had access to our proprietary information, nor can be we certain that our agreements will not be breached. If any of the parties to these confidentiality agreements breaches or violates the terms of such agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result.

Even if we are able to adequately protect our trade secrets and proprietary information, our trade secrets could otherwise become known or could be independently discovered by our competitors. If our trade secrets are not adequately protected so as to protect our market against competitors' products, others may be able to exploit our proprietary peptide product candidate discovery technologies to identify and develop competing product candidates, and thus our competitive position could be adversely affected, as could our business.

We may be involved in lawsuits and other legal proceedings to protect or enforce our intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our issued patents or any patents issued as a result of our pending or future patent applications. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable or may refuse to stop the other party in such infringement proceeding from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly, and could put any of our patent applications at risk of not yielding an issued patent. Issued patents and patent applications may be challenged in the courts and in the patent office in the United States and abroad. An adverse determination in any such challenge could prevent the issuance of, reduce the scope of, invalidate or render unenforceable our patent rights, result in the loss of exclusivity, or limit our ability to stop others from using or commercializing our platform technology and products. Any such adverse result or determination could have a material adverse effect on our business, financial condition and results of operations.

Any issued patents covering our product candidates, including any patent that may issue as a result of our pending or future patent applications, could be found invalid or unenforceable if challenged in court in the United States or abroad.

As more groups become engaged in scientific research and product development in fields related to our product candidates, such as hepcidin mimetics or IL-23R, the risk of our patents, or patents that we have in-licensed, being challenged through patent interferences, derivation proceedings, oppositions, re-examinations, litigation or other means will likely increase. An adverse outcome in a patent dispute could have a material adverse effect on our business by:

- causing us to lose patent rights in the relevant jurisdiction(s);
- subjecting our collaboration partners or us to litigation, or otherwise preventing the commercialization of product candidates in the relevant jurisdiction(s); or
- requiring our collaboration partners or us to obtain licenses to the disputed patents, cease using the disputed technology or develop or obtain alternative technologies.

An adverse outcome in a patent dispute could severely harm our collaborations or cause our collaboration partners to terminate their respective agreements.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, are unpredictable and generally expensive and time-consuming and, even if resolved in our favor, are likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the market price of our common stock. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Third-party claims of intellectual property infringement may prevent or delay our drug discovery and development efforts.

Our commercial success depends in part on our ability to develop, manufacture, market and sell our drug candidates and use our proprietary technologies without infringing or otherwise violating the patents and proprietary rights of third parties. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates, and there may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates and technologies.

Third parties may initiate legal proceedings against us alleging that we are infringing or otherwise violating their patent or other intellectual property rights. Given the vast number of patents in our field of technology, marketing of our product candidates or practice of our technologies could infringe existing patents or patents granted in the future. There may be applications now pending of which we are unaware that may later result in issued patents that may be infringed by the practice of our peptide therapeutics technology platform or the manufacture, use or sale of our product candidates. If any third-party patents were to be held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product or formulation itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire. As our industry expands and more patents are issued, the risk increases that our product candidates or technologies may give rise to claims of infringement of the patent rights of others.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to commercialize our product candidates. Even if we are successful in defending against any infringement claims, litigation is expensive and time-consuming and is likely to divert management's attention and substantial resources from our core business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, limit our uses, pay royalties or redesign our infringing product candidates, which may be impossible or require substantial time and monetary expenditure. We may choose to seek, or may be required to seek, a license from the third-party patent holder and would most likely be required to pay license fees or royalties or both, each of which could be substantial. These licenses may not be available on commercially reasonable terms, however, or at all. Even if we were able to obtain a license, the rights we obtain may be nonexclusive, which would provide our competitors access to the same intellectual property rights upon which we are forced to rely. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In such an event, we would be unable to further practice our technologies or develop and commercialize any of our product candidates at issue, which could harm our business significantly.

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

Many of our employees and consultants, including our senior management and our scientific founders, have been employed or retained at universities or by other biotechnology or pharmaceutical companies, including potential competitors. Some of our employees and consultants, including each member of our senior management and each of our scientific founders, executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment or retention. We may be subject to claims that we or these employees, consultants or independent contractors have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's or consultant's former or other employer. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

We may be subject to claims challenging the inventorship or ownership of our issued patents, any patents issued as a result of our pending or future patent applications and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an ownership interest in our issued patents, any patents issued as a result of our pending or future applications or other intellectual property. We have had in the past, and we may have in the future, ownership disputes arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates and technologies. Litigation may be necessary to defend against these and other claims.

In addition, some of our intellectual property rights were generated through the use of U.S. government funding and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980 and implementing regulations. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us or our licensors to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party in certain circumstances (also referred to as “march-in rights”).

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we expect to rely on third parties in the development and manufacture of our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor’s discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have an adverse effect on our business and results of operations.

Intellectual property rights do not necessarily address all potential threats to our business.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business. The following examples are illustrative:

- others may be able to make compounds or formulations that are similar to our product candidates, but that are not covered by the claims of any patents that we own, license or control;
- we or any strategic partners might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own;
- we may not have been the first to file patent applications covering certain of our inventions;
- others may independently develop the same, similar, or alternative technologies without infringing, misappropriating or violating our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents may not provide us with any competitive advantages, or may be narrowed or held invalid or unenforceable, including as a result of legal challenges;

- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and may then use the information learned from such activities to develop competitive products for sale in our major commercial markets;

- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such trade secrets or know-how; and

- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could have a material adverse impact on our business and financial condition.

Risks Related to Ownership of our Common Stock

Our stock price has been and will likely continue to be volatile and may decline regardless of our operating performance.

Our stock price has fluctuated in the past and is likely to be volatile in the future. From January 1, 2024 through December 31, 2024, the reported sale price of our common stock has fluctuated between $21.43 and $48.89 per share. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may experience losses on their investment in our common stock, including due to the factors discussed in these "Risk Factors" and elsewhere in this Annual Report.

Volatility in our share price could subject us to securities class action litigation.

Securities class action litigations have often been brought against companies following a decline in the market price of their securities. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

We are required to develop and maintain proper and effective internal controls over financial reporting and any failure to maintain the adequacy of these internal controls may adversely affect investor confidence in our company and, as a result, the value of our common stock.

We are required, pursuant to Section 404 of the Sarbanes-Oxley Act ("Section 404"), to furnish a report by management on the effectiveness of our internal control over financial reporting. This assessment needs to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. Our independent registered public accounting firm is required to attest to the effectiveness of our internal control over financial reporting.

Maintaining adequate internal controls 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. We currently do not have an internal audit group, and we may need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge and continue the costly and challenging process of compiling the system and processing documentation necessary to perform the evaluation needed to comply with Section 404. We may not complete our continued evaluation, testing and any required remediation in a timely fashion. During our evaluation of our internal control, if we identify one or more material weaknesses in our internal control over financial reporting or fail to remediate any material weaknesses, we will be unable to assert that our internal control over financial reporting is effective. In addition, if we have a material weakness, we will receive an adverse opinion regarding our internal control over financial reporting from our independent registered public accounting firm. Any material weakness or other failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition or results of operations. If we are not able to comply with the requirements of Section 404 or if we or our independent registered public accounting firm are unable to attest to the effectiveness of our internal control over

financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities, which would require additional financial and management resources.

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

Our amended and restated certificate of incorporation ("Certificate of Incorporation") provides that the Court of Chancery of the State of Delaware will be the exclusive forum for certain actions and proceedings. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. The choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes, which may discourage such lawsuits. Alternatively, if a court were to find the choice of forum provision contained in our Certificate of Incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions.

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

There are provisions in our Certificate of Incorporation and Bylaws, such as the existence of a classified Board and the authorization of "blank-check" preferred stock, that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change in control was considered favorable by our stockholders. These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our Board, who are responsible for appointing the members of our management.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibit a person who owns 15% or more of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. Any provision in our Certificate of Incorporation, our Bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock and could also affect the price that some investors are willing to pay for our common stock.

General Risk Factors

Our ability to use net operating loss carryforwards to offset future taxable income, and our ability to use tax credit carryforwards, may be subject to certain limitations.

Our ability to use our federal and state net operating losses ("NOLs") to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income, and we cannot predict with certainty when, or whether, we will generate sufficient taxable income to use our NOLs. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire.

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than fifty percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research and development tax credits) to offset its post-change taxable income or tax liability may be limited. We have experienced ownership changes in the past, resulting in annual limitations in our ability to use our NOLs and credits. In addition, we may experience subsequent ownership changes as a result of future equity offerings or other changes in the ownership of our stock, some of which

are beyond our control. As a result, the amount of the NOLs and tax credit carryforwards presented in our financial statements could be limited and may expire unused. Any such material limitation or expiration of our NOLs may harm our future operating results by effectively increasing our future tax obligations.

If the estimates we make, or the assumptions on which we rely, in preparing our consolidated financial statements prove inaccurate, our actual results may vary from those reflected in our accruals.

Our consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges accrued by us and related disclosure of contingent assets and liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. We cannot assure you, however, that our estimates, or the assumptions underlying them, will be correct.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

In the ordinary course of our business, we collect, use, store, and transmit confidential, sensitive, proprietary, and personal information. The secure maintenance of this information and our IT systems is important to our operations and business strategy. We understand the growing challenges associated with cybersecurity threats and have established a strong cybersecurity program intended to continue to monitor and improve our cybersecurity posture .

Risk Management Approach

We have documented cybersecurity policies and standards, and we assess risks from cybersecurity threats and monitor information systems for potential cybersecurity issues. These processes are managed and monitored by a dedicated cybersecurity team, including third-party service providers, and led by our Head of IT, and include mechanisms, controls, technologies, systems, and other processes designed to help prevent or mitigate data loss, theft, misuse, or other security incidents or vulnerabilities affecting the data and help maintain a stable information technology environment. For example, we use processes, tools and external services to conduct regular vulnerability testing, penetration testing, data recovery testing, security audits, and ongoing risk assessments, including due diligence on and audits of our key technology vendors, CROs, and other contractors and suppliers .

We work to maintain a strong cybersecurity posture through a multi-layered approach. Our endpoint detection and response (“EDR”) system helps monitor and analyze endpoint devices, and is designed to assist us in quickly identifying and responding to emerging threats. Complementing our EDR capabilities, our managed detection and response service assists with threat monitoring, proactive threat hunting, and rapid incident response. Furthermore, we employ data loss prevention tools to help enforce strict data security policies, prevent unauthorized access and protect the transmission of sensitive information. These integrated technologies help us to detect, mitigate, and respond to cyber threats, with the goal of minimizing potential disruptions to our business operations.

We have an incident response plan designed to help quickly detect, contain and remediate cybersecurity incidents. This plan outlines clear escalation procedures, roles and responsibilities to help us respond in a timely manner to potential threats. We also conduct regular employee training on matters such as phishing and email security best practices, among other topics. In addition, we consult with outside advisors and experts when appropriate to assist with assessing, identifying, and managing cybersecurity risks, including to help anticipate future threats and trends, and their impact on our risk environment.

Governance

Our current Head of IT reports directly to our Chief Financial Officer and has over twenty years of experience managing information technology and cybersecurity matters, holds a Master of Science degree in Telecommunications and Computer Networks and is Project Management Professional, Certified Scrum Master and IT Infrastructure Library certified. We have established a cybersecurity council, facilitated by the Head of IT, which includes senior leadership from various departments. The council meets quarterly to review cybersecurity strategies, assess emerging threats, and receive updates on regulatory and industry best practices .

Our Board as a whole has oversight for the most significant risks facing us and for our processes to help identify, prioritize, assess, manage, and mitigate those risks, including oversight of cybersecurity risks. Our Board receives at least two updates each year on cybersecurity and information technology matters and related risk exposures from our Head of IT as well as other members of our senior leadership team.

We consider cybersecurity, along with other significant risks that we face, within our overall enterprise risk management framework. Since the beginning of the last fiscal year, we have identified and mitigated certain known cybersecurity threats, which we determined are not reasonably likely to materially affect us and have strengthened our cybersecurity ecosystem. However, cybersecurity attack techniques change frequently, and with increased volume and sophistication of such attacks, there can be no guarantee that we will not be the subject of future successful attacks, threats or incidents that could materially affect us. Additional information on the cybersecurity risks we face is discussed in Part I, Item 1A, “Risk Factors - Significant disruptions of information technology systems or cybersecurity incidents could adversely affect our business.”

Item 2. Properties

We lease approximately 75,600 square feet of office and laboratory space in Newark, California under a lease agreement, as amended, that expires in November 2029. We believe that our existing facilities are adequate to meet our current business needs. We anticipate that additional space will be available on commercially reasonable terms, if required.

Item 3. Legal Proceedings

From time to time, we may become subject to litigation and claims arising in the ordinary course of business. We are not currently a party to any material legal proceedings, and we are not currently aware of any pending or threatened legal proceeding against us that we believe could have a material adverse effect on our business, operating results, financial condition or cash flows. Refer to Note 9 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for additional information on our historical legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Information

Our common stock trades on The Nasdaq Stock Market, LLC under the symbol "PTGX."

Stockholders

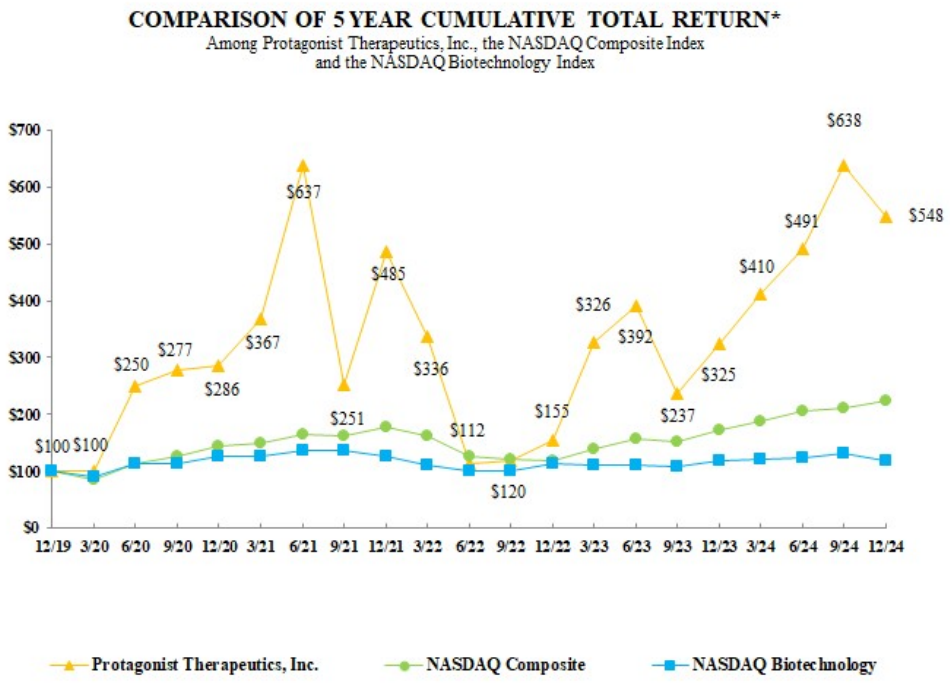
As of the close of business on February 19, 2025, there were two stockholders of record of our common stock. The number of stockholders of record is based upon the actual number of stockholders registered at such date and does not include holders of shares in "street names" or persons, partnerships, associates, or corporations, or other entities identified in security listings maintained by depositories.

Dividends

We have never declared or paid any cash dividends. We currently expect to retain all future earnings, if any, for use in the operation and expansion of our business, and therefore do not anticipate paying any cash dividends in the foreseeable future.

Performance Graph

The following is not deemed "filed" with the Securities and Exchange Commission and shall not be incorporated by reference into any filing we make under the Exchange Act or the Securities Act of 1933, as amended, whether made before or after the date hereof and irrespective of any general incorporation by reference language in such filing. The graph below shows the cumulative total stockholder return assuming an investment on December 31, 2019 in each of our common stock, the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The graph compares the performance of a $100 investment in our common stock and in each index (assuming reinvestment of all dividends) from December 31, 2019 to December 31, 2024.



**The comparisons in the graph are based on historical data and are not indicative of, or intended to forecast, future performance of our common stock.*

Recent Sales of Unregistered 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

OVERVIEW

We are a discovery through late-stage development biopharmaceutical company focused on peptide therapeutics. Our clinical programs fall into two broad categories of diseases: (i) hematology and blood disorders, and (ii) inflammatory and immunomodulatory ("I&I") diseases. Two novel peptides derived from our proprietary discovery technology platform, rusfertide and icotrokinra (formerly known as JNJ-2113), are currently in advanced Phase 3 clinical development, with New Drug Application ("NDA") submissions to the U.S. Food and Drug Administration ("FDA") potentially in 2025.

Rusfertide, an injectable mimetic of the natural hormone hepcidin, is currently in Phase 3 development for treatment of the rare blood disorder polycythemia vera ("PV"). Rusfertide is being co-developed and will be co-commercialized with Takeda Pharmaceuticals, Inc. ("Takeda") and the Company remains primarily responsible for development through NDA filing. Icotrokinra is a first-in-class investigational targeted oral peptide that selectively blocks the Interleukin-23 receptor ("IL-23R") and is licensed to J&J Innovative Medicines ("JNJ"), formerly Janssen Biotech, Inc. Following icotrokinra's joint discovery by us and JNJ scientists pursuant to our IL-23R collaboration, we were primarily responsible for the development of icotrokinra through Phase 1, with JNJ assuming responsibility for development in Phase 2 and beyond.

We also have a number of pre-clinical stage oral drug discovery programs to address clinically and commercially validated targets, including IL-17 oral peptide antagonist PN-881, an oral metabolic/obesity peptide program, and an oral hepcidin mimetic/ferroportin blocker program.

Rusfertide

Rusfertide is currently in Phase 3 development for the treatment of PV. VERIFY (ClinicalTrials.gov identifier NCT05210790) is a global double-blind, placebo-controlled Phase 3 clinical trial of rusfertide in PV for approximately 250 patients. The trial evaluates the efficacy, symptom burden and safety of once-weekly, subcutaneously self-administered rusfertide in patients with uncontrolled hematocrit who are phlebotomy dependent despite standard of care treatment. The trial enrolled patients across North and South America, Europe, Asia and Australia. We expect to announce top-line data for the trial's 32-week primary efficacy endpoint in March 2025, potentially leading to an NDA filing in the fourth quarter of 2025.

Our rusfertide Phase 2 clinical trials include the following:

- REVIVE (NCT04057040) – A Phase 2 proof of concept ("POC") trial, was initiated in the fourth quarter of 2019. We completed enrollment of patients in the first quarter of 2022 and 70 patients were enrolled through the end of the randomized withdrawal portion of the trial, which was completed during the first quarter of 2023 and is continuing in an ongoing open-label extension ("OLE");
- THRIVE (NCT06033586) – A Phase 2 long-term OLE for REVIVE patients on years three through five of treatment; and
- PACIFIC (NCT04767802) – Another Phase 2 trial for rusfertide for patients diagnosed with PV and with routinely elevated hematocrit levels (>48%), was initiated during the first quarter of 2021, and the 52-week trial was completed during the second quarter of 2023.

Final results from the REVIVE trial presented at the American Society of Hematology ("ASH") 2024 Annual Meeting in December 2024 showed that 54% of patients with PV experienced more than 2.5 years of durable hematocrit control (<45%), decreased phlebotomy use, long-term tolerability and improvements in patient-reported outcomes.

In January 2024, we entered into a worldwide license and collaboration agreement for rusfertide with Takeda (the "Takeda Collaboration Agreement"). We are primarily responsible for the development of rusfertide through a potential NDA filing. Under the terms of the agreement, we received a one-time, non-refundable upfront payment of $300.0 million in April 2024, and we are eligible to receive additional worldwide development, regulatory and commercial milestone payments for rusfertide of up to $330.0 million, inclusive of the following potential upcoming milestones:

- $25.0 million upon successful achievement of the primary endpoint in the Phase 3 VERIFY trial for rusfertide in PV; and
- $50.0 million upon FDA approval of an NDA for rusfertide in PV (or $75.0 million if we exercise our full right to opt-out of the 50:50 U.S. profit and loss sharing arrangement).

We are also eligible to receive tiered royalties from 10% to 17% on ex-U.S. net sales of rusfertide and other specified second-generation injectable hepcidin memetic compounds (the "Licensed Products"). We and Takeda will also share equally in profits and losses (50% to us and 50% to Takeda) of the Licensed Products in the United States, if approved. See Note 3 to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K for further details related to the agreement, including our right to opt-out of the 50:50 U.S. profit and loss sharing arrangement.

Icotrokinra

Our IL-23R antagonist compound icotrokinra, licensed to J&J, is an orally delivered drug that is designed to block biological pathways currently targeted by marketed injectable antibody drugs. Our orally stable peptide approach may offer a targeted therapeutic approach for gastrointestinal and systemic compartments as needed. We believe that, compared to antibody drugs, icotrokinra has the potential to provide clinical improvement in an oral medication with increased convenience and compliance and the opportunity for the earlier introduction of targeted oral therapy.

JNJ has initiated the following icotrokinra trials:

- ICONIC-LEAD (NCT06095115) – A 684-patient randomized, controlled Phase 3 trial to evaluate the safety and efficacy of icotrokinra compared with placebo in participants with moderate-to-severe plaque psoriasis, with PASI-90 (90% improvement in skin lesions as measured by the Psoriasis Area and Severity Index ("PASI") and Investigator's Global Assessment ("IGA") scores of 0 (clear) or 1 (almost clear) as co-primary endpoints;
- ICONIC-TOTAL (NCT06095102) – A 311-patient randomized, controlled Phase 3 trial to evaluate the efficacy and safety of icotrokinra compared with placebo for the treatment of plaque psoriasis in participants with at least moderate severity affecting special areas (scalp, genital, and/or palms of the hands and soles of the feet) with overall IGA scores of 0 or 1 as the primary endpoint;
- ICONIC-ADVANCE 1 (NCT06143878) – A 774-patient randomized, controlled Phase 3 trial to evaluate the effectiveness of icotrokinra in participants with moderate-to-severe plaque psoriasis compared to placebo and Sotyktu® ("deucravacitinib"). The trial's primary co-endpoints are PASI-90 and IGA scores of 0 or 1;
- ICONIC-ADVANCE 2 (NCT06220604) – A 731-patient Phase 3 trial similarly designed to ICONIC ADVANCE 1 in participants with moderate-to-severe plaque psoriasis;
- Pustular/Erythrodermic Psoriasis (NCT06295692) – A 19-patient open label Phase 3 trial to evaluate the effectiveness of icotrokinra in participants with pustular or erythrodermic psoriasis;
- ICONIC-PsA 2 (NCT06807424) – A 750-patient randomized, controlled Phase 3 trial to evaluate the efficacy and safety of icotrokinra compared with placebo in biologic-experienced patients with active psoriatic arthritis ("PsA"); and
- ANTHEM-UC (NCT06049017) – A 252-patient randomized, controlled Phase 2b trial to evaluate the safety and effectiveness of icotrokinra compared with placebo in participants with moderate-to-severely active ulcerative colitis ("UC").

In the fourth quarter of 2024, we announced positive topline results for the ICONIC-LEAD and ICONIC-TOTAL Phase 3 trials. In the ICONIC-LEAD trial, once daily icotrokinra showed significant skin clearance versus placebo in adults and adolescents with moderate to-severe plaque psoriasis. At week 16, nearly two-thirds (64.7%) of patients treated with icotrokinra achieved IGA scores of 0 or 1 and 49.6% achieved PASI-90, compared to 8.3% and 4.4% on placebo, respectively. In addition, topline results from the Phase 3 ICONIC-TOTAL trial showed that once daily icotrokinra met the primary endpoint of IGA scores of 0 or 1 at week 16 as compared to placebo. Comprehensive results from both ICONIC-LEAD and ICONIC-TOTAL are expected to be presented at upcoming medical congresses and shared with health authorities in planned submissions.

Topline results for the ANTHEM trial for icotrokinra in UC are expected in the first quarter of 2025. Topline results for the ICONIC-ADVANCE 1, ICONIC-ADVANCE 2, and pustular/erythrodermic psoriasis trials are expected in the second quarter of 2025.

On July 27, 2021, we entered into an Amended and Restated License and Collaboration Agreement with JNJ, which amended and restated the License and Collaboration Agreement, effective July 13, 2017, by and between the Company and JNJ, as amended by the first amendment, effective May 7, 2019 (together, the “JNJ License and Collaboration Agreement”) for the development and commercialization of icotrokinra. During the fourth quarter of 2023, we earned a $50.0 million milestone payment in connection with the dosing of the third patient in the ICONIC-TOTAL Phase 3 clinical trial of icotrokinra in patients with moderate-to-severe psoriasis and a $10.0 million milestone payment upon the dosing of the third patient in the ANTHEM Phase 2b trial in patients with moderately-to-severely active UC. The JNJ License and Collaboration Agreement was further amended in November 2024 to:

- increase the milestone payment for a Phase 3 clinical trial of any licensed product for any indication meeting its primary endpoint by $50.0 million, from $115.0 million to $165.0 million;
- eliminate the $35.0 million milestone payment previously due for the acceptance of an NDA filing by the FDA for a licensed product for any indication; and
- eliminate the $15.0 million milestone payment previously due for the dosing of the third patient in the first Phase 3 clinical trial of a licensed product for a second indication.

We earned the $165.0 million milestone payment described above during the fourth quarter of 2024. We have earned a total of $337.5 million in nonrefundable payments from JNJ from 2017 through December 31, 2024. We are eligible to receive up to $630.0 million in future development and sales milestone payments, inclusive of the following potential upcoming milestones:

- $50.0 million milestone upon approval of an NDA for icotrokinra in any indication;
- $25.0 million milestone upon the acceptance of an NDA filing by the FDA for icotrokinra in a second indication; and
- $45.0 million milestone upon the approval of an NDA for icotrokinra in a second indication.

We also remain eligible to receive upward tiering royalties on net product sales at percentages ranging from 6% percent to 10% percent, with 10% percent applicable for net sales over $4.0 billion. See Note 3 to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information.

PN-881

In the fourth quarter of 2024, we announced the selection of PN-881, a potential best-in-class oral peptide IL-17 antagonist, as a development candidate for the treatment of immune-mediated skin diseases. PN-881 targets three IL-17 dimers (IL-17 AA, AF and FF), which may offer potential treatment options for hidradenitis suppurativa (“HS”), spondyloarthritis, plaque psoriasis and psoriatic arthritis (“PsA”). Investigational New Drug (“IND”), or foreign equivalent, enabling studies are ongoing, and we expect to initiate a PN-881 Phase 1 study in the fourth quarter of 2025.

Discovery Platform

Our clinical and pre-clinical assets are all derived from our proprietary discovery platform. Our platform enables us to engineer novel, structurally constrained peptides that are designed to retain key advantages of both orally delivered small molecules and injectable antibody drugs while overcoming many of their limitations as therapeutic agents. Importantly, constrained peptides can be designed to potentially alleviate the fundamental instability inherent in traditional peptides to allow different delivery forms, such as oral, subcutaneous, intravenous, and rectal. Our discovery pipeline has strategically focused on (i) hematology and blood disorders, (ii) I&I diseases and (iii) metabolic diseases, including obesity.

We have a pre-clinical stage program to identify an orally administered hepcidin mimetic/ferroportin blocker, which we believe to be complementary to the injectable rusfertide for offering the best treatment options for PV and other potential erythropoietic and iron imbalance disorders, and we expect to nominate a development candidate in the fourth quarter of 2025. We also have an oral peptide-based metabolic/obesity program and expect to nominate a development candidate in the second quarter of 2025.

Risks and Uncertainties

We describe the respective risks, uncertainties and assumptions that could affect our business, financial condition and/or results of operations in Part I, Item 1A. “Risk Factors” herein.

Operations

We have incurred cumulative net losses from inception through December 31, 2024 of $340.5 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant research and development expenses and other expenses related to our ongoing operations, product development, pre-clinical discovery programs and pre-commercialization activities. As a result, we may incur losses in the future as we continue the development of, and seek regulatory approval for, our product candidates.

Critical Accounting Polices and Estimates

Our management’s discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles (“GAAP”). The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent liabilities at the date of the consolidated financial statements, as well as the reported revenue generated, and the expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, and the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management’s judgments and estimates.

Use of Estimates

The preparation of the consolidated financial statements in conformity with GAAP requires management to make estimates, assumptions and judgments that affect the reported amounts of assets and liabilities and disclosure of contingent liabilities as of the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. On an ongoing basis, we evaluate our estimates, including those related to revenue recognition, accruals for research and development activities, stock-based compensation, income taxes, marketable securities and leases. Estimates related to revenue recognition include assumptions used to determine standalone selling price utilized to allocate the transaction price between distinct performance obligations, assumptions used to recognize revenue over time for certain performance obligations for which a cost-based input method is used as the measure of

progress and estimates of whether contingent consideration should be included in the transaction price at each reporting period. We base these estimates on historical and anticipated results, trends and various other assumptions that we believe are reasonable under the circumstances, including assumptions as to forecasted amounts and future events. Actual results may differ materially from these estimates.

There has been uncertainty and disruption in the global economy and financial markets due to a number of factors, including geopolitical instability, inflationary pressures, high interest rates, a recessionary environment, domestic and global monetary and fiscal policy, changes in trade policies, including tariffs or other trade restrictions or the threat of such actions, banking and other financial institution instability and other factors. We have taken into consideration any known impacts in our accounting estimates to date and are not aware of any additional specific events or circumstances that would require any additional updates to our estimates or judgments or a revision of the carrying value of our assets or liabilities as of the date of the filing of this Annual Report on Form 10-K. These estimates may change as new events occur, circumstances change, and additional information is obtained. Actual results could differ materially from these estimates under different assumptions or conditions.

Revenue Recognition

Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers* requires us to allocate the arrangement consideration on a relative standalone selling price basis for each performance obligation after determining the transaction price of the contract and identifying the performance obligations to which that amount should be allocated. The relative standalone selling price is defined as the price at which an entity would sell a promised good or service separately to a customer. If other observable transactions in which we have sold the same performance obligation separately are not available, we estimate the standalone selling price of each performance obligation. Key assumptions to determine the standalone selling price may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

Whenever we determine that goods or services promised in a contract should be accounted for as a combined performance obligation over time, we determine the period over which the performance obligations will be performed and revenue will be recognized. Revenue is recognized using the proportional performance method. Costs incurred or labor hours are typically used as the measure of performance. Management's judgment is required in determining the level of effort required under an arrangement and the period over which we expect to complete our performance obligations. If we determine that the performance obligation is satisfied over time, any upfront payment received is initially recorded as deferred revenue on our consolidated balance sheets.

Research and Development Costs

Research and development costs are expensed as incurred, unless there is an alternate future use in other research and development projects or otherwise. Research and development costs include salaries and benefits, stock-based compensation expense, laboratory supplies and facility-related overhead, outside contracted services, including clinical and pre-clinical trial costs, manufacturing and process development costs for both clinical and preclinical materials, research costs, development milestone payments under license and collaboration agreements, and other consulting services.

We accrue for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of pre-clinical studies and clinical trials, and contract manufacturing activities. We record the estimated costs of research and development activities based upon the estimated services provided but not yet invoiced and we include these costs in accrued expenses and other payables in our consolidated balance sheets and within research and development expense in our consolidated statements of operations. We accrue for these costs based on various factors such as estimates of the work completed and in accordance with agreements established with our third-party service providers. As actual costs become known, we adjust our accrued liabilities. We have not experienced any material differences between accrued liabilities and actual costs incurred. However, the status and timing of actual services performed, number of patients enrolled, the rate of patient enrollment and the number and location of sites activated may vary from our estimates and may result in adjustments to our research and development expenses in future

periods. Changes in these estimates that result in material changes to our accruals could materially affect the results of our operations.

Recent Accounting Pronouncements

Information regarding recent accounting pronouncements applicable to us is included in Note 2 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K.

Components of Our Results of Operations

License and Collaboration Revenue

Our license and collaboration revenue is derived from payments we receive under the Takeda Collaboration Agreement and the JNJ License and Collaboration Agreement. See Note 3 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for additional information.

Research and Development Expenses

Research and development expenses represent costs incurred to conduct research, such as the discovery and development of our product candidates. We recognize all research and development costs as they are incurred unless there is an alternative future use in other research and development projects or otherwise. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received, rather than when payment has been made. In instances where we enter into agreements with third parties to provide research and development services to us, costs are expensed as services are performed. Amounts due under such arrangements may be either fixed fee or fee for service and may include upfront payments, monthly payments, and payments upon the completion of milestones or the receipt of deliverables.

Research and development expenses consist primarily of the following:

- expenses incurred under agreements with clinical trial sites that conduct research and development activities on our behalf;
- employee-related expenses, which include salaries, benefits and stock-based compensation;
- laboratory vendor expenses related to the preparation and conduct of pre-clinical studies and clinical trials;
- costs related to production of clinical supplies and pre-clinical materials, including fees paid to contract manufacturers;
- license fees and milestone payments under license and collaboration agreements; and
- facilities and other allocated expenses, which include expenses for rent and maintenance of facilities, information technology, depreciation and amortization expense and administrative and other supplies.

We recognize the amounts related to our Australian research and development refundable tax offset that are not subject to refund provisions as a reduction in research and development expenses. The research and development tax offsets are recognized when there is reasonable assurance that the offset will be received, the relevant expenditure has been incurred and the amount of the consideration can be reliably measured. We evaluate our eligibility under the tax incentive program as of each balance sheet date and make accruals and related adjustments based on the most current and relevant data available. We may alternatively be eligible for a nonrefundable tax offset.

We allocate direct and indirect costs incurred to product candidates when they enter clinical development. For product candidates in clinical development, direct costs consist primarily of clinical, pre-clinical, and drug discovery costs, costs of supplying drug substance and drug product for use in clinical and pre-clinical studies, including clinical manufacturing costs, contract research organization fees, and other contracted services pertaining to specific clinical and pre-clinical studies. Indirect costs allocated to our product candidates on a program-specific basis include research and development employee salaries, benefits, and stock-based compensation, and indirect overhead and other administrative support costs. Program-specific costs are unallocated when the related expenses are incurred for our early-stage research and drug discovery projects as our internal resources, employees and infrastructure are not tied to any one research or drug discovery project and are typically deployed across multiple projects. As such, we do not provide financial information regarding the costs incurred for early stage pre-clinical and drug discovery programs on a program-specific basis prior to the clinical development stage.

We expect our research and development expenses to increase in the near term as compared to prior year periods as we continue to focus our resources toward (i) progressing our rusfertide program into late stage clinical trials and preparing for regulatory filings and commercialization, and (ii) advancing our pre-clinical and drug discovery research programs, including progressing our recently nominated product development candidate PN-881 through IND-enabling studies, or foreign equivalents. We do not intend to dedicate further internal resources to clinical development or contract manufacturing activities for our PN-943 clinical program. The process of conducting research, identifying potential product candidates, conducting pre-clinical studies and clinical trials necessary to obtain regulatory approval and commencing pre-commercialization activities is costly and time intensive. We may never succeed in achieving marketing approval for our product candidates regardless of our costs and efforts. The probability of success of our product candidates may be affected by numerous factors, including pre-clinical data, clinical data, competition, manufacturing capability, our cost of goods to be sold, our ability to receive, and the timing of, regulatory approvals, market conditions, and our ability to successfully commercialize our products if they are approved for marketing. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will be able to generate revenue from the commercialization and sale of any of our product candidates. Our research and development programs are subject to change from time to time as we evaluate our priorities and available resources.

General and Administrative Expenses

General and administrative expenses consist of personnel costs, allocated facilities costs and other expenses for outside professional services, including legal, human resources, audit and accounting services, IT and pre-commercialization expenses, including selling and marketing costs. Personnel costs consist of salaries, benefits and stock-based compensation. Allocated expenses consist of expenses for rent and maintenance of facilities, information technology, depreciation and amortization expense and other administrative supplies. We expect to continue to incur expenses to support our continued operations as a public company, including expenses related to compliance with the rules and regulations of the SEC and those of the national securities exchange on which our securities are traded, insurance expenses, investor relations expenses, audit fees, professional services and general overhead and administrative costs.

Interest Income

Interest income consists of interest earned on our cash, cash equivalents, and marketable securities, which is comprised of contractual interest, premium amortization and discount accretion.

Other Income (Expense), Net

Other income (expense), net consists primarily of amounts related to foreign exchange gains and losses and related items.

Results of Operations

Comparison of the Years Ended December 31, 2024 and 2023

	Year Ended December 31,		Dollar	%
	2024	2023	Change	Change
	(Dollars in thousands)			
Revenue:				
License and collaboration revenue	$ 434,433	$ 60,000	$ 374,433	*
Operating expenses:				
Research and development [1]	138,128	120,161	17,967	15
General and administrative [2]	43,462	33,491	9,971	30
Total operating expenses	181,590	153,652	27,938	18
Income (loss) from operations	252,843	(93,652)	346,495	*
Interest income	26,315	14,898	11,417	77
Other income (expense), net	250	(201)	451	*
Income (loss) before income tax expense	279,408	(78,955)	358,363	*
Income tax expense	4,220	—	4,220	*
Net income (loss)	$ 275,188	$ (78,955)	$ 354,143	*

*Percentage not meaningful.

[1] Includes $20.9 million and $17.1 million of non-cash stock-based compensation expense for the years ended December 31, 2024 and 2023, respectively.
[2] Includes $16.6 million and $12.2 million of non-cash stock-based compensation expense for the years ended December 31, 2024 and 2023, respectively.

License and Collaboration Revenue

License and collaboration revenue was comprised of the following for the years presented:

	Year Ended December 31,		Dollar	%
	2024	2023	Change	Change
	(Dollars in thousands)			
License and collaboration revenue:				
Takeda Collaboration Agreement revenue	$ 269,433	$ —	$ 269,433	*
JNJ License and Collaboration Agreement revenue	165,000	60,000	105,000	175
Total license and collaboration revenue	$ 434,433	$ 60,000	$ 374,433	*

*Percentage not meaningful.

License and collaboration revenue increased by $374.4 million from $60.0 million for the year ended December 31, 2023 to $434.4 million for the year ended December 31, 2024.

Takeda Collaboration Agreement revenue of $269.4 million for the year ended December 31, 2024 was comprised of (i) $254.1 million of the $300.0 million upfront cash payment allocated to the delivery of the rusfertide license to Takeda upon effectiveness of the agreement in March 2024, and (ii) $15.3 million allocated to development services provided by us during the period based on the cost input method. The remaining balance of $30.6 million was recorded as deferred revenue as of December 31, 2024, which will be recognized over time based on a measure of our efforts toward satisfying our performance obligation relative to the total expected efforts or inputs to satisfy the performance obligation (e.g. costs incurred compared to total budget).

JNJ License and Collaboration Agreement revenue represents the achievement of non-refundable milestone payments pursuant to the JNJ License and Collaboration Agreement, as amended in November 2024, of $165.0 million and $60.0 million for the years ended December 31, 2024 and 2023, respectively.

We do not have any commercialized products, and our revenue is derived from licensing and collaboration agreements. Revenue from licensing and collaboration agreements, by its very nature, is highly variable and dependent upon factors such as the timing of when regulatory and sales milestones are achieved, if at all, and the accounting for any upfront payments and performance obligations associated with any existing or new agreements.

As discussed above, our revenue for the year ended December 31, 2024 was significantly higher than in prior years due to the partial recognition of an upfront payment of $300.0 million upon execution of the Takeda Collaboration Agreement and the achievement of a $165.0 million milestone pursuant to the terms of the JNJ License and Collaboration Agreement, as amended in November 2024. Our revenue for the year ended December 31, 2025 is expected to be comprised of (i) the proportionate recognition of the $30.6 million recorded in deferred revenue as of December 31, 2024, and (ii) any milestones achieved during the year, which are expected to be substantially lower than in 2024. Accordingly, revenue in 2025 is expected to reduce significantly, which will also impact our net income.

Research and Development Expenses

	Year Ended December 31,		Dollar	%
	2024	2023	Change	Change
	(Dollars in thousands)			
Clinical and development expense — rusfertide	$ 97,862	$ 98,060	$ (198)	-
Clinical and development expense — PN-943	150	1,058	(908)	(86)
Clinical and development expense — other	176	99	77	78
Pre-clinical and drug discovery research expense	39,940	20,944	18,996	91
Total research and development expenses	$ 138,128	$ 120,161	$ 17,967	15

Research and development expenses increased $18.0 million, or 15%, from $120.2 million for the year ended December 31, 2023 to $138.1 million for the year ended December 31, 2024. The increase was primarily due to an increase of $19.0 million in pre-clinical and drug discovery research expense, including costs related to PN-881, our recently nominated IL-17 development candidate, partially offset by a decrease of $0.9 million in expenses for our PN-943 program as further development work was deprioritized in 2023.

We had 98 and 85 full-time equivalent research and development employees as of December 31, 2024 and 2023, respectively. Research and development personnel-related expenses for the year ended December 31, 2024 increased by $10.0 million as compared to the year ended December 31, 2023, including increases of $6.1 million in personnel-related expenses and $3.9 million in stock-based compensation expense.

General and Administrative Expenses

General and administrative expenses increased $10.0 million, or 30%, from $33.5 million for the year ended December 31, 2023 to $43.5 million for the year ended December 31, 2024. This increase was primarily due to a $4.6 million increase in advisory and legal fees related to the Takeda Collaboration agreement and a $4.4 million increase in stock-based compensation expense.

We had 28 and 27 full-time equivalent general and administrative employees as of December 31, 2024 and 2023, respectively.

Interest Income

Interest income increased $11.4 million, or 77%, from $14.9 million for the year ended December 31, 2023 to $26.3 million for the year ended December 31, 2024. This increase was primarily due to higher invested balances, including the $300.0 million one-time, nonrefundable upfront payment received under the Takeda Collaboration Agreement in April 2024.

Income Tax Expense

Income tax expense was $4.2 million and $0 for the year ended December 31, 2024 and 2023, respectively. Income tax expense for the year ended December 31, 2024 was a result of taxable income from the recognition of revenue in connection with the Takeda Collaboration Agreement and the JNJ License and Collaboration Agreement. The effective tax rate was 1.5% and 0.0% for the years ended December 31, 2024 and 2023, respectively.

Comparison of the Years Ended December 31, 2023 and 2022

See Part II, Item 7—Results of Operations—Comparison of the Years Ended December 31, 2023 and 2022 in our Annual Report on Form 10-K for the year ended December 31, 2023, filed on February 17, 2024, for a discussion of our results of operations for the year ended December 31, 2023 compared to the year ended December 31, 2022.

Liquidity and Capital Resources

Sources of Liquidity

Historically we have funded our operations primarily from net proceeds from the sale of shares of our common stock and receipt of payments under collaboration agreements.

Proceeds from Sales of Our Common Stock

In April 2023, we completed an underwritten public offering of 5,000,000 shares of our common stock at a public offering price of $20.00 per share and issued an additional 750,000 shares of common stock at a price of $20.00 per share following the underwriters' exercise of their option to purchase additional shares. Net proceeds, after deducting underwriting commissions and offering costs paid by us, were approximately $107.8 million.

In August 2022, we entered into an Open Market Sale Agreement℠, pursuant to which we may offer and sell up to $100.0 million shares of our common stock from time to time in "at-the-market" offerings (the "2022 ATM Facility"). During the year ended December 31, 2023, we sold 1,749,199 shares of our common stock under the 2022 ATM Facility for net proceeds of $24.3 million, after deducting issuance costs. There were no sales of our common stock under the 2022 ATM Facility during the years ended December 31, 2024 and 2022.

Pre-Funded Warrants

In August 2018, we entered into a Securities Purchase Agreement with certain accredited investors (each, an "Investor" and, collectively, the "Investors"), pursuant to which we sold an aggregate of 2,750,000 shares of our common stock at a price of $8.00 per share for aggregate net proceeds of $21.7 million, after deducting offering expenses payable by us. In a concurrent private placement, we issued the Investors warrants to purchase an aggregate of 2,750,000 shares of our common stock (each, a "Warrant" and, collectively, the "Warrants"). Each Warrant was exercisable from August 8, 2018 through August 8, 2023. Warrants to purchase 1,375,000 shares of our common stock had an exercise price of $10.00 per share and Warrants to purchase 1,375,000 shares of our common stock had an exercise price of $15.00 per share.

In August 2023, prior to the expiration of the Warrants, we entered into certain agreements with the Investors and their affiliates under which we agreed to allow the Warrants to be exercised in exchange for pre-funded warrants representing the same number of Warrant Shares underlying the Warrants with an exercise price of $0.001 per share (the "Pre-Funded Warrants"). Subsequent to the execution of the agreements and prior to the expiration of the Warrants, all outstanding Warrants were exercised for gross proceeds of $34.4 million in exchange for 44,748 shares of our common stock and Pre-Funded Warrants to purchase 2,705,252 shares of common stock (subject to adjustment in the event of any stock dividends and splits, reverse stock split, recapitalization, reorganization or similar transaction, as described in the Pre-Funded Warrants) with an exercise price of $0.001 per share. The Pre-Funded Warrants will expire upon the day they are exercised in full. The Pre-Funded Warrants are exercisable at any time prior to expiration except that the Pre-Funded Warrants cannot be exercised by the Investors if, after giving effect thereto, the Investors would beneficially

own more than 9.99% of our common stock, subject to certain exceptions. The common stock and Pre-Funded Warrants met the criteria for equity classification and the net proceeds from the transaction were recorded as a credit to additional paid-in capital. In accordance with Accounting Standards Topic 260, *Earnings Per Share*, outstanding Pre-Funded Warrants are included in the computation of basic net loss per share because the exercise price is negligible, and they are fully vested and exercisable after the original issuance date. During the year ended December 31, 2024, Pre-Funded Warrants to purchase 1,205,252 shares were net exercised, resulting in the issuance of 1,205,225 shares of common stock. As of December 31, 2024, Pre-Funded Warrants to purchase 1,500,000 shares of common stock remained outstanding.

Receipt of Payments Under Collaboration Agreements

In March 2024, we earned a $300.0 million one-time, nonrefundable upfront payment from Takeda upon the closing of the Takeda Collaboration Agreement, which we received in April 2024.

Pursuant to the Takeda Collaboration Agreement, we may be eligible to receive clinical development, regulatory and sales milestones, if and when achieved. Upcoming potential development milestones under the Takeda Collaboration Agreement include:

- $25.0 million upon successful achievement of the primary endpoint in the Phase 3 VERIFY trial for rusfertide in PV; and
- $50.0 million upon FDA approval of an NDA for rusfertide in PV (or $75.0 million if we exercise our full right to opt out of the 50:50 U.S. profit and loss sharing arrangement in exchange for enhanced economics).

Under the JNJ License and Collaboration Agreement, we earned a $50.0 million milestone payment upon the dosing of the third patient in the ICONIC-TOTAL Phase 3 trial in late October 2023, which we received in December 2023. We earned a $10.0 million milestone payment upon the dosing of the third patient in the ANTHEM Phase 2b trial in patients with UC in December 2023, which we received in January 2024. The JNJ License and Collaboration Agreement was further amended in November 2024 to:

- increase the milestone payment for a Phase 3 clinical trial of any licensed product for any indication meeting its primary endpoint by $50.0 million, from $115.0 million to $165.0 million;
- eliminate the $35.0 million milestone payment previously due for the acceptance of an NDA filing by the FDA for use of licensed product for any indication; and
- eliminate the $15.0 million milestone payment previously due for the dosing of the third patient in the first Phase 3 clinical trial of a licensed product for a second indication.

We earned the $165.0 million milestone payment described above during the fourth quarter of 2024. We earned a total of $337.5 million in nonrefundable payments from JNJ from 2017 through December 31, 2024. We have also received payments for services provided under the collaboration agreement and we may make in-kind payment reimbursements to JNJ for certain costs they have incurred pursuant to the cost sharing terms of the agreement.

Pursuant to the JNJ License and Collaboration Agreement, we may be eligible to receive clinical development, regulatory and sales milestones, if and when achieved. Upcoming potential development milestones under the JNJ License and Collaboration Agreement include:

- $50.0 million milestone upon approval of an NDA for icotrokinra in any indication;
- $25.0 million milestone upon the acceptance of an NDA filing by the FDA for icotrokinra in a second indication; and
- $45.0 million milestone upon the approval of an NDA for icotrokinra in a second indication.

Capital Requirements

As of December 31, 2024, we had $559.2 million of cash, cash equivalents and marketable securities and an accumulated deficit of $340.5 million. Our capital expenditures were $1.4 million, $0.6 million and $0.8 million for the years ended December 31, 2024, 2023 and 2022, respectively. Our primary uses of cash are to fund our operating expenses, including our research and development expenditures and general and administrative costs. We expect that our existing cash, cash equivalents and marketable securities will be sufficient to fund our operations for at least the next twelve months from the date of this Annual Report on Form 10-K based on current operating plans and financial forecasts.

We may require additional funding to advance our early discovery pipeline and to develop, acquire, or in-license other potential product candidates. Our future funding requirements will depend on many factors, including:

- the progress, timing, scope, results and costs of advancing our clinical trials for our product candidates, including the ability to enroll patients in a timely manner for our clinical trials;
- the costs of and our ability to obtain clinical supplies for our current product candidates and any other product candidates we may identify and develop;
- our ability to successfully commercialize our current product candidates with our collaboration partners and any other product candidates we may identify and develop;
- the success of our existing or future collaborations with third parties;
- the selling and marketing costs associated with rusfertide, which is being co-developed and co-commercialized with Takeda under the Takeda Collaboration Agreement, and any other product candidates we may identify and develop, including the costs and timing of expanding our sales and marketing capabilities;
- the achievement of development, regulatory and sales milestones resulting in payments to us from JNJ under the JNJ License and Collaboration Agreement, Takeda under the Takeda Collaboration Agreement or other such arrangements that we may enter into, and the timing of receipt of such payments, if any;
- the timing, receipt and amount of royalties from JNJ under the JNJ License and Collaboration Agreement or Takeda under the Takeda Collaboration Agreement upon regulatory approval or clearance, if any;
- the amount and timing of sales and other revenues from our current product candidates and any other product candidates we may identify and develop, including the sales price and the availability of adequate third-party reimbursement;
- the cash requirements of any future acquisitions or discoveries of product candidates;
- the time and costs necessary to respond to technological and market developments; and
- the extent to which we may acquire or in-license other product candidates and technologies.

Such additional funding may come from various sources, including raising additional capital, seeking access to debt, and seeking additional collaborative or other arrangements with partners, but such funding may not be available on terms acceptable to us, if at all. As discussed in Part I, Item 1A, “Risk Factors,” we are currently operating in a period of economic uncertainty and capital markets disruption, which has been significantly impacted by domestic and global monetary and fiscal policy, changes in trade policies, including tariffs or other restrictions or the threat of such actions, geopolitical instability, inflationary pressures, high interest rates and banking and other financial institution instability, among other factors. A future recession or market correction, including those due to significant geopolitical or macroeconomic events, could materially affect our business and our access to credit and financial markets.

Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. Further, our operating plans may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials, other research and development activities and pre-commercialization costs. If we do raise additional capital through public or private equity offerings or convertible debt securities, the ownership interest of our existing stockholders could be diluted, and the terms of these securities could include liquidation or other preferences that could adversely affect our stockholders' rights. If we raise additional capital through debt financing, we could be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to fully estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated product development programs. For additional information, see Part I, Item 1A, "Risk Factors — Risks Related to our Financial Position and Capital Requirements."

The following table summarizes our cash flows for the periods indicated:

	Year Ended December 31,		
	2024	2023	2022
Consolidated Statements of Cash Flows Data:	(Dollars in thousands)		
Cash provided by (used) in operating activities	$ 184,152	$ (70,236)	$ (108,137)
Cash (used in) provided by investing activities	$ (299,483)	$ (39,258)	$ 91,468
Cash provided by financing activities	$ 25,853	$ 170,477	$ 18,838
Stock-based compensation	$ 37,554	$ 29,293	$ 24,202
Deferred revenue	$ 30,567	$ —	$ —

Cash Provided by (Used in) Operating Activities

Cash provided by operating activities for the year ended December 31, 2024 was $184.2 million and consisted primarily of our net income of $275.2 million and certain non-cash items, including $37.6 million of stock-based compensation, partially offset by a net change of $122.6 million in net operating assets and liabilities. The change in net operating assets and liabilities was driven primarily by a change of $155.0 million in receivable from a collaboration partner related to a milestone payment under the JNJ License and Collaboration Agreement, partially offset by a change of $30.6 million in deferred revenue related to the Takeda Collaboration Agreement. The $254.4 million increase in cash provided by operating activities during the year ended December 31, 2024, as compared to the year ended December 31, 2023, was primarily due to the receipt of a $300.0 million one-time, non-refundable upfront payment related to the Takeda Collaboration Agreement.

Cash used in operating activities for the year ended December 31, 2023 was $70.2 million and consisted primarily of our net loss of $79.0 million and a net change of $19.5 million in net operating assets and liabilities, partially offset by certain non-cash items, including $29.2 million of stock-based compensation expense. The $37.9 million decrease in cash used in operating activities for the year ended December 31, 2023, as compared to the year ended December 31, 2022, was primarily due to a $48.4 million decrease in our net loss and a $5.1 million increase in stock-based compensation expense, partially offset by a $4.0 million decrease in accretion of discount on marketable securities and an $11.7 million net change in net operating assets and liabilities.

Cash (Used in) Provided by Investing Activities

Cash used in investing activities for the year ended December 31, 2024 was $299.5 million and consisted of purchases of securities of $621.7 million and purchases of property and equipment of $1.4 million, partially offset by proceeds from maturities of marketable securities of $323.6 million. The $260.2 million increase in cash used in investing activities for the year ended December 31, 2024, as compared to the year ended December 31, 2023, was primarily due to the investment made with a portion of the proceeds from the $300.0 million payment from the Takeda Collaboration Agreement. Purchases of property and equipment were primarily related to purchases of leasehold improvements and laboratory equipment.

Cash used in investing activities for the year ended December 31, 2023 was $39.3 million and consisted of purchases of marketable securities of $191.1 million and purchases of property and equipment of $0.6 million, partially offset by proceeds from maturities of marketable securities of $152.4 million. The $130.7 million decrease in cash provided by investing activities for the year ended December 31, 2023, as compared to the year ended December 31, 2022, was primarily related to a decrease in the net activity of purchases and maturities of marketable securities. Purchases of property and equipment were primarily related to purchases of laboratory and computer equipment.

Cash Provided by Financing Activities

Cash provided by financing activities for the year ended December 31, 2024 was $25.9 million and consisted of net cash proceeds of $26.5 million from the issuance of common stock upon exercises of stock options and purchases of stock under our employee stock purchase plan ("ESPP"), partially offset by $0.6 million in tax withholding payments related to the net settlement of restricted stock units. The $144.6 million decrease in cash provided by financing activities for year ended December 31, 2024, as compared to the year ended December 31, 2023, was primarily due to $107.8 million of proceeds received from a public offering of our common stock in April 2023, $24.3 million of proceeds from ATM sales of our common stock in 2023, and $34.3 million in proceeds from exercises of warrants in 2023 in exchange for Pre-Funded Warrants and common stock. These changes were partially offset by a $21.7 million increase in proceeds from the issuance of common stock upon exercise of options and purchases of common stock under our ESPP.

Cash provided by financing activities for the year ended December 31, 2023 was $170.5 million and consisted primarily of net cash proceeds of $107.8 million from the April 2023 public offering of our common stock, $24.3 million from sales of our common stock under the 2022 ATM Facility, $34.4 million from the exercise of the Warrants in exchange for issuance of Pre-Funded Warrants and common stock, and $4.8 million in proceeds from the issuance of common stock upon exercise of stock options and purchases of common stock under our ESPP. The $151.6 million increase in cash provided by financing activities for the year ended December 31, 2023, as compared to the year ended December 31, 2022, was primarily due to a $107.8 million increase in net cash proceeds from the April 2023 public offering, a $9.7 million increase in cash proceeds from ATM sales and a $34.4 million increase in net cash proceeds from the exercise of the Warrants.

Contractual Obligations and Other Commitments

In the normal course of business, we enter into agreements with contract service providers to assist in the performance of our research and development activities and clinical and commercial manufacturing activities. Subject to the required notice periods and our obligations under certain binding commitments, we can elect to discontinue the work under these agreements at any time. However, the financial terms of some of these agreements may include non-refundable upfront payments, payments by us for options to acquire certain rights, contingent obligations by us for potential development and regulatory milestone payments and/or sales-based milestone payments and royalty payments. These obligations are recorded in our consolidated statements of operations as incurred, which is generally when the corresponding events become probable. Certain payments are contingent upon the occurrence of various future events that have a high degree of uncertainty. We expect to enter into additional clinical development, contract research, clinical and commercial manufacturing, supplier and collaborative research agreements in the future, which may require upfront payments and long-term commitments of capital resources.

Our contractual obligations include minimum lease payments under our operating lease obligations. In May 2024, we entered into a third amendment to our facility lease agreement dated as of March 2017 to extend the lease term for our existing office and laboratory space from one to 66 months and to lease approximately 17,700 rentable square feet of additional office space. See Note 8 to the Consolidated Financial Statements elsewhere in this Annual Report on Form 10-K for additional information.

Under the Takeda Collaboration Agreement, we may share with Takeda certain development, manufacturing and commercialization costs. The actual amounts that we may pay Takeda or that Takeda may pay us will depend on a number of factors, some of which are outside of our control and some of which are contingent upon the success, if

achieved, of certain development and regulatory activities. See Note 3 to the Consolidated Financial Statements elsewhere in this Annual Report on Form 10-K for additional information.

In January 2020, we initiated arbitration proceedings with the International Court of Arbitration of the International Chamber of Commerce against Zealand Pharma A/S ("Zealand") related to a collaboration agreement we and Zealand entered into in 2012 and terminated in 2014. The agreement provides for certain post-termination payment obligations to Zealand with respect to compounds related to the collaboration that we elect to further develop and that meet specified conditions. In August 2021, we and Zealand agreed to resolve the dispute and reached an Arbitration Resolution Agreement. Under the Arbitration Resolution Agreement, we recognized $4.0 million in development milestone payments to Zealand in the third quarter of 2021 and are obligated to pay Zealand certain milestone and royalty payments for rusfertide. The potential future payments include (i) up to $2.75 million in future development milestone payments, (ii) a low single digit royalty on worldwide net sales, and (iii) sales milestones for achievement of annual net sales amounts in specific geographies. See Note 7 and Note 9 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for additional information.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities related to our interest-earning investments and inflation risk affecting labor costs and clinical trial costs.

Interest Rate Fluctuation Risk

We had $559.2 million and $341.6 million in cash, cash equivalents and marketable securities at December 31, 2024 and 2023, respectively. Our cash and cash equivalents consist of cash, money market funds, commercial paper and government bonds. Marketable securities consist of certificates of deposit, corporate bonds, commercial paper and government bonds. A portion of our investments may be subject to interest rate risk and could decline in value if market interest rates increase. Based on our interest rate sensitivity analysis, an immediate 100 basis point increase in interest rates would increase our annual interest income by approximately $2.8 million, while an immediate 100 basis point decrease in interest rates would decrease our annual interest income by approximately $2.8 million.

Approximately $0.6 million and $0.9 million of our cash balance was located in Australia at December 31, 2024 and 2023, respectively. Our expenses, except those related to our Australian operations, are generally denominated in U.S. dollars. For our operations in Australia, the majority of our expenses are denominated in Australian dollars. To date, we have not had a formal hedging program with respect to foreign currency, but we may do so in the future if our exposure to foreign currency becomes more significant. A 10% increase or decrease in current exchange rates would not have a material effect on the results of our operations.

Inflation Fluctuation Risk

Inflation generally affects us by increasing our costs, such as the cost of labor and research and development contract costs. We do not believe inflation has had a material adverse effect on the results of our operations during the year ended December 31, 2024.

Item 8. Financial Statements and Supplementary Data

PROTAGONIST THERAPEUTICS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Protagonist Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Protagonist Therapeutics, Inc. (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations, comprehensive income (loss), stockholders' equity and cash flows for each of the three years in the period ended December 31, 2024, 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, 2024 and 2023, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 21, 2025 expressed an unqualified opinion thereon.

Basis for Opinion

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

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

Critical Audit Matter

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

Takeda Collaboration Agreement

Description of the Matter

As described in Note 3, the Company entered into a Collaboration and License Agreement with Takeda Pharmaceuticals USA, Inc. (Takeda), pursuant to which the Company and Takeda will collaborate on the development and commercialization of rusfertide (Takeda Agreement). As further described in Note 3, the transaction price was allocated at the inception of the agreement to all identified performance obligations based on the relative standalone selling price.

Auditing the Company's revenue recognition for the Takeda Agreement was complex and required the evaluation of significant judgments made by management, including the determination of the standalone selling price of the license obligation. The estimated standalone selling price for the performance obligation related to the license of intellectual property reflects management's assumptions, which includes forecasted revenues, development timelines, discount rates and probabilities of technical and regulatory success. Changes to these assumptions can have a material effect on the allocation of the transaction price to the performance obligations as well as the amount and timing of revenue recognized.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls addressing the risks of material misstatement related to the accounting for the Takeda Agreement. For example, we tested management's controls over the identification of performance obligations, the determination of the significant assumptions described above with respect to the estimation of the standalone selling price of the performance obligations related to the licensed compounds, and the accuracy and completeness of underlying data used in estimating the standalone selling price and the transaction price.

Our audit procedures included, among others, obtaining and reading the Takeda Agreement and evaluating the completeness of the performance obligations identified by management. We also evaluated management's estimates of the standalone selling price for identified performance obligations. For example, we evaluated the reasonableness and consistency of significant assumptions used in the determination of standalone selling price. We also performed a sensitivity analysis to evaluate the impact that changes in the significant assumptions would have on the estimated standalone selling price of performance obligations and the resulting impact on the allocation of transaction price to each performance obligation, as well as revenue recognized during the period. We involved our valuation professionals to assist in the assessment of certain assumptions used in the determination of the estimated standalone selling price of the license performance obligation.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2020.
San Mateo, California
February 21, 2025

PROTAGONIST THERAPEUTICS, INC.
Consolidated Balance Sheets
(In thousands, except share data)

	December 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 97,249	$ 186,727
Marketable securities	321,664	154,890
Receivable from collaboration partner	165,000	10,000
Prepaid expenses and other current assets	7,728	3,960
Total current assets	591,641	355,577
Marketable securities - noncurrent	140,252	—
Property and equipment, net	3,190	1,195
Restricted cash - noncurrent	225	225
Operating lease right-of-use asset	9,417	954
Total assets	$ 744,725	$ 357,951
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,615	$ 772
Payable to collaboration partner	—	3
Accrued expenses and other payables	23,693	19,358
Deferred revenue	18,891	—
Income taxes payable	2,689	—
Operating lease liability	510	1,141
Total current liabilities	47,398	21,274
Deferred revenue - noncurrent	11,676	—
Operating lease liability - noncurrent	10,356	—
Total liabilities	69,430	21,274
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock, $ 0.00001 par value, 10,000,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $ 0.00001 par value, 180,000,000 and 90,000,000 shares authorized as of December 31, 2024 and 2023, respectively; 61,035,139 and 57,708,613 shares issued and outstanding as of December 31, 2024 and 2023, respectively	1	1
Additional paid-in capital	1,015,898	952,491
Accumulated other comprehensive loss	(82)	(105)
Accumulated deficit	(340,522)	(615,710)
Total stockholders' equity	675,295	336,677
Total liabilities and stockholders' equity	$ 744,725	$ 357,951

The accompanying notes are an integral part of these consolidated financial statements.

PROTAGONIST THERAPEUTICS, INC.
Consolidated Statements of Operations
(In thousands, except share and per share data)

	Year Ended December 31,		
	2024	2023	2022
License and collaboration revenue	$ 434,433	$ 60,000	$ 26,581
Operating expenses:			
Research and development	138,128	120,161	126,215
General and administrative	43,462	33,491	31,739
Total operating expenses	181,590	153,652	157,954
Income (loss) from operations	252,843	(93,652)	(131,373)
Interest income	26,315	14,898	4,060
Other income (expense), net	250	(201)	(80)
Income (loss) before income tax expense	279,408	(78,955)	(127,393)
Income tax expense	4,220	—	—
Net income (loss)	$ 275,188	$ (78,955)	$ (127,393)
Net income (loss) per share, basic	$ 4.47	$ (1.39)	$ (2.60)
Net income (loss) per share, diluted	$ 4.23	$ (1.39)	$ (2.60)
Weighted-average shares used to compute net income (loss) per share, basic	61,566,989	56,763,559	49,042,232
Weighted-average shares used to compute net income (loss) per share, diluted	65,077,722	56,763,559	49,042,232

The accompanying notes are an integral part of these consolidated financial statements.

PROTAGONIST THERAPEUTICS, INC.
Consolidated Statements of Comprehensive Income (Loss)
(In thousands)

	Year Ended December 31,		
	2024	2023	2022
Net income (loss)	$ 275,188	$ (78,955)	$ (127,393)
Other comprehensive income (loss):			
Unrealized gain on marketable securities	23	60	89
Gain (loss) on translation of foreign operations	—	194	(149)
Comprehensive income (loss)	$ 275,211	$ (78,701)	$ (127,453)

The accompanying notes are an integral part of these consolidated financial statements.

PROTAGONIST THERAPEUTICS, INC.
Consolidated Statements of Stockholders' Equity
(In thousands, except share data)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive (Loss) Gain	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2021	47,838,330	$ —	$ 709,682	$ (299)	$ (409,362)	$ 300,021
Issuance of common stock pursuant to at-the-market offering, net of issuance costs	422,367	—	14,553	—	—	14,553
Issuance of common stock under equity incentive and employee stock purchase plans	686,284	—	4,448	—	—	4,448
Issuance of common stock upon exercise of Exchange Warrants	399,997	—	—	—	—	—
Shares withheld for net settlement of tax withholding upon vesting of restricted stock units	(7,726)	—	(188)	—	—	(188)
Stock-based compensation expense	—	—	24,202	—	—	24,202
Issuance costs related to prior period common stock offering	—	—	25	—	—	25
Other comprehensive income (loss)	—	—	—	(60)	—	(60)
Net income (loss)	—	—	—	—	(127,393)	(127,393)
Balance at December 31, 2022	49,339,252	—	752,722	(359)	(536,755)	215,608
Issuance of common stock pursuant to public offerings, net of issuance costs	5,750,000	—	107,798	—	—	107,798
Issuance of common stock pursuant to at-the-market offering, net of issuance costs	1,749,199	1	24,301	—	—	24,302
Exercise of Warrants in exchange for issuance of Pre-Funded Warrants	—	—	33,813	—	—	33,813
Issuance of common stock upon exercise of Warrants	44,748	—	559	—	—	559
Issuance of common stock under equity incentive and employee stock purchase plans	857,377	—	4,774	—	—	4,774
Shares withheld for net settlement of tax withholding upon vesting of restricted stock units	(31,963)	—	(769)	—	—	(769)
Stock-based compensation expense	—	—	29,293	—	—	29,293
Other comprehensive income (loss)	—	—	—	254	—	254
Net income (loss)	—	—	—	—	(78,955)	(78,955)
Balance at December 31, 2023	57,708,613	1	952,491	(105)	(615,710)	336,677
Issuance of common stock under equity incentive and employee stock purchase plans	2,142,094	—	26,453	—	—	26,453
Issuance of common stock upon exercise of Pre-Funded Warrants	1,205,225	—	—	—	—	—
Shares withheld for net settlement of tax withholding upon vesting of restricted stock units	(20,793)	—	(600)	—	—	(600)
Stock-based compensation expense	—	—	37,554	—	—	37,554
Other comprehensive income (loss)	—	—	—	23	—	23
Net income (loss)	—	—	—	—	275,188	275,188
Balance at December 31, 2024	61,035,139	$ 1	$ 1,015,898	$ (82)	$ (340,522)	$ 675,295

The accompanying notes are an integral part of these consolidated financial statements.

PROTAGONIST THERAPEUTICS, INC.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2024	2023	2022
Cash Flows from Operating Activities			
Net income (loss)	$ 275,188	$ (78,955)	$ (127,393)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Stock-based compensation	37,554	29,293	24,202
Operating lease right-of-use asset amortization	2,069	2,335	2,335
Depreciation	826	977	1,034
Accretion of discount on marketable securities	(8,875)	(4,569)	(549)
Other	—	194	—
Changes in operating assets and liabilities:			
Receivable from collaboration partner	(155,000)	(9,990)	1,556
Prepaid expenses and other assets	(3,768)	1,753	3,754
Research and development tax incentive receivable	—	—	2,686
Accounts payable	842	(2,868)	2,045
Payable to collaboration partner	(3)	(66)	(830)
Accrued expenses and other payables	4,289	(5,597)	(12,715)
Deferred revenue	30,567	—	(1,601)
Income taxes payable	2,689	—	—
Operating lease liability	(2,226)	(2,743)	(2,661)
Net cash provided by (used in) operating activities	184,152	(70,236)	(108,137)
Cash Flows from Investing Activities			
Purchase of marketable securities	(621,702)	(191,045)	(214,874)
Proceeds from maturities of marketable securities	323,574	152,396	307,137
Purchases of property and equipment	(1,355)	(609)	(795)
Net cash (used in) provided by investing activities	(299,483)	(39,258)	91,468
Cash Flows from Financing Activities			
Proceeds from issuance of common stock upon exercise of stock options and purchases under employee stock purchase plan	26,453	4,774	4,448
Tax withholding payments related to net settlement of restricted stock units	(600)	(769)	(188)
Proceeds from public offering of common stock, net of issuance costs	—	107,798	—
Proceeds from at-the-market offering, net of issuance costs	—	24,302	14,553
Proceeds from exercise of Warrants in exchange for issuance of Pre-Funded Warrants	—	33,813	—
Proceeds from issuance of common stock upon exercise of Warrants	—	559	—
Issuance costs related to prior period common stock offering	—	—	25
Net cash provided by financing activities	25,853	170,477	18,838
Effect of exchange rate changes on cash, cash equivalents and restricted cash	—	—	(90)
Net (decrease) increase in cash, cash equivalents and restricted cash	(89,478)	60,983	2,079
Cash, cash equivalents and restricted cash, beginning of period	186,952	125,969	123,890
Cash, cash equivalents and restricted cash, end of period	$ 97,474	$ 186,952	$ 125,969
Supplemental Disclosure of Cash Flow Information:			
Cash paid for taxes	$ 1,530	$ —	$ —
Supplemental Disclosure of Non-Cash Financing and Investing Information:			
Right-of-use asset obtained in exchange for lease obligation	$ 10,511	$ —	$ —
Leasehold improvements obtained under tenant improvement allowance	$ 1,421	$ —	$ —
Purchases of property and equipment in accounts payable and accrued liabilities	$ 46	$ 61	$ 19

The accompanying notes are an integral part of these consolidated financial statements.

PROTAGONIST THERAPEUTICS, INC.
Notes to Consolidated Financial Statements

Note 1. Organization and Description of Business

Protagonist Therapeutics, Inc. (the "Company") is a discovery through late-stage development biopharmaceutical company focused on peptide therapeutics. The Company's clinical programs fall into two broad categories of diseases: (i) hematology and blood disorders, and (ii) inflammatory and immunomodulatory ("I&I") diseases. Two novel peptides derived from the Company's proprietary discovery technology platform, rusfertide and icotrokinra (formerly known as JNJ-2113), are currently in advanced Phase 3 clinical development.

Rusfertide, an injectable mimetic of the natural hormone hepcidin partnered with Takeda Pharmaceuticals, Inc. ("Takeda"), is currently in Phase 3 development for treatment of the rare blood disorder polycythemia vera ("PV"). Icotrokinra is a first-in-class investigational targeted oral peptide that selectively blocks the Interleukin-23 receptor ("IL-23R"), which is licensed to J&J Innovative Medicines ("JNJ"), formerly Janssen Biotech, Inc. Icotrokinra is an orally delivered drug that is designed to block biological pathways currently targeted by marketed injectable antibody drugs. Following Icotrokinra's joint discovery by the Company and JNJ scientists pursuant to their IL-23R collaboration, the Company was primarily responsible for the development of icotrokinra through Phase 1, with JNJ assuming responsibility for development in Phase 2 and beyond.

The Company also has a number of pre-clinical stage oral drug discovery programs to address clinically and commercially validated targets, including IL-17 oral peptide antagonist PN-881, an oral metabolic/obesity peptide program, and an oral hepcidin mimetic/ferroportin blocker program.

The Company is headquartered in Newark, California and has one wholly owned subsidiary, Protagonist Pty Limited ("Protagonist Australia"), located in Brisbane, Queensland, Australia.

Liquidity

As of December 31, 2024, the Company had cash, cash equivalents and marketable securities of $ 559.2 million. The Company has incurred an accumulated deficit from inception through December 31, 2024 of $ 340.5 million. The Company's ultimate success depends upon the outcome of its research and development and collaboration activities. The Company may incur additional losses in the future as it continues the development of rusfertide through Phase 3 development and a potential NDA filing and invests in its pre-clinical discovery programs and may need to raise additional capital to continue to execute its long-range business plan. Since the Company's initial public offering in August 2016, it has financed its operations primarily through proceeds from offerings of common stock and payments received under license and collaboration agreements.

Note 2. Summary of Significant Accounting Policies

Basis of Presentation and Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiary, Protagonist Australia, and have been prepared in conformity with accounting principles generally accepted in the United States ("GAAP") and applicable rules and regulations of the Securities and Exchange Commission ("SEC"). All intercompany balances and transactions have been eliminated upon consolidation.

Use of Estimates

The preparation of the consolidated financial statements in conformity with GAAP requires management to make estimates, assumptions and judgments that affect the reported amounts of assets and liabilities and disclosure of contingent liabilities as of the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. On an ongoing basis, management evaluates its estimates, including those related to revenue recognition, accruals for research and development activities, stock-based compensation, income taxes,

marketable securities and leases. Estimates related to revenue recognition include assumptions used to determine standalone selling price utilized to allocate the transaction price between distinct performance obligations, assumptions used to recognize revenue over time for certain performance obligations for which a cost-based input method is used as the measure of progress and estimates of whether contingent consideration should be included in the transaction price at each reporting period. Management bases these estimates on historical and anticipated results, trends and various other assumptions that the Company believes are reasonable under the circumstances, including assumptions as to forecasted amounts and future events.

There has been uncertainty and disruption in the global economy and financial markets due to a number of factors, including geopolitical instability, inflationary pressures, high interest rates, a recessionary environment, domestic and global monetary and fiscal policy, changes in trade policies, including tariffs or other trade restrictions or the threat of such actions, banking and other financial institution instability and other factors. The Company has taken into consideration any known impacts in its accounting estimates to date and is not aware of any additional specific events or circumstances that would require any additional updates to its estimates or judgments or a revision of the carrying value of its assets or liabilities as of the filing date of this Annual Report on Form 10-K. These estimates may change as new events occur and additional information is obtained. Actual results could differ materially from these estimates under different assumptions or conditions.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents and marketable securities. Substantially all of the Company's cash is held by three financial institutions that management believes are of high credit quality. Such deposits generally exceed federally insured limits. The primary focus of the Company's investment strategy is to preserve capital and to meet liquidity requirements. The Company's cash equivalents and marketable securities are managed by external managers within the guidelines of the Company's investment policy. The Company's investment policy addresses the level of credit exposure by limiting concentration in any one corporate issuer and establishing a minimum allowable credit rating. To manage its credit risk exposure, the Company maintains its U.S. portfolio of cash equivalents and marketable securities in fixed income securities denominated and payable in U.S. dollars. Permissible investments of fixed income securities include obligations of the U.S. government and its agencies, money market instruments including commercial paper and negotiable certificates of deposit, and highly rated corporate debt obligations and money market funds.

Cash Equivalents

Cash equivalents that are readily convertible to cash are stated at cost, which approximates fair value. The Company considers all highly liquid investments purchased with an original maturity of three months or less to be cash equivalents.

Restricted Cash

Restricted cash consists of cash balances held as security in connection with a letter of credit related to the Company's facility lease entered into in March 2017, as subsequently amended. The Company's letter of credit balance was $ 0.2 million at December 31, 2024, 2023 and 2022 pursuant to the terms of the facility lease.

Cash as Reported in Consolidated Statements of Cash Flows

Cash as reported in the consolidated statements of cash flows includes the aggregate amounts of cash and cash equivalents and the restricted cash as presented on the consolidated balance sheets.

Cash as reported in the consolidated statements of cash flows consisted of (in thousands):

	December 31,		
	2024	2023	2022
Cash and cash equivalents	$ 97,249	$ 186,727	$ 125,744
Restricted cash - noncurrent	225	225	225
Total cash reported on consolidated statements of cash flows	$ 97,474	$ 186,952	$ 125,969

Marketable Securities

All marketable securities have been classified as “available-for-sale” and are carried at estimated fair value as determined based upon quoted market prices or pricing models for similar securities. Management determines the appropriate classification of its marketable securities at the time of purchase and reevaluates such designation as of each balance sheet date. Short-term marketable securities have maturities greater than three months but not longer than 365 days as of the balance sheet date. Long-term marketable securities have maturities of 365 days or longer as of the balance sheet date. Unrealized gains and losses are excluded from earnings and are reported as a component of comprehensive income (loss). Realized gains and losses, if any, on available-for-sale securities are included in interest income. The cost of securities sold is based on the specific-identification method. Interest on marketable securities is included in interest income.

Fair Value of Financial Instruments

Fair value accounting is applied to all financial assets and liabilities that are recognized or disclosed at fair value in the consolidated financial statements on a recurring basis (at least annually). The carrying amount of the Company’s financial instruments, including cash equivalents, receivables from its collaboration partner, accounts payable, payables to its collaboration partner and accrued expenses and other payables approximate fair value due to their short-term maturities. See Note 4 to the Consolidated Financial Statements for additional information regarding the fair value of the Company’s other financial assets and liabilities.

Investment Impairment

As of each reporting date, the Company assesses each of its investments in available-for-sale debt securities whose fair value is below its cost basis to determine if the investment’s impairment is due to credit-related factors or noncredit-related factors. Factors considered in determining whether an impairment is credit-related include the extent to which the investment’s fair value is less than its cost basis, declines in published credit ratings, issuer default on interest or principal payments, and declines in the financial condition and near-term prospects of the issuer. Credit-related impairments on available-for-sale debt securities are recognized as an allowance for credit losses with a corresponding adjustment to other income (expense), net. The portion of the impairment that is not credit-related is recorded as a reduction of other comprehensive income (loss), net of applicable taxes.

Pursuant to Accounting Standard Update 2016-13, *Financial Instruments - Credit Losses (Topic 326)* , the Company has elected to exclude accrued interest from both the fair value and the amortized cost basis of the available-for-sale debt securities for the purposes of identifying and measuring an impairment. The Company writes off accrued interest as a reduction of interest income when an issuer has defaulted on interest payments due on a security.

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, ranging from three to five years . Leasehold improvements are amortized over the shorter of the lease term or the estimated useful lives of the assets. Maintenance and repairs are charged to expense as incurred. When assets are retired or otherwise disposed of, the cost and accumulated depreciation are removed from the consolidated balance sheet and any resulting gain or loss is reflected in operations in the period realized.

Leases

The Company determines if an arrangement is a lease at inception. Pursuant to Accounting Standards Codification Topic 842, *Leases* ("ASC Topic 842"), operating leases are included in operating lease right-of-use ("ROU") asset, operating lease liability, and noncurrent operating lease liability on the consolidated balance sheets. Operating lease ROU asset and operating lease liability are recognized based on the net present value of the future minimum lease payments over the lease term at commencement date. If the Company's leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on information available at the commencement date in determining the present value of future payments. The operating lease ROU asset also includes any lease payments made and excludes lease incentives and initial direct costs incurred. Lease terms include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term.

The Company records tenant improvement allowances as a reduction to the ROU asset with the impact of the decrease recognized prospectively over the remaining lease term. The leasehold improvements are amortized over the shorter of their useful life or the remaining term of the lease.

Impairment of Long-Lived Assets

The Company reviews long-lived assets, primarily comprised of property, equipment and operating lease ROU assets, for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparison of the carrying amount to the future net cash flows which the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured as the amount by which the carrying amount of the assets exceeds the projected discounted future net cash flows arising from the asset. There have been no such impairments of long-lived assets for any of the periods presented.

Comprehensive Income (Loss)

Comprehensive income (loss) includes net income (loss) as well as other changes in stockholders' equity that result from transactions and economic events other than those from stockholders. The Company's foreign currency translation and unrealized gains and losses on available-for-sale securities represent the only components of other comprehensive income (loss) that are excluded from reported net income (loss) and that are presented in the consolidated statements of comprehensive income (loss).

Income Taxes

The Company uses the asset and liability method to account for income taxes in accordance with the authoritative guidance for income taxes. Under this method, deferred tax assets and liabilities are determined based on future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases, and tax loss and credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates applied to taxable income in the 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 the period that includes the enactment date. A valuation allowance is established when necessary to reduce deferred tax assets to the amount expected to be realized.

The Company recognizes the effect of income tax positions only if those positions are more likely than not of being sustained. Recognized income tax positions are measured at the largest amount that is greater than a 50% likelihood of being realized. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs. The Company records interest and penalties related to unrecognized tax benefits in income tax expense. To date, there have been no interest or penalties recorded in relation to unrecognized tax benefits.

Collaborative Arrangements

The Company analyzes its collaborative arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards and therefore are within the scope of Accounting Standards Codification Topic 808, *Collaborative Arrangements* ("ASC Topic 808"). For collaborative arrangements that contain multiple elements, the Company determines which units of account are deemed to be within the scope of ASC Topic 808 and which units of account are more reflective of a vendor-customer relationship and therefore are within the scope of Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers* ("ASC Topic 606"). For units of account that are accounted for pursuant to ASC Topic 808, an appropriate recognition method is determined and applied consistently, either by analogy to appropriate accounting literature or by applying a reasonable accounting policy election. For collaborative arrangements that are within the scope of ASC Topic 808, the Company evaluates the income statement classification for presentation of amounts due to or owed from other participants associated with multiple units of account in a collaborative arrangement based on the nature of each activity. Payments or reimbursements that are the result of a collaborative relationship instead of a customer relationship, such as co-development and co-commercialization activities, are recorded as increases or decreases to research and development expense or general and administrative expense, as appropriate.

Revenue Recognition

Under ASC Topic 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC Topic 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. The Company applies the five-step model to contracts when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, the Company assesses the goods or services promised within each contract, determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligations when (or as) the performance obligations are satisfied. The Company constrains its estimate of the transaction price up to the amount (the "variable consideration constraint") that a significant reversal of recognized revenue is not probable.

Licenses of intellectual property: If a license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in an arrangement, the Company recognizes revenue from non-refundable, upfront 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. For licenses that are bundled with 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 proportional performance for purposes of recognizing revenue from non-refundable, upfront fees. The Company evaluates the measure of proportional performance each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone payments: At the inception of each arrangement or amendment that includes development, regulatory or commercial milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price. ASC Topic 606 suggests two alternatives to use when estimating the amount of variable consideration: the expected value method and the most likely amount method. Under the expected value method, an entity considers the sum of probability-weighted amounts in a range of possible consideration amounts. Under the most likely amount method, an entity considers the single most likely amount in a range of possible consideration amounts. Whichever method used should be consistently applied throughout the life of the contract; however, it is not necessary for the Company to use the same approach for all contracts. The Company expects to use the most likely amount method for development and regulatory milestone payments. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered

probable of being achieved until those approvals are received. If there is more than one performance obligation, the transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis. The Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability or achievement of each such milestone and any related constraint, and if necessary, adjusts its estimates of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

Any potential milestone payments that the Company determines are not associated with performance obligations as defined under the contract are excluded from the transaction price and are recognized as the triggering event occurs.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, where 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).

Upfront payments and fees are recorded as deferred revenue upon receipt or when due and may require deferral of revenue recognition to a future period until the Company performs its obligations under these arrangements. Amounts payable to the Company are recorded as accounts receivable when the Company's right to consideration is unconditional. Amounts payable to the Company and not yet billed to the collaboration partner are recorded as contract assets. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less.

Contractual cost sharing payments made to a customer or collaboration partner are accounted for as a reduction to the transaction price if such payments are not related to distinct goods or services received from the customer or collaboration partner.

Contracts may be amended to account for changes in contract specifications and requirements. Contract modifications exist when the amendment either creates new, or changes existing, enforceable rights and obligations. When contract modifications create new performance obligations and the increase in consideration approximates the standalone selling price for goods and services related to such new performance obligations, as adjusted for specific facts and circumstances of the contract, the modification is considered to be a separate contract. If a contract modification is not accounted for as a separate contract, the Company accounts for the promised goods or services not yet transferred at the date of the contract modification (the remaining promised goods or services) prospectively, as if it were a termination of the existing contract and the creation of a new contract, if the remaining goods or services are distinct from the goods or services transferred on or before the date of the contract modification. The Company accounts for a contract modification as if it were a part of the existing contract if the remaining goods or services are not distinct and, therefore, form part of a single performance obligation that is partially satisfied at the date of the contract modification. In such case the effect that the contract modification has on the transaction price, and on the entity's measure of progress toward complete satisfaction of the performance obligation, is recognized as an adjustment to revenue (either as an increase in or a reduction of revenue) at the date of the contract modification (the adjustment to revenue is made on a cumulative catch-up basis).

Research and Development Costs

Research and development costs are expensed as incurred, unless there is an alternate future use in other research and development projects or otherwise. Research and development costs include salaries and benefits, stock-based compensation expense, laboratory supplies and facility-related overhead, outside contracted services, including clinical trial costs, manufacturing and process development costs for clinical and pre-clinical materials, research costs, development milestone payments under license and collaboration agreements, and other consulting services.

The Company accrues for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of pre-clinical and non-clinical studies, clinical trials and contract manufacturing activities. The Company records the estimated costs of research and development activities based upon the estimated

services provided but not yet invoiced and includes these costs in accrued expenses and other payables in the consolidated balance sheets and within research and development expense in the consolidated statements of operations. The Company accrues for these costs based on various factors such as estimates of the work completed and in accordance with agreements established with its third-party service providers. As actual costs become known, the Company adjusts its accrued liabilities. The Company has not experienced any material differences between accrued liabilities and actual costs incurred. However, the status and timing of actual services performed, the number of patients enrolled, the rate of patient enrollment and the number and location of sites activated may vary from the Company's estimate and may result in adjustments to research and development expenses in future periods. Changes in these estimates that result in material changes to the Company's accruals could materially affect the Company's results of operations.

Research and Development Tax Incentive

The Company is eligible under the AusIndustry research and development tax incentive program to obtain either a refundable tax offset or a nonrefundable tax offset from the Australian Taxation Office. The refundable cash offset is available to the Company on the basis of specific criteria with which the Company must comply. Specifically, the Company must have aggregated annual turnover of less than AUD 20.0 million and cannot be controlled by income tax exempt entities. The refundable tax offset is recognized as a reduction to research and development expense when the right to receive has been attained and funds are considered to be collectible. The Company may alternatively be eligible for a nonrefundable tax offset in years when the aggregated annual turnover exceeds AUD 20.0 million. The Company evaluates its eligibility under tax incentive programs as of each balance sheet date and makes accrual and related adjustments based on the most current and relevant data available. Unused nonrefundable tax offsets may be carried forward to future years, subject to satisfying specific criteria.

Stock-based Compensation

The Company has granted stock options, restricted stock units ("RSUs") and performance share units ("PSUs").

Stock-based compensation expense associated with stock options is based on the estimated grant date fair value using the Black-Scholes valuation model, which requires the use of subjective assumptions related to expected stock price volatility, option term, risk-free interest rate and dividend yield. The Company recognizes compensation expense over the vesting period of the awards that are ultimately expected to vest.

Stock-based compensation expense associated with RSUs is based on the fair value of the Company's common stock on the grant date, which equals the closing market price of the Company's common stock on the grant date. For RSUs, the Company recognizes compensation expense over the vesting period of the awards that are ultimately expected to vest. PSUs allow the recipients of such awards to earn fully vested shares of the Company's common stock upon the achievement of pre-established performance objectives. Stock-based compensation expense associated with PSUs is based on the fair value of the Company's common stock on the grant date, which equals the closing market price of the Company's common stock on the grant date and is recognized when the performance objective is expected to be achieved. The Company evaluates the probability of achieving the performance criteria on a quarterly basis. The cumulative effect on current and prior periods of a change in the estimated number of PSUs expected to be earned is recognized as compensation expense or as reduction of previously recognized compensation expense in the period of the revised estimate.

The Company recognizes forfeitures of stock-based awards as they occur.

If stock-based awards are granted in contemplation of or shortly before a planned release of material nonpublic information, and such information is expected to result in a material increase in the Company's share price, the Company considers whether an adjustment to the observable market price is required when estimating fair values.

Net Income (Loss) per Share

The computation of basic net income (loss) per share of common stock is based on the weighted-average number of shares of common stock outstanding during each period. The computation of diluted net income (loss) per share of

common stock is based on the weighted-average number of shares of common stock outstanding during the period plus, when their effect is dilutive, incremental shares consisting of shares subject to stock options, RSUs, PSUs, the Company's employee stock purchase plan ("ESPP"), and warrants. In accordance with Accounting Standards Codification Topic 260, *Earnings Per Share* ("ASC Topic 260"), outstanding Exchange and Pre-Funded Warrants (as defined in Note 10. Stockholders' Equity) are included in the computation of weighted-average shares of common stock, basic because the exercise price was negligible, and they were fully vested and exercisable after the original issuance date.

In periods when the Company has net income, the dilutive effect of all potentially outstanding shares is computed using the treasury stock method. In periods in which the Company reports a net loss, all common stock equivalents are deemed anti-dilutive such that basic net loss per share of common stock and diluted net loss per share of common stock are equal.

Recently Adopted Accounting Pronouncements

In August 2020, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update No. 2020-06, *Debt - Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging - Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity* ("ASU 2020-06"), which simplified accounting for convertible instruments by removing major separation models required under current GAAP. ASU 2020-06 also removed certain settlement conditions that were required for equity-linked contracts to qualify for the derivative scope exception, and it simplified the diluted earnings per share calculation in certain areas. ASU 2020-06 is effective for the Company beginning January 1, 2024. The adoption of this guidance did not have a material impact on the Company's consolidated financial statements or related disclosures.

In November 2023, the FASB issued Accounting Standards Update No. 2023-07 *Segment Reporting (Topic 280) – Improvements to Reportable Segment Disclosures* ("ASU 2023-07"), which requires public entities to disclose incremental segment information on an annual and interim basis. ASU 2023-07 requires all public entities, including public entities with a single reportable segment, to provide one or more measures of segment profit or loss used by the chief operating decision maker to allocate resources and assess performance. Additionally, the guidance requires disclosures of significant segment expenses and other segment items as well as incremental qualitative disclosures. ASU 2023-07 is effective for the Company for fiscal years beginning on January 1, 2024, and interim periods within fiscal years beginning on January 1, 2025. The Company currently operates as one reportable segment and the impact of the adoption of this standard was limited to certain enhanced disclosures in the consolidated financial statements. See Note 15 to these consolidated financial statements for disclosures related to the adoption of this guidance.

Recently Issued Accounting Pronouncements Not Yet Adopted as of December 31, 2024

In December 2023, the FASB issued Accounting Standards Update No. 2023-09 *Income Taxes (Topic 740) – Improvements to Income Tax Disclosures* ("ASU 2023-09"), which requires public business entities to disclose specific categories in the income tax rate reconciliation annually and provide additional information for reconciling items that meet a qualitative threshold. ASU 2023-09 also requires that entities disclose annually additional information about income taxes paid and disaggregated information for certain items. The standard can be applied prospectively or retrospectively. ASU 2023-09 is effective for the Company beginning on January 1, 2025. The Company will adopt this guidance in its 2025 Annual Report on Form 10-K but does not expect the adoption of this guidance to have a material impact on its financial position, results of operations or cashflows.

In November 2024, the FASB issued Accounting Standards Update No. 2024-03 *Income Statement – Reporting Comprehensive Income – Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses* ("ASU 2024-03"), which requires detailed disclosures about specified categories of expenses (including employee compensation, depreciation, and amortization) included in certain expense captions presented on the face of the income statement. ASU 2024-03 is effective for the Company or fiscal years beginning on January 1, 2027, and for interim periods within fiscal years beginning on January 1, 2028. Early adoption is permitted. The guidance may be applied either (1) prospectively to financial statements issued for reporting periods after the effective date of ASU 2024-03 or (2) retrospectively to all prior periods presented in the financial statements. The Company does not expect the adoption of this guidance to have a material effect on its consolidated financial statements and continues to evaluate disclosure presentation alternatives.

Note 3. License and Collaboration Agreements

Takeda Collaboration Agreement

In January 2024, the Company entered into the Takeda Collaboration Agreement, which became effective in March 2024.

Pursuant to the Takeda Collaboration Agreement, the Company and Takeda are jointly developing and commercializing rusfertide and potentially other specified second-generation injectable hepcidin mimetic compounds (the "Licensed Products") in the United States (the "Profit-Share Territory"). Takeda is solely and exclusively responsible for the development and commercialization of the Licensed Products in all other countries (the "Takeda Territory"). The Company and Takeda share the costs of the development, manufacture and commercialization activities for the Licensed Products in the Profit-Share Territory, provided that (i) the Company leads, and is solely responsible for its costs associated with, completion of the ongoing Phase 3 VERIFY program evaluating rusfertide for the treatment of PV as well as associated U.S. regulatory activities; (ii) Takeda leads, and is solely responsible for its costs associated with, pre-commercialization activities related to rusfertide in the Profit-Share Territory; and (iii) Takeda leads commercialization of rusfertide in the Profit-Share Territory, with the Company holding an option to co-detail. Takeda is solely responsible for all costs for the development, manufacture and commercialization of the Licensed Products in the Takeda Territory. The Company granted Takeda a non-transferable, sublicensable and, except for certain specified exceptions, exclusive license to certain intellectual property of the Company to exercise its rights and perform its obligations under the Takeda Collaboration Agreement.

The Company received a one-time, non-refundable upfront payment of $ 300.0 million in April 2024. In addition, the Company is eligible to receive additional worldwide development, regulatory and commercial milestone payments for rusfertide of up to $ 330.0 million, and tiered royalties from 10 % to 17 % on net sales of the Licensed Products in the Takeda Territory. The Company and Takeda also share equally in profits and losses (50 % to the Company and 50 % to Takeda) for Licensed Products in the Profit-Share Territory. Takeda will book sales of the Licensed Products globally.

The Company has the right to opt-out entirely of profit- and loss-sharing in the Profit-Share Territory for rusfertide and all other Licensed Products (the "Full Opt-out Right") (i) during the 90-day period beginning 120 days after the filing of an NDA with the FDA for rusfertide for PV (the "Initial Opt-out Period"); and (ii) for convenience without receipt of the Opt-out Payment (as defined below) (generally following the Initial Opt-out Period). In addition, if the Company does not exercise the Full Opt-out Right, the Company may opt-out of any Licensed Product other than rusfertide on a Licensed Product-by-Licensed Product basis (each, a "Partial Opt-out Right" and either the Full Opt-out Right or a Partial Opt-out right being an "Opt-out Right"). Following the Company's exercise of an Opt-out Right, the Company has agreed to transition applicable development and commercial activities to Takeda, and Takeda has agreed to assume sole operational and financial responsibility for such activities in the United States.

The Takeda Collaboration Agreement provides for aggregate development, regulatory and commercial milestone payments from Takeda to the Company for rusfertide of up to $ 975 million if the Company exercises the Full Opt-out Right. In addition to these milestone payments, in the event the Company exercises the Full Opt-out Right during the Initial Opt-out Period, the Company will receive: (i) a $ 200 million payment following its exercise of the Full Opt-out Right; and (ii) an additional $ 200 million payment following FDA approval of the NDA for rusfertide for PV (together, the "Opt-out Payment"). If the Company exercises an Opt-out Right, Takeda has agreed to pay the Company royalties of 14 % to 29 % on worldwide net sales of the Licensed Products with respect to which the Company has exercised an Opt-out Right.

Upcoming potential development and regulatory milestones under the Takeda Collaboration Agreement include:

- $ 25.0 million upon successful achievement of the primary endpoint in the Phase 3 VERIFY clinical trial for rusfertide in PV; and
- $ 50.0 million upon FDA approval of an NDA for rusfertide in PV (or $ 75.0 million if the Company exercises the Full Opt-out Right).

The Company evaluated the Takeda Collaboration Agreement and concluded that it has elements that are within the scope of ASC Topic 606 and ASC Topic 808. As of the effective date of the Takeda Collaboration Agreement, the Company identified two distinct performance obligations: (i) the rusfertide license delivered upon the effectiveness of the Takeda Collaboration Agreement and (ii) certain development services to be provided prior to the Initial Opt-out Period, including the Company's responsibilities to complete the VERIFY Phase 3 clinical trial in PV and to file an NDA with the FDA upon successful completion of the VERIFY trial and associated manufacturing services.

The Company determined that the initial transaction price totaled $ 300.0 million, comprised of the upfront payment. The Company has excluded any future estimated milestones or royalties from this transaction price to date, all of which are either currently constrained or subject to the sales-and usage-based royalty exception. As part of the Company's evaluation of this variable consideration constraint, it determined that the potential payments are contingent upon developmental and regulatory milestones that are uncertain and are highly susceptible to factors outside of its control. The Company allocated $ 254.1 million of the initial transaction price to the license and $ 45.9 million to the development services based upon the relative standalone selling price of each performance obligation. The estimate of standalone selling price for the license was determined based on discounted cash flows for the expected development and commercialization of rusfertide and includes assumptions for forecasted revenues, development timelines and expenses, discount rates, and probabilities of technical and regulatory success. The estimate of standalone selling price for the development services was determined based on forecasted costs and expenses over the expected development period. For the license of rusfertide, the Company determined that Takeda could benefit from the license at the time the license was granted and therefore, the related performance obligation was satisfied at a point in time.

The amount allocated to the license, which represents functional intellectual property that was transferred at a point in time, was satisfied upon transfer of the license to Takeda. The amount allocated to development services will be recognized over time based on a measure of the Company's efforts toward satisfying the performance obligation relative to the total expected efforts or inputs to satisfy the performance obligation (e.g., costs incurred compared to total budget). The Company recognized $ 15.3 million of revenue allocated to development services with respect to the period from the effective date of the contract through December 31, 2024.

The Company determined that the Takeda Collaboration Agreement met the definition of a collaborative arrangement under ASC Topic 808. Both parties are active participants in directing and carrying out the development of the Licensed Products and both are exposed to the significant risk and rewards related to the commercial success of the Products. If the Company does not exercise an Opt-out Right ("Company Opt-in"), the Company and Takeda would co-detail the Licensed Products in the U.S. and share in the economic results through a profit-sharing structure. The Company determined that development costs subsequent to the Company Opt-in date are within the scope of ASC Topic 808, which does not provide recognition and measurement guidance. As such, the Company determined that Accounting Standards Codification Topic 730, "*Research and Development"* was appropriate to analogize to based on the cost-sharing provisions of the agreement. The Company concluded that payments to or reimbursements from Takeda related to these services will be accounted for as an increase to or reduction of research and development expense, respectively.

JNJ License and Collaboration Agreement

On July 27, 2021, the Company entered into an Amended and Restated License and Collaboration Agreement with JNJ, formerly Janssen Biotech, Inc., which amended and restated the License and Collaboration Agreement, effective July 13, 2017, by and between the Company and JNJ, as amended effective May 7, 2019 and November 14, 2024 (together, the "JNJ License and Collaboration Agreement"). Prior to January 1, 2023, JNJ was a related party to us as Johnson & Johnson Innovation - JJDC, Inc. was a significant (greater than 5%) stockholder of the Company, and both companies are subsidiaries of Johnson & Johnson. The JNJ License and Collaboration Agreement relates to the development, manufacture and commercialization of oral IL-23 receptor antagonist drug candidates and enables JNJ to develop collaboration compounds for multiple indications. Under the JNJ License and Collaboration Agreement, JNJ is required to use commercially reasonable efforts to develop at least one collaboration compound for at least two indications.

During the fourth quarter of 2023, the Company earned a $ 50.0 million milestone payment in connection with the dosing of the third patient in the ICONIC-TOTAL Phase 3 clinical trial of icotrokinra (formerly JNJ-2113) in patients with moderate-to-severe psoriasis and a $ 10.0 million milestone payment upon the dosing of the third patient in the

ANTHEM Phase 2b trial moderately-to-severely active UC. The JNJ License and Collaboration Agreement was further amended in November 2024 to:

- increase the milestone payment for a Phase 3 clinical trial of any licensed product for any indication meeting its primary endpoint by $ 50.0 million, from $ 115.0 million to $ 165.0 million;
- eliminate the $ 35.0 million milestone payment previously due for the acceptance of an NDA filing by the FDA for use of a licensed product for any indication; and
- eliminate the $ 15.0 million milestone payment previously due for the dosing of the third patient in the first Phase 3 clinical trial of a licensed product for a second indication.

The Company earned the $ 165.0 million milestone payment described above during the fourth quarter of 2024. The Company has earned a total of $ 337.5 million in non-refundable payments from JNJ from inception in 2017 through December 31, 2024.

Upcoming potential development and regulatory milestones include:

- $ 50.0 million upon FDA approval of an NDA in any indication;
- $ 25.0 million upon the acceptance of an NDA filing by the FDA for a second indication; and
- $ 45.0 million upon FDA approval of an NDA for a second indication.

Pursuant to the agreement, the Company is eligible to receive future sales milestone payments and tiered royalties on net product sales at percentages ranging from 6 % to 10 %.

Revenue Recognition

For the year ended December 31, 2024, the Company recognized $ 434.4 million of license and collaboration revenue. This was comprised of $ 269.4 million related to the Takeda Collaboration Agreement, including (i) $ 254.1 million allocated to the rusfertide license delivered to Takeda upon the effectiveness of the agreement in March 2024 and (ii) $ 15.3 million for development services provided by the Company during the period based on the cost-based input method, and $ 165.0 million related to the JNJ License and Collaboration Agreement, as described above.

For the year ended December 31, 2023, the Company recognized $ 60.0 million of collaboration revenue related to the JNJ License and Collaboration Agreement, which included a $ 50.0 million milestone payment earned in October 2023 in connection with the dosing of the third patient in the ICONIC-TOTAL Phase 3 trial of icotrokinra in patients with moderate-to-severe psoriasis, and a $ 10.0 million milestone payment earned in December 2023 upon the dosing of the third patient in the ANTHEM Phase 2b trial for patients with UC.

For the year ended December 31, 2022, the Company recognized $ 26.6 million of collaboration revenue related to the JNJ License and Collaboration Agreement, which was primarily related to the transaction price under the Restated Agreement recognized based on proportional performance. The Company completed its performance obligation under the collaboration as of June 30, 2022.

During the years ended December 31, 2024 and 2023, no revenue was recognized from amounts included in the deferred revenue balance at the beginning of the year. During the year ended December 31, 2022, the Company recognized revenue of $ 0.9 million from amounts included in the deferred revenue balance at the beginning of the year. None of the costs to obtain or fulfill the contracts were capitalized.

The remaining unrecognized transaction price amount of $ 30.6 million related to the Takeda Collaboration Agreement was recorded as deferred revenue on the Company's consolidated balance sheet as of December 31, 2024 and will be recognized over time based on a measure of the Company's efforts toward satisfying the performance obligation relative to the total expected efforts or inputs to satisfy the performance obligation (e.g. costs incurred compared to total budget).

Note 4. Fair Value Measurements

Financial assets and liabilities are recorded at fair value. The accounting guidance for fair value provides a framework for measuring fair value, clarifies the definition of fair value and expands disclosures regarding fair value measurements. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. The accounting guidance establishes a three-tiered hierarchy, which prioritizes the inputs used in the valuation methodologies in measuring fair value as follows:

Level 1—Inputs are unadjusted quoted prices in active markets for identical assets or liabilities at the measurement date.

Level 2—Inputs (other than quoted market prices included in Level 1) are either directly or indirectly observable for the asset or liability through correlation with market data at the measurement date and for the duration of the instrument's anticipated life.

Level 3—Inputs reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

In determining fair value, the Company utilizes quoted market prices, broker or dealer quotations, or valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible and considers counterparty credit risk in its assessment of fair value.

The following tables present the fair value of the Company's financial assets determined using the inputs defined above (in thousands):

	December 31, 2024			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 19,563	$ —	$ —	$ 19,563
Certificates of deposit	—	15,835	—	15,835
U.S. Treasury and agency securities	—	299,217	—	299,217
Commercial paper	—	110,832	—	110,832
Corporate debt securities	—	102,705	—	102,705
Total financial assets	$ 19,563	$ 528,589	$ —	$ 548,152

	December 31, 2023			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 19,212	$ —	$ —	$ 19,212
Certificates of deposit	—	13,004	—	13,004
U.S. Treasury and agency securities	—	145,085	—	145,085
Commercial paper	—	130,296	—	130,296
Corporate debt securities	—	7,672	—	7,672
Total financial assets	$ 19,212	$ 296,057	$ —	$ 315,269

The Company's certificates of deposit, U.S. Treasury and agency securities, including U.S. Treasury bills, commercial paper, and corporate debt securities are classified as Level 2 as they were valued based upon quoted market prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets that are not active and model-based valuation techniques, for which all significant inputs are observable in the market or can be corroborated by observable market data for substantially the full term of the assets.

The carrying amount of the Company's remaining financial assets and liabilities, including cash, receivables and payables, approximates their fair value due to their short-term nature.

Note 5. Cash Equivalents and Marketable Securities

Cash equivalents and marketable securities consisted of the following (in thousands):

	December 31, 2024			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	$ 19,563	$ —	$ —	$ 19,563
Certificates of deposit	15,820	22	(7)	15,835
U.S. Treasury and agency securities	299,211	429	(423)	299,217
Commercial paper	110,815	28	(11)	110,832
Corporate debt securities	102,714	103	(112)	102,705
Total cash equivalents and marketable securities	$ 548,123	$ 582	$ (553)	$ 548,152
Classified as:				
Cash equivalents				$ 86,236
Marketable securities - current				321,664
Marketable securities - noncurrent				140,252
Total cash equivalents and marketable securities				$ 548,152

	December 31, 2023			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	$ 19,212	$ —	$ —	$ 19,212
Certificates of deposit	12,998	6	—	13,004
U.S. Treasury and agency securities	145,024	63	(2)	145,085
Commercial paper	130,351	5	(60)	130,296
Corporate debt securities	7,678	—	(6)	7,672
Total cash equivalents and marketable securities	$ 315,263	$ 74	$ (68)	$ 315,269
Classified as:				
Cash equivalents				$ 160,379
Marketable securities - current				154,890
Total cash equivalents and marketable securities				$ 315,269

All of the Company's marketable securities are classified as available-for-sale. Current marketable securities of $ 321.7 million and $ 154.9 million held as of December 31, 2024 and 2023, respectively, had contractual maturities of less than one year. Noncurrent marketable securities of $ 140.3 million held as of December 31, 2024 had contractual maturities of at least one year but no more than two years . The Company does not intend to sell its securities that are in an unrealized loss position, and it is not more likely than not that the Company will be required to sell its securities before recovery of their amortized cost basis, which may be at maturity. There were no material realized gains or realized losses on marketable securities for the periods presented. The Company evaluated securities with unrealized losses to determine whether such losses, if any, were due to credit-related factors and determined that there were no credit-related losses to be recognized as of December 31, 2024 and 2023.

Note 6. Balance Sheet Components

Prepaid Expenses and Other Current Assets

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

	December 31,	
	2024	2023
Accrued interest receivable	$ 3,242	$ 256
Prepaid clinical and research related expenses	1,830	649
Prepaid insurance	1,159	1,410
Prepaid licenses	600	529
Other prepaid expenses	649	1,040
Other receivable	248	76
Prepaid expenses and other current assets	$ 7,728	$ 3,960

Property and Equipment, Net

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

	December 31,	
	2024	2023
Laboratory equipment	$ 6,354	$ 5,323
Furniture and computer equipment	1,447	1,143
Leasehold improvements	2,424	963
Total property and equipment	10,225	7,429
Accumulated depreciation	(7,035)	(6,234)
Property and equipment, net	$ 3,190	$ 1,195

Depreciation expense for the years ended December 31, 2024, 2023 and 2022, was $ 894,000 , $ 977,000 and $ 1,032,000 , respectively. As of December 31, 2024, 2023 and 2022, $ 47,000 , $ 56,000 and $ 156,000 , respectively, of the Company's property and equipment, net, was located in Australia. The remainder of the Company's property and equipment, net was located in the United States.

Accrued Expenses and Other Payables

Accrued expenses and other payables consisted of the following (in thousands):

	December 31,	
	2024	2023
Accrued clinical and research related expenses	$ 11,923	$ 11,841
Accrued employee related expenses	11,078	6,786
Accrued professional service fees	618	632
Other	74	99
Total accrued expenses and other payables	$ 23,693	$ 19,358

Note 7. Research Collaboration and License Agreement

Pursuant to a collaboration agreement between the Company and Zealand Pharma A/S ("Zealand") entered into in June 2012 and a related arbitration resolution agreement entered into in August 2021, the Company is obligated to pay Zealand certain milestone and royalty payments for rusfertide. The potential future payments include: (i) up to $ 2.75 million in future development milestone payments; (ii) a low single digit royalty on worldwide net sales; and (iii) sales milestones for achievement of annual net sales amounts in specified geographies.

See Note 9. Commitments and Contingencies – Legal Proceedings for additional information on the results of arbitration proceedings related to this research and collaboration agreement.

Milestone payments to collaboration partners are recorded as research and development expense in the period that the expense is incurred. No expense was recorded under this agreement for the years ended December 31, 2024, 2023 or 2022.

Note 8. Lease

The Company applies ASC Topic 842 to recognize assets and liabilities for leases with lease terms of more than 12 months on the balance sheet. The Company has elected to account for each separate lease component and non-lease component as one single component for all lease assets. Leases with terms of 12 months or less are not recorded on the balance sheet, and the related lease expenses are recognized on a straight-line basis over the lease term.

The Company has one operating lease agreement originally entered into in March 2017 for approximately 42,900 square feet for laboratory and office space located in Newark, California. In July 2021, the Company entered into a second amendment to its original facility lease agreement, as amended, for 15,000 square feet of additional office space in Newark, California.

On May 6, 2024, the Company amended its facility lease agreement (the “Amended Lease”) to extend the lease term for its existing office and laboratory space from one to 66 months and lease approximately 17,700 rentable square feet of additional office space, all located in Newark, California. The Company began occupying the additional space under the Amended Lease on July 1, 2024. The Amended Lease, which expires in November 2029, provides for an agreed-upon period of rent abatement and a tenant improvement allowance of $ 1.8 million. As a result of this amendment, the Company recorded an additional right-of-use-asset and the related liability of $ 10.5 million.

The Company provided the landlord with a $ 225,000 letter of credit collateralized by restricted cash as security deposit for the operating lease agreement. No additional security deposit was required pursuant to the Amended Lease, and the Company is responsible for its proportional share of operating expenses and tax obligations.

Balance sheet information related to the Company’s operating lease is as follows for the periods presented (in thousands):

	December 31,	
Operating Lease:	**2024**	**2023**
Operating lease right-of-use asset	$ 9,417	$ 954
Operating lease liability - current	$ 510	$ 1,141
Operating lease liability - noncurrent	10,356	—
Total operating lease liabilities	$ 10,866	$ 1,141
Weighted-average remaining lease term (years)	4.9	0.4
Weighted-average discount rate	5.7 %	10.4 %

Other information related to the Company’s operating lease is as follows for the periods presented (in thousands):

	Year Ended December 31,		
	2024	**2023**	**2022**
Operating lease cost	$ 2,459	$ 2,335	$ 2,335
Short-term rent expense	51	—	—
Less: Sublease income	(34)	(137)	(123)
Total lease expense	$ 2,476	$ 2,198	$ 2,212

Supplemental cash flow information is as follows for the periods presented (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Operating cash flow used by operating leases	$ 2,226	$ 2,743	$ 2,661
New operating lease asset obtained in exchange for operating lease liability	$ 10,511	$ —	$ —

Future lease payments required under lease obligations as of December 31, 2024 are as follows (in thousands):

Year Ending December 31:	Amount
2025	$ 1,159
2026	2,786
2027	2,882
2028	2,983
Thereafter	2,825
Total future minimum lease payments	12,635
Less: Imputed interest	(1,769)
Present value of lease liabilities	$ 10,866

Note 9. Commitments and Contingencies

Contract Service Providers

In the normal course of business, the Company enters into agreements with contract service providers to assist in the performance of its research and development activities and clinical and commercial manufacturing activities. Subject to the required notice periods and the Company's obligations under binding purchase orders, the Company can elect to discontinue the work under these agreements at any time. However, the financial terms of some of these agreements may include non-refundable upfront payments, payments by the Company for options to acquire certain rights, contingent obligations by the Company for potential development and regulatory milestone payments and/or sales-based milestone payments and royalty payments. These obligations are recorded in the Company's consolidated statements of operations as incurred, which is generally when the corresponding events become probable. Certain payments are contingent upon the occurrence of various future events that have a high degree of uncertainty. The Company expects to enter into additional clinical development, contract research, clinical and commercial manufacturing, supplier and collaborative research agreements in the future, which may require upfront payments and long-term commitments of capital resources.

Indemnification Agreements

In the ordinary course of business, the Company enters into agreements that may include indemnification provisions. Pursuant to such agreements, the Company may indemnify, hold harmless and defend an indemnified party for losses suffered or incurred by the indemnified party. Some of the provisions will limit losses to those arising from third-party actions. In some cases, the indemnification will continue after the termination of the agreement. The maximum potential amount of future payments the Company could be required to make under these provisions is not determinable. The Company has also entered into indemnification agreements with its directors and officers that may require the Company to indemnify its directors and officers against liabilities that may arise by reason of their status or service as directors or officers to the fullest extent permitted by law. The Company carries a directors' and officers' insurance policy. To date, the Company has not incurred material costs to defend lawsuits or settle claims related to the indemnification agreements. The Company believes that the fair value of these indemnification agreements is minimal and has not accrued any amounts for the obligations.

Legal Proceedings

The Company recognizes accruals for legal actions to the extent that it concludes that a loss is both probable and reasonably estimable. The Company accrues for the best estimate of a loss within a range; however, if no estimate in the

range is better than any other, it accrues the minimum amount in the range. If the Company determines that a loss is reasonably possible and the loss or range of loss can be estimated, it discloses the possible loss.

In January 2020, the Company initiated arbitration proceedings with the International Court of Arbitration of the International Chamber of Commerce against Zealand related to a collaboration agreement the Company and Zealand entered into in 2012 and terminated in 2014. The agreement provides for certain post-termination payment obligations to Zealand with respect to compounds related to the collaboration that the Company elects to further develop and meet specified conditions. In August 2021, the Company and Zealand agreed to resolve the dispute and reached an Arbitration Resolution Agreement. Under the Arbitration Resolution Agreement, the Company recognized $ 4.0 million in development milestone payments to Zealand in the third quarter of 2021 and is obligated to pay Zealand certain milestone and royalty payments for rusfertide. The potential future payments include (i) up to $ 2.75 million in future development milestone payments, (ii) a low single digit royalty on worldwide net sales, and (iii) sales milestones for achievement of annual net sales amounts in specific geographies.

The Company considered the outcome of these arbitration proceedings as being related to its research and development projects; therefore, payments or milestone payments were recorded as research and development expenses.

Note 10. Stockholders' Equity

Shares of Common Stock Authorized for Issuance

At the Company's 2024 Annual Meeting of Stockholders held on June 20, 2024, the Company's stockholders approved an amendment to the Company's Amended and Restated Certificate of Incorporation (the "Certificate of Incorporation") to increase the number of authorized shares of the Company's common stock from 90,000,000 to 180,000,000 , which also has the effect of increasing the total number of authorized shares from 100,000,000 to 190,000,000 (the "Amendment"). On June 21, 2024, the Company filed a Certificate of Amendment to the Certificate of Incorporation with the Secretary of State of the State of Delaware to effect the Amendment, which became effective immediately upon such filing.

Public Offering

In April 2023, the Company completed an underwritten public offering of 5,000,000 shares of its common stock at a public offering price of $ 20.00 per share and issued an additional 750,000 shares of common stock at a price of $ 20.00 per share following the underwriters' exercise of their option to purchase additional shares. Net proceeds, after deducting underwriting commissions and offering costs paid by the Company, were $ 107.8 million.

ATM Offering

In August 2022, the Company entered into an Open Market Sale Agreement ^{SM} , pursuant to which the Company may offer and sell up to $ 100.0 million shares of its common stock from time to time in "at-the-market" offerings (the "2022 ATM Facility"). During the year ended December 31, 2023, the Company sold 1,749,199 shares of its common stock under the 2022 ATM Facility for net proceeds of $ 24.3 million, after deducting issuance costs. There were no sales of the Company's common stock under the 2022 ATM Facility during the years ended December 31, 2024 and 2022.

Exchange Warrants

In December 2018, the Company entered into an exchange agreement (the "Exchange Agreement") with an investor and its affiliates (the "Exchanging Stockholders"), pursuant to which the Company exchanged an aggregate of 1,000,000 shares of the Company's common stock, par value $ 0.00001 per share, owned by the Exchanging Stockholders for pre-funded warrants (the "Exchange Warrants") to purchase an aggregate of 1,000,000 shares of common stock (subject to adjustment in the event of any stock dividends and splits, reverse stock split, recapitalization, reorganization or similar transaction, as described in the Exchange Warrants), with an exercise price of $ 0.00001 per share. The Exchange Warrants expired ten years from the date of issuance. The Exchange Warrants were exercisable at any time prior to expiration except that the Exchange Warrants could not be exercised by the Exchanging Stockholders if, after giving

effect thereto, the Exchanging Stockholders would beneficially own more than 9.99 % of the Company's common stock, subject to certain exceptions. In accordance with Accounting Standards Codification Topic 505, *Equity*, the Company recorded the retirement of the common stock exchanged as a reduction of common stock shares outstanding and a corresponding debit to additional paid-in-capital at the fair value of the Exchange Warrants on the issuance date. The Exchange Warrants met the criteria for equity classification and the fair value of the Exchange Warrants was recorded as a credit to additional paid-in capital and was not subject to remeasurement. The Company determined that the fair value of the Exchange Warrants was substantially similar to the fair value of the retired shares on the issuance date due to the negligible exercise price for the Exchange Warrants. During the year ended December 31, 2022, the remaining Exchange Warrants to purchase 400,000 shares of the Company's common stock were net exercised, resulting in the issuance of 399,997 shares of common stock. As of December 31, 2024, there were no outstanding Exchange Warrants.

Pre-Funded Warrants

In August 2018, the Company entered into a Securities Purchase Agreement with certain accredited investors (each, an "Investor" and, collectively, the "Investors"), pursuant to which the Company sold an aggregate of 2,750,000 shares of its common stock at a price of $ 8.00 per share for aggregate net proceeds of $ 21.7 million, after deducting offering expenses payable by the Company. In a concurrent private placement, the Company issued the Investors warrants to purchase an aggregate of 2,750,000 shares of its common stock (each, a "Warrant" and, collectively, the "Warrants"). Each Warrant was exercisable from August 8, 2018 through August 8, 2023 . Warrants to purchase 1,375,000 shares of the Company's common stock had an exercise price of $ 10.00 per share and Warrants to purchase 1,375,000 shares of the Company's common stock had an exercise price of $ 15.00 per share.

In August 2023, prior to the expiration of the Warrants, the Company entered into certain agreements with the Investors and their affiliates under which the Company agreed to allow the Warrants to be exercised in exchange for pre-funded warrants representing the same number of Warrant Shares underlying the Warrants with an exercise price of $ 0.001 per share (the "Pre-Funded Warrants"). Subsequent to the execution of the agreements and prior to the expiration of the Warrants, all outstanding Warrants were exercised for gross proceeds of $ 34.4 million in exchange for 44,748 shares of the Company's common stock and Pre-Funded Warrants to purchase 2,705,252 shares of common stock (subject to adjustment in the event of any stock dividends and splits, reverse stock split, recapitalization, reorganization or similar transaction, as described in the Pre-Funded Warrants) with an exercise price of $ 0.001 per share. The Pre-Funded Warrants will expire upon the day they are exercised in full. The Pre-Funded Warrants are exercisable at any time prior to expiration except that the Pre-Funded Warrants cannot be exercised by the Investors if, after giving effect thereto, the Investors would beneficially own more than 9.99 % of the Company's common stock, subject to certain exceptions. The common stock and Pre-Funded Warrants met the criteria for equity classification and the net proceeds from the transaction were recorded as a credit to additional paid-in capital. In accordance with ASC Topic 260, outstanding Pre-Funded Warrants are included in the computation of basic net loss per share because the exercise price is negligible, and they are fully vested and exercisable after the original issuance date. During the year ended December 31, 2024, Pre-Funded Warrants to purchase 1,205,252 shares were net exercised, resulting in the issuance of 1,205,225 shares of common stock. As of December 31, 2024, Pre-Funded Warrants to purchase 1,500,000 shares of common stock remained outstanding.

Note 11. Equity Plans

Equity Incentive Plan

In May 2007, the Company established the 2007 Stock Option and Incentive Plan (“2007 Plan”) which provided for the granting of stock options to employees and consultants of the Company. Options granted under the 2007 Plan were either incentive stock options (“ISOs”) or nonqualified stock options (“NSOs”). ISOs were granted only to Company employees. NSOs were granted to Company employees, non-employee members of the Company’s Board of Directors (“Board”) and consultants. Options under the 2007 Plan have a term of ten years and generally vested over a four-year period.

In July 2016, the Company’s Board and stockholders approved the 2016 Equity Incentive Plan (“2016 Plan”) to replace the 2007 Plan. Under the 2016 Plan, 1,200,000 shares of the Company’s common stock were initially reserved for the issuance of stock options, restricted stock units and other awards to employees, directors and consultants. Pursuant to the “evergreen” provision contained in the 2016 Plan, the number of shares reserved for issuance under the 2016 Plan automatically increases on January 1 of each year, starting on January 1, 2017 and continuing through (and including) January 1, 2026, by 4 % of the total number of shares of the Company’s capital stock outstanding on December 31 of the preceding fiscal year, or a lesser number of shares determined by the Company’s Board. Upon adoption of the 2016 Plan, no additional stock awards were issued under the 2007 Plan. Options granted under the 2007 Plan that were outstanding on the date the 2016 Plan became effective remain subject to the terms of the 2007 Plan. The number of options available for grant under the 2007 Plan was ceased and the number was added to the common stock reserved for issuance under the 2016 Plan. As of December 31, 2024, approximately 1,109,629 shares of common stock were available for issuance under the 2016 Plan.

The 2016 Plan is administered by the Board, or a committee appointed by the Board, which determines the types of awards to be granted, including the number of shares subject to the awards, the exercise price and the vesting schedule. Options granted under the 2016 Plan expire no later than ten years from the date of grant. The exercise price of each option may not be less than 100 % of the fair market value of the common stock at the date of grant. Options may be granted to stockholders possessing more than 10 % of the total combined voting power of all classes of stocks of the Company at an exercise price at least 110 % of the fair value of the common stock at the date of grant and the options are not exercisable after the expiration of 10 years from the date of grant. Employee stock options generally vest over a period of approximately four years . Employee RSUs generally vest over a period of approximately three or four years . Non-employee Board director initial stock options generally vest monthly over a period of approximately three years . Non-employee Board director annual refresher options and RSUs generally vest over a period of approximately one year .

Inducement Plan

In May 2018, the Company’s Board approved the 2018 Inducement Plan, as subsequently amended. The 2018 Inducement Plan is a non-stockholder approved stock plan, under which awards options and restricted stock unit awards to persons that were not previously employees or directors of the Company, or following a bona fide period of non-employment, as an inducement material to such persons entering into employment with the Company, within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules. The 2018 Inducement Plan is administered by the Board or the Compensation Committee of the Board, which determines the types of awards to be granted, including the number of shares subject to the awards, the exercise price and the vesting schedule. Awards granted under the 2018 Inducement Plan expire no later than ten years from the date of grant. Employee stock options granted under the 2018 Inducement Plan generally vest over a period of approximately four years . As of December 31, 2024, approximately 645,858 shares of common stock were available for issuance under the 2018 Inducement Plan, as amended.

Stock Options

Stock option activity under the Company's equity incentive and inducement plans is set forth below:

	Options Outstanding	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Life (years)	Aggregate Intrinsic Value [1]
				(in millions)
Balances at December 31, 2023	7,922,043	$ 17.21		
Options granted	2,068,570	24.39		
Options exercised	(1,766,092)	14.33		
Options forfeited	(407,365)	27.57		
Balances at December 31, 2024	7,817,156	$ 19.22	6.89	$ 152.9
Options exercisable – December 31, 2024	4,877,064	$ 18.60	5.96	98.5
Options vested and expected to vest – December 31, 2024	7,817,156	$ 19.22	6.89	$ 152.9

[1] The aggregate intrinsic values were calculated as the difference between the exercise price of the options and the closing price of the Company's common stock on December 31, 2024. The calculation excludes options with an exercise price higher than the closing price of the Company's common stock on December 31, 2024.

The aggregate intrinsic value of options exercised was $ 40.7 million, $ 3.3 million and $ 5.4 million for the years ended December 31, 2024, 2023 and 2022, respectively.

During the years ended December 31, 2024, 2023 and 2022, the estimated weighted-average grant-date fair value of common stock underlying options granted was $ 20.07 , $ 10.81 and $ 17.52 per share, respectively.

For the years ended December 31, 2024, 2023 and 2022, the aggregate fair value of stock options that vested during the year was $ 30.3 million, $ 25.9 million and $ 23.3 million, respectively.

Stock Options Valuation Assumptions

The fair value of stock option awards was estimated at the date of grant using a Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,		
	2024	2023	2022
Expected term (in years)	5.27 - 6.08	5.27 - 6.08	5.27 - 6.08
Expected volatility	96.6 % - 106.2 %	105.7 % - 110.1 %	96.3 % - 101.7 %
Risk-free interest rate	3.46 % - 4.71 %	3.57 % - 4.86 %	1.64 % - 4.23 %
Dividend yield	—	—	—

In determining the fair value of the options granted, the Company uses the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective, and generally requires judgment to determine.

Expected Term—The Company's expected term represents the period that the Company's options granted are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term). The Company has limited historical exercise information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for its stock option grants.

Expected Volatility— Beginning January 1, 2023, the Company's expected volatility is estimated based upon the volatility of the Company's stock price over a period equal to the expected term of the stock option grants. For the year ended December 31, 2022, the Company's expected volatility was estimated based upon a mix of 25 % of the average

volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants and 75 % of the volatility of the Company's stock price since its initial public offering in August 2016.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of the option.

Expected Dividend—The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

RSUs

An RSU is an agreement to issue shares of the Company's common stock at the time of vesting. RSUs generally vest annually in equal installments over three or four years on approximately the anniversary of the grant date. RSUs granted to certain non-executive employees in 2022 vested 100 % on approximately the first anniversary of the grant date.

RSU activity under the Company's equity incentive plans is set forth below:

	Number of Shares		Weighted Average Grant Date Fair Value
Unvested RSUs at December 31, 2023	664,491	$	18.40
Granted	564,465		23.56
Vested	(316,748)		18.93
Forfeited	(67,500)		23.31
Unvested RSUs at December 31, 2024	844,708	$	21.03

Stock-based compensation expense associated with RSUs is based on the fair value of the Company's common stock on the grant date, which equals the closing market price of the Company's common stock on the grant date. For RSUs, the Company recognizes compensation expense over the vesting period of the awards that are ultimately expected to vest.

For the years ended December 31, 2024, 2023 and 2022, the aggregate fair value of RSUs that vested during the year was $ 6.0 million, $ 5.9 million and $ 1.7 million, respectively.

PSUs

PSU activity under the Company's equity incentive plans is set forth below:

	Number of Shares		Weighted Average Grant Date Fair Value
Unvested PSUs at December 31, 2023	75,500	$	23.57
Granted	—		—
Vested	—		—
Forfeited	—		—
Unvested PSUs at December 31, 2024	75,500	$	23.57

The terms of the PSUs provide for 100 % of shares to be earned based on the achievement of certain pre-determined performance objectives, subject to the participant's continued employment. The PSUs will vest, if at all, upon certification by the Compensation Committee of the Board of the actual achievement of the performance objectives, subject to specified change of control exceptions.

Stock-based compensation expense associated with PSUs is based on the fair value of the Company's common stock on the grant date, which equals the closing market price of the Company's common stock on the grant date. The Company recognizes compensation expense over the vesting period of the awards that are ultimately expected to vest when the achievement of the related performance objective becomes probable.

During the year ended December 31, 2023, the Compensation Committee of the Board certified the actual achievement of performance objectives related to certain PSUs. As a result, recipients earned a total of 114,000 shares of common stock. The total fair market value of the PSUs at vest date during the year ended December 31, 2023 was $ 3.0 million. No PSUs vested during the years ended December 31, 2024 and 2022.

The total fair value of grant date fair value of unvested PSUs outstanding as of December 31, 2024 was $ 1.8 million. As of December 31, 2024, the achievement of the related performance objectives was deemed not probable and, accordingly, no stock-based compensation expense for unvested PSUs has been recognized as of December 31, 2024.

Employee Stock Purchase Plan

In July 2016, the Company's Board and stockholders approved the 2016 Employee Stock Purchase Plan ("2016 ESPP"). The 2016 ESPP is intended to qualify as an employee stock purchase plan under Section 423 of the Internal Revenue Code of 1986, as amended, and is administered by the Company's Board and the Compensation Committee of the Board. Under the 2016 ESPP, 150,000 shares of the Company's common stock were initially reserved for employee purchases of the Company's common stock. Pursuant to the "evergreen" provision contained in the 2016 ESPP, the number of shares reserved for issuance automatically increases on January 1 of each year, starting on January 1, 2017 and continuing through (and including) January 1, 2026 by the lesser of (i) 1 % of the total number of shares of common stock outstanding on December 31 of the preceding fiscal year (ii) 300,000 shares, or (iii) such other number of shares determined by the Board.

The 2016 ESPP allows eligible employees to purchase shares of the Company's common stock at a discount through payroll deductions of up to 15 % of their eligible compensation. At the end of each offering period, eligible employees are able to purchase shares at 85 % of the lower of the fair market value of the Company's common stock at the beginning of the offering period or at the end of each applicable purchase period. During the year ended December 31, 2024, a total of 59,254 shares of common stock were issued under the 2016 ESPP, and approximately 1,700,648 shares of common stock were available for issuance as of December 31, 2024.

The fair value of the rights granted under the 2016 ESPP was calculated using the Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,		
	2024	2023	2022
Expected term (in years)	0.50	0.50	0.50
Expected volatility	48.2 % - 52.6 %	82.6 % - 128.2 %	117.5 % - 128.2 %
Risk-free interest rate	4.65 % - 5.35 %	3.56 % - 5.17 %	0.75 % - 3.56 %
Dividend yield	—	—	—

Stock-Based Compensation

Total stock-based compensation expense was as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Research and development	$ 20,919	$ 17,061	$ 14,719
General and administrative	16,635	12,232	9,483
Total stock-based compensation expense	$ 37,554	$ 29,293	$ 24,202

As of December 31, 2024, total unrecognized stock-based compensation expense was approximately $ 56.9 million, which the Company expects to recognize over a weighted-average period of approximately 2.3 years.

Note 12. 401(k) Plan

The Company has a retirement and savings plan under Section of 401(k) of Internal Revenue Code (the "401(k) Plan") covering all U.S. employees. The 401(k) Plan allows employees to make pre- and post-tax contributions up to the maximum allowable amount set by the Internal Revenue Service. The Company may make contributions to this plan at its discretion. The Company matched 50 % of each employee's contribution up to a maximum of $ 4,000 for the years ended December 31, 2024, 2023 and 2022, resulting in recognized expense of approximately $ 0.4 million, $ 0.4 million and $ 0.3 million for the years ended December 31, 2024, 2023 and 2022, respectively.

Note 13. Income Taxes

The following table presents domestic and foreign components of net loss before income taxes (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Domestic	$ 279,379	$ (76,779)	$ (124,208)
Foreign	29	(2,176)	(3,185)
Total net income (loss) before taxes	$ 279,408	$ (78,955)	$ (127,393)

The federal, state and foreign components of the income tax expense are summarized as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Current:			
Federal	$ 4,078	$ —	$ —
State	142	—	—
Other	—	—	—
Total current tax expense	4,220	—	—
Deferred:			
Federal	—	—	—
State	—	—	—
Other	—	—	—
Total deferred tax expense	—	—	—
Total income tax expense	$ 4,220	$ —	$ —

The effective tax rate of the provision for income taxes differs from the federal statutory rate as follows:

	Year Ended December 31,		
	2024	2023	2022
Federal statutory income tax rate	21.0 %	21.0 %	21.0 %
State taxes, net of federal benefit	2.1	8.1	1.4
Tax credits	(2.9)	8.5	5.9
Foreign tax rate difference	—	0.2	0.2
Change in valuation allowance	(18.2)	(34.4)	(25.8)
Other	(0.5)	(3.4)	(2.7)
Provision for income taxes	1.5 %	— %	— %

The components of the deferred tax assets are as follows (in thousands):

	December 31,	
	2024	2023
Deferred tax assets:		
Net operating loss carryforwards	$ 8,876	$ 70,469
Depreciation	2,717	950
Accruals and other	2,246	1,430
Operating lease liability	2,430	265
Research and development and foreign credits	30,852	38,759
Section 174 capitalized research and development expenditures	58,630	43,841
Stock-based compensation	11,759	10,772
Total deferred tax assets	117,510	166,486
Deferred tax liabilities:		
Operating right-of-use asset	(2,105)	(221)
Total deferred tax liabilities	(2,105)	(221)
Valuation allowance	(115,405)	(166,265)
Net deferred tax assets	$ —	$ —

Accounting Standards Codification Topic 740, *Income Taxes*, requires that the tax benefit of net operating losses, temporary differences and credit carryforwards be recorded as an asset to the extent that management assesses that realization is “more likely than not.” Realization of the future tax benefits is dependent on the Company’s ability to generate sufficient taxable income within the carryforward period. Because of the Company’s recent history of operating losses, management believes that recognition of the deferred tax assets arising from the above-mentioned future tax benefits is currently not likely to be realized and, accordingly, has provided a valuation allowance. The valuation allowance decreased by approximately $ 50.9 million during the year ended December 31, 2024, and increased by $ 28.1 million and $ 34.2 million during the years ended December 31, 2023 and 2022, respectively.

Federal and state laws impose substantial restrictions on the utilization of net operating loss and tax credit carryforwards in the event of an ownership change for tax purposes, as defined in Section 382 of the Internal Revenue Code. As a result of such ownership changes, the annual limitation may result in the expiration of net operating losses and credits before utilization. The Company performed a Section 382 analysis through December 31, 2024. The Company has experienced ownership changes in the past. The ownership changes will not result in a limitation that will materially reduce the total amount of net operating loss carryforwards and credits that can be utilized. Subsequent ownership changes may affect the limitation in future years.

As of December 31, 2024, the Company had $ 29.2 million of federal net operating loss carryforwards and $ 215.8 million of state net operating loss carryforwards. $ 5.9 million of the federal net operating loss carryforwards will begin to expire in 2037, if not utilized, and the remaining $ 23.3 million have no expiration date. The state net operating loss carryforwards will begin to expire in 2035, if not utilized.

As of December 31, 2024, the Company had $ 35.6 million of federal and $ 7.7 million of state research and development tax credit carryforwards available to reduce future income taxes. The federal research and development tax credits will begin to expire in 2035, if not utilized. The state research and development tax credits have no expiration date.

As of December 31, 2024, the Company had AUD 5.7 million ($ 3.5 million) of Australian research and development tax credit carryforwards available to reduce future income taxes. The Australian research and development tax credits have no expiration date.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Balance at beginning of year	$ 28,025	$ 25,295	$ 33,159
Decreases based on tax positions related to prior years	(902)	—	(10,779)
Increases based on tax positions related to current year	3,450	2,730	2,915
Balance at end of year	$ 30,573	$ 28,025	$ 25,295

At December 31, 2024, the Company had unrecognized tax benefits of $ 30.6 million, which are subject to a valuation allowance and would not affect the effective tax rate if recognized. The Company does not anticipate that the total amount of unrecognized tax benefits will significantly increase or decrease in the next 12 months. The Company's policy is to include interest and penalties related to unrecognized tax benefits within the provision for income taxes, as necessary. Management determined that no accrual for interest or penalties was required as of December 31, 2024, 2023 and 2022.

The Company files income tax returns in the United States federal jurisdiction, the State of California, the State of Florida, and Australia. The Company is not currently under examination by income tax authorities in federal, state or other jurisdictions. The Company's tax returns remain open for examination for all years.

Protagonist Australia had an accumulated deficit at December 31, 2024 and, accordingly, no provision has been provided thereon for any unremitted earnings.

The Company has received orphan drug designation from the FDA for its clinical asset rusfertide (PTG-300) for the treatment of polycythemia vera and beta-thalassemia and may qualify for a related 25 % U.S. Federal income tax credit on qualifying clinical trial expenditures.

Note 14. Net Income (Loss) per Share

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

	Year Ended December 31,		
	2024	2023	2022
Numerator:			
Net income (loss)	$ 275,188	$ (78,955)	$ (127,393)
Denominator:			
Weighted-average shares of common stock, basic	61,566,989	56,763,559	49,042,232
Dilutive effect of common stock equivalents	3,510,733	—	—
Weighted-average shares of common stock, dilutive	65,077,722	56,763,559	49,042,232
Net income (loss) per share of common stock			
Basic net income (loss) per share of common stock	$ 4.47	$ (1.39)	$ (2.60)
Diluted net income (loss) per share of common stock	$ 4.23	$ (1.39)	$ (2.60)

Approximately 2.9 million potentially dilutive shares of common stock (consisting of shares subject to outstanding stock options, RSUs, and under the ESPP) were excluded from the diluted net income per share of common stock computations for the year ended December 31, 2024 because their effect was anti-dilutive. Approximately 8.7 million and 9.9 million potentially dilutive shares of common stock (consisting of shares subject to outstanding stock options, RSUs, PSUs, warrants and under the ESPP, as applicable) were excluded from the diluted net loss per share of common stock computations for the years ended December 31, 2023 and 2022, respectively, due to the Company's net losses for these periods.

Note 15. Segment Reporting

Operating segments are components of an enterprise for which separate financial information is available and which are evaluated by a company's chief operating decision maker ("CODM"), in deciding how to allocate resources and to assess performance.

The Company operates and manages its business as one operating segment, which primarily focuses on the discovery and development of innovative medicines in areas of unmet medical need. The Company's Chief Executive Officer serves as the Company's CODM and manages and allocates resources to the operations of the Company on an entity-wide basis. Managing and allocating resources on an entity-wide basis enables the CODM to assess the overall level of resources available and how to best deploy these resources across functions and research and development projects based on unmet medical need, scientific data, probability of technical and regulatory successful development, market potential and other considerations, and, as necessary, reallocate resources among our internal research and development portfolio and external opportunities to best support the long-term growth of our business. The Company's CODM reviews financial information on an aggregate basis for the purposes of allocating resources and evaluating financial performance, including segment net income (loss), which is also reported on the consolidated statement of operations as consolidated net income (loss).

The Company derives revenues from its collaboration partners, consisting of nonrefundable upfront and milestone payments and cost sharing payments under its license and collaboration agreements. The Company's customers are comprised of its two collaboration partners, Takeda and JNJ, formerly Janssen Biotech. Takeda and JNJ accounted for 62 % and 38 % of the Company's revenues for the year ended December 31, 2024, respectively. JNJ accounted for 100 % of the Company's revenues for the years ended December 31, 2023 and 2022. All of the Company's revenues for the years ended December 31, 2024, 2023 and 2022 were generated in the United States. See Note 3 to the consolidated financial statements for additional information.

Segment information was as follows for the years presented (dollars in thousands):

	Year Ended December 31,		
	2024	2023	2022
Revenue	$ 434,433	$ 60,000	$ 26,581
Discovery department expenses [1]	(13,411)	(5,471)	(11,608)
Development department expenses [1]	(62,262)	(65,574)	(66,941)
General and administrative department expenses [1]	(24,249)	(19,620)	(21,702)
Employee wages and benefits - discovery	(6,601)	(4,531)	(6,162)
Employee wages and benefits - development	(23,365)	(19,301)	(19,279)
Employee wages and benefits - general and administrative	(14,148)	(9,862)	(8,060)
Stock-based compensation	(37,554)	(29,293)	(24,202)
Other segment items [2]	250	(201)	(80)
Interest income	26,315	14,898	4,060
Income tax expense	(4,220)	—	—
Segment profit (loss)	$ 275,188	$ (78,955)	$ (127,393)
Reconciliation of profit (loss)			
Adjustments and reconciling items	$ —	$ —	$ —
Consolidated net income (loss)	$ 275,188	$ (78,955)	$ (127,393)
Other segment information			
Segment assets [3]	$ 744,725	$ 357,951	$ 247,928
Long-lived assets [4]	$ 12,607	$ 2,149	$ 4,626
Expenditures for long-lived assets	$ 1,355	$ 609	$ 795

[1] Amounts exclude employee wages and benefits, stock-based compensation and expense allocations.
[2] Other segment items include foreign currency related income (expense) and other miscellaneous income (expense).
[3] The measure of segment assets is reported on the consolidated balance sheet as total assets.
[4] Long-lived assets include property and equipment, net and operating lease right-of-use asset.

The accounting policies of the Company's operating segment are the same as those described in the summary of significant accounting policies. Substantially all of the Company's long-lived assets are in the United States. See Note 6 to the consolidated financial statements for depreciation expense for the periods presented.

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Management, under the supervision and with the participation of our Chief Executive Officer (Principal Executive Officer) and Chief Financial Officer (Principal Financial Officer), has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2024. Based on the evaluation of our disclosure controls and procedures, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures as of December 31, 2024 were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our management, including our Chief Executive Officer and Chief Financial Officer, conducted an evaluation of the effectiveness of our internal control over financial reporting based on the criteria set forth in *Internal Control-Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on its evaluation under the criteria set forth in *Internal Control-Integrated Framework*, our management concluded that our internal control over financial reporting was effective as of December 31, 2024.

Our independent registered public accounting firm, Ernst & Young LLP, has audited the financial statements included in the Annual Report and has issued a report on the effectiveness of our internal control over financial reporting as of December 31, 2024. The report of Ernst & Young LLP is included below.

Limitations on Effectiveness of Controls and Procedures and Internal Control over Financial Reporting

In designing and evaluating the disclosure controls and procedures and internal control over financial reporting, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures and internal control over financial reporting must reflect the fact that there are resource constraints, and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting that occurred during our most recent fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Protagonist Therapeutics, Inc.

Opinion on Internal Control Over Financial Reporting

We have audited Protagonist Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), (the COSO criteria). In our opinion, Protagonist Therapeutics, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2024 and 2023, the related consolidated statements of operations, comprehensive income (loss), stockholders' equity and cash flows for each of the three years in the period ended December 31, 2024, and the related notes and our report dated February 21, 2025 expressed an unqualified opinion thereon.

Basis for Opinion

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

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

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

Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ Ernst & Young LLP

San Mateo, California
February 21, 2025

Item 9B. Other Information

b) Trading Plans

On December 15, 2024 , William D. Waddill , a member of our Board , adopted a trading plan intended to satisfy Rule 10b5-1(c) to sell up to 24,000 shares of the Company's common stock through December 31, 2025 , or such earlier date when all transactions under the trading plan are completed, subject to certain conditions. During the quarter ended December 31, 2024, none of our other Section 16 officers or directors adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement, as such terms are defined under Item 408(a) of Regulation S-K.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers, and Corporate Governance

Except as set forth below, the information required by this item is incorporated herein by reference to information in our Definitive Proxy Statement on Schedule 14A relating to our 2025 Annual Meeting of Stockholders, which we expect to be filed with the SEC within 120 days of our fiscal year ended December 31, 2024 (the "Proxy Statement"), including under the headings "Election of Class III Director Nominees," "Executive Officers," "Information Regarding Committees of the Board," "Insider Trading Policy," and, if applicable, "Delinquent Section 16(a) Reports."

We have adopted a Code of Business Conduct and Ethics that applies to all directors, officers and employees, including our principal executive, principal financial and principal accounting officers, or persons performing similar functions. The Code of Business Conduct and Ethics is posted on our website at www.protagonist-inc.com.

We intend to disclose future amendments to certain provisions of the Code of Business Conduct and Ethics, and waivers of the Code of Business Conduct and Ethics granted to executive officers and directors, on our website listed above within four business days following the date of the amendment or waiver.

Item 11. Executive Compensation

The information required by this item is incorporated herein by reference to information in our Proxy Statement, including under the headings "Information Regarding Committees of the Board – Compensation Committee Interlocks and Insider Participation," "Report of the Compensation Committee of the Board," "Executive Compensation," and "Director Compensation."

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

The information required by this item is incorporated herein by reference to information in our Proxy Statement, including under the headings "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information."

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

The information required by this item is incorporated herein by reference to information in our Proxy Statement, including under the headings "Transactions with Related Persons" and "Information Regarding the Board of Directors and Corporate Governance – Independence of the Board of Directors."

Item 14. Principal Accountant Fees and Services

The information required by this item is incorporated by reference to information in our Proxy Statement, including under the heading “Ratification of Selection of Independent Registered Public Accounting Firm.”

PART IV

Item 15. Exhibits, Financial Statement Schedules

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

(1) FINANCIAL STATEMENTS

The financial statements filed as part of this Annual Report on Form 10-K are included in Part II, Item 8 of this Annual Report on Form 10-K.

(2) FINANCIAL STATEMENT SCHEDULES

Financial statement schedules have been omitted in this Annual Report on Form 10-K because they are not applicable, not required under the instructions, or the information requested is set forth in the financial statements or related notes thereto.

(3) EXHIBITS

The exhibits listed in the accompanying Exhibit Index are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K.

(4) EXHIBIT INDEX

Exhibit Number	Exhibit Description	Incorporation By Reference				Filed or Furnished Herewith
		Form	SEC File No.	Exhibit	Filing Date	
3.1	Amended and Restated Certificate of Incorporation.	8-K	001-37852	3.1	8/16/2016	
3.2	Certificate of Amendment to the Amended and Restated Certificate of Incorporation.	8-K	001-37852	3.1	6/26/2024	
3.3	Amended and Restated Bylaws.	S-1/A	333-212476	3.2(b)	8/1/2016	
4.1	Specimen stock certificate evidencing the shares of common stock.	S-1/A	333-212476	4.1	8/1/2016	
4.2	Description of Protagonist Therapeutics, Inc.'s Securities Registered Pursuant to Section 12 of the Exchange Act.					X
4.3	Form of Pre-Funded Warrant	10-Q	001-37852	10.1	11/2/2023	
10.1+	Protagonist Therapeutics, Inc. 2007 Stock Option and Incentive Plan, as amended and restated, and form of option agreement, exercise notice, joinder, and adoption agreement thereunder.	S-1	333-212476	10.1	7/11/2016	
10.2+	Protagonist Therapeutics, Inc. 2016 Equity Incentive Plan and forms of stock option grant notice, option agreement, notice of exercise, restricted stock unit grant notice and restricted stock unit agreement thereunder.	S-1/A	333-212476	10.2	8/1/2016	
10.3+	Protagonist Therapeutics, Inc. 2016 Employee Stock Purchase Plan.	S-1/A	333-212476	10.3	8/1/2016	
10.4+	Form of Indemnity Agreement for Directors and Officers.	S-1/A	333-212476	10.4	8/1/2016	
10.5+	Protagonist Therapeutics, Inc. Amended and Restated 2018 Inducement Plan, and forms of stock option grant notice, option agreement, restricted stock unit grant notice and restricted stock unit agreement thereunder.	S-8	333-263097	99.3	2/28/2022	
10.6	Lease, dated March 6, 2017, by and between the Registrant and BMR-Pacific Research Center LP.	10-K	001-37852	10.9	3/7/2017	
10.7+	Severance Agreement, dated August 1, 2016, by and between the Registrant and Dinesh Patel.	S-1/A	333-212476	10.9	8/1/2016	
10.8†	Research and Collaboration Agreement, dated June 16, 2012, by and among the Registrant, Protagonist Pty. Ltd. and Zealand Pharma A/S.	S-1	333-212476	10.17	7/11/2016	

Exhibit Number	Exhibit Description	Incorporation By Reference				Filed or Furnished Herewith
		Form	SEC File No.	Exhibit	Filing Date	
10.9†	Contract Extension Letter of Agreement, dated June 1, 2013, by and among the Registrant, Protagonist Pty. Ltd. and Zealand Pharma A/S.	S-1	333-212476	10.18	7/11/2016	
10.10†	Agreement on Addition of Additional Collaboration Program, dated September 16, 2013, by and among the Registrant, Protagonist Pty. Ltd. and Zealand Pharma A/S.	S-1	333-212476	10.19	7/11/2016	
10.11†	Protagonist Assumption of Responsibility, dated January 28, 2014, by and between the Registrant and Zealand Pharma A/S.	S-1	333-212476	10.20	7/11/2016	
10.12†	Agreement to Assign Patent Applications, dated February 7, 2014, by and between the Registrant, Protagonist Pty. Ltd. and Zealand Pharma A/S.	S-1	333-212476	10.21	7/11/2016	
10.13†	Abandonment Agreement, dated February 28, 2014, by and among the Registrant, Protagonist Pty. Ltd. and Zealand Pharma A/S.	S-1	333-212476	10.22	7/11/2016	
10.14	Registration Rights Agreement, dated August 8, 2018, by and between the Registrant and certain parties identified on the signature pages thereto.	8-K	001-37852	4.3	8/7/2018	
10.15	Securities Purchase Agreement, dated August 6, 2018, by and between the Registrant and certain purchasers identified on the signature pages thereto.	S-3	333-227216	10.1	9/7/2018	
10.16	Exchange Agreement, dated December 21, 2018, by and between the Registrant and Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P. and Biotechnology Value Trading Fund OS, L.P.	8-K	001-37852	10.1	12/31/2018	
10.17	First Amendment, dated January 31, 2019, to Lease, dated March 6, 2017, by and between Protagonist Therapeutics, Inc., as Tenant, and BMR-Pacific Research Center LP, as Landlord.	10-Q	001-37852	10.3	5/8/2019	
10.18+	Severance Agreement, dated March 14, 2019, by and among Protagonist Therapeutics, Inc. and Suneel Gupta, Ph.D.	10-Q	001-37852	10.4	5/8/2019	

Exhibit Number	Exhibit Description	Incorporation By Reference				Filed or Furnished Herewith
		Form	SEC File No.	Exhibit	Filing Date	
10.19	Open Market Sale Agreement℠, dated August 5, 2022, by and between Protagonist Therapeutics, Inc. and Jefferies LLC.	S-3	333-266595	1.2	8/5/2022	
10.20	Second Amendment, dated July 2, 2021, to Lease, dated March 6, 2017, by and between Protagonist Therapeutics, Inc., as Tenant, and BMR-Pacific Research Center, LP as Landlord.	10-Q	001-37852	10.3	11/3/2021	
10.21†	Amended and Restated License and Collaboration Agreement, dated July 27, 2021, by and between Protagonist Therapeutics, Inc. and Janssen Biotech, Inc.	10-Q	001-37852	10.1	11/3/2021	
10.22†	Arbitration Resolution Agreement, dated August 4th, 2021, by and among Protagonist Therapeutics, Inc. and Zealand Pharma, A/S.	10-Q	001-37852	10.2	11/3/2021	
10.23+	Employment Offer Letter, by and between Protagonist Therapeutics Inc. and Asif Ali, dated March 25, 2022.	10-Q	001-37852	10.1	5/5/2022	
10.24+	Offer Letter, by and between Protagonist Therapeutics Inc. and Arturo Molina, M.D., Ph.D., dated November 1, 2022.	10-K	001-37852	10.25	3/15/2022	
10.25+	Severance Agreement, by and between Protagonist Therapeutics Inc. and Arturo Molina, M.D., Ph.D., dated November 7, 2022.	10-K	001-37852	10.26	3/15/2022	
10.26†	License and Collaboration Agreement by and between Protagonist Therapeutics, Inc. and Takeda Pharmaceuticals USA, Inc., dated January 31, 2024.	10-Q	001-37852	10.1	5/7/2024	
10.27	Third Amendment, dated May 6, 2024, to Lease, dated March 6, 2017, by and between Protagonist Therapeutics, Inc. as Tenant and BMR-Pacific Research Center, LP, as Landlord.	10-Q	001-37852	10.1	8/6/2024	
10.28†	Amendment 1, dated November 14, 2024, to Amended and Restated License and Collaboration Agreement, dated July 27, 2021, by and between Protagonist Therapeutics, Inc. and Janssen Biotech, Inc.					X
19.1	Insider Trading Policy					X
21.1	List of Subsidiaries.					X

Exhibit Number	Exhibit Description	Incorporation By Reference				Filed or Furnished Herewith
		Form	SEC File No.	Exhibit	Filing Date	
23.1	Consent of Independent Registered Public Accounting Firm.					X
24.1	Power of Attorney (included in signature page of this Form 10-K).					X
31.1	Certification of Chief Executive Officer required by Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
31.2	Certification of Chief Financial Officer required by Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
32.1*	Certification of Chief Executive Officer and Chief Financial Officer, as required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
97.1	Compensation Recoupment ("Clawback") Policy, adopted by Protagonist Therapeutics Inc. November 23, 2023.	Form 10-K	001-37852	97.1	2/27/2024	
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL Document.					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document.					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document.					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.					X
104	Cover Page Interactive Data File – the cover page interactive data file does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.					

+ Indicates management contract or compensatory plan, contract or agreement.

† Certain identified information has been omitted by means of marking such information with asterisks in reliance on Item 601(b)(10)(iv) of Regulation S-K because it is both (i) not material and (ii) the type that the registrant treats as private or confidential.

* This certification attached as Exhibit 32.1 that accompanies this Annual Report on Form 10-K is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Protagonist Therapeutics, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of the Form 10-K, irrespective of any general incorporation language contained in such filing.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements 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.

PROTAGONIST THERAPEUTICS, INC.

Date: February 21, 2025

By: /s/ Dinesh V. Patel, Ph.D.
Dinesh V. Patel, Ph.D.
President, Chief Executive Officer and Director
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Dinesh V. Patel and Asif Ali, and each of them, his or her true and lawful attorneys-in-fact, with full power of substitution, for him in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith with the Securities and Exchange Commission, hereby ratifying and confirming all that said attorneys-in-fact or any of them or their substitute or substitutes may lawfully do or cause to be done by virtue thereof.

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 in the capacities and on the dates indicated:

Signature	Title	Date
/s/ Dinesh V. Patel, Ph.D. Dinesh V. Patel, Ph.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	February 21, 2025
/s/ Asif Ali Asif Ali	Executive Vice President, Chief Financial Officer *(Principal Financial and Accounting Officer)*	February 21, 2025
/s/ Harold E. Selick, Ph.D. Harold E. Selick, Ph.D.	Chairman of the Board of Directors	February 21, 2025
/s/ Bryan Giraudo Bryan Giraudo	Director	February 21, 2025
/s/ Sarah O'Dowd Sarah O'Dowd	Director	February 21, 2025
/s/ William D. Waddill William D. Waddill	Director	February 21, 2025
/s/ Lewis T. Williams, M.D., Ph.D. Lewis T. Williams, M.D., Ph.D.	Director	February 21, 2025

Exhibit 4.2

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following is a description of the authorized capital stock of Protagonist Therapeutics, Inc., a Delaware Corporation ("we," "us," "our," or the "Company"). The following summaries and descriptions are not complete and are subject to and qualified by reference to the actual provisions of the Company's Amended and Restated Certificate of Incorporation, as amended from time to time (the "Charter") and Amended and Restated Bylaws (the "Bylaws"), both of which have been filed with the Securities and Exchange Commission and are incorporated by reference herein. We encourage you to read our Charter, our Bylaws, and the applicable provisions of the Delaware General Corporation Law for more information.

General

Pursuant to our Charter, the Company is authorized to issue up to 180,000,000 shares of common stock, par value $0.00001 per share ("Common Stock"), and up to 10,000,000 shares of preferred stock, par value $0.00001 per share ("Preferred Stock").

Common Stock

Voting Rights

Holders of our Common Stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders, including the election of directors, and do not have cumulative voting rights. Accordingly, the holders of a majority of the outstanding shares of our Common Stock entitled to vote in any election of directors can elect all of the directors standing for election, if they so choose, other than any directors that holders of any Preferred Stock we may issue may be entitled to elect.

Dividend Rights

Subject to preferences that may be applicable to any then outstanding Preferred Stock, holders of our Common Stock are entitled to receive ratably those dividends, if any, as may be declared by the board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our Common Stock will be entitled to share ratably in the assets legally available for distribution to stockholders after the payment of or provision for all of our debts and other liabilities, subject to the prior rights of holders of any Preferred Stock then outstanding.

Rights and Preferences

Holders of our Common Stock have no preemptive or conversion rights or other subscription rights and there are no redemption or sinking funds provisions applicable to our Common Stock. The rights, preferences and privileges of holders of our Common Stock are subject to and may be adversely affected by the rights of the holders of any series of Preferred Stock that we may designate and issue in the future.

Anti-Takeover Effects of Delaware Law, our Charter and our Bylaws

Some provisions of Delaware law, our Charter and our Bylaws contain provisions that could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in

their best interest or in our best interests, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated Preferred Stock—The ability to authorize undesignated Preferred Stock makes it possible for our board of directors to issue Preferred Stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management of the Company.

Stockholder Meetings—Our Bylaws provide that a special meeting of stockholders may be called only by our chairman of the board, chief executive officer or president, or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals —Our Bylaws establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent —Our Charter and Bylaws eliminate the right of stockholders to act by written consent without a meeting.

Staggered Board—Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third-party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Removal of Directors—Our Charter provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two thirds of the total voting power of all of our outstanding voting stock then entitled to vote in the election of directors.

Stockholders Not Entitled to Cumulative Voting —Our Charter does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our Common Stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our Preferred Stock may be entitled to elect.

Delaware Anti-Takeover Statute —We are subject to Section 203 of the Delaware General Corporation Law, which prohibits persons deemed to be “interested stockholders” from engaging in a “business combination” with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an “interested stockholder” is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status owned, 15% or more of a corporation’s voting stock. Generally, a “business combination” includes a merger, consolidation, asset or stock sale, other transaction resulting in an increase of interested stockholder’s share of the stock of the corporation or any receipt by the interested stockholder of any financial benefit by or through the corporation. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Choice of Forum—Our Charter provides that, unless we consent in writing to the selection of an alternative form, the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our Charter or Bylaws; or (4) any action asserting a claim governed by the internal affairs doctrine. This provision does not apply to suits brought to enforce a duty or liability created by the Securities Exchange Act of 1934, as amended, or any other claim for which the U.S. federal courts have exclusive jurisdiction. Our Charter also provides that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision. It is possible that a court of law could rule that the choice of forum provision contained in our Charter is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

Amendment of Charter Provisions—The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue Preferred Stock, would require approval by holders of at least two thirds of the total voting power of all of our outstanding voting stock.

The provisions of Delaware law, our Charter and our Bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our Common Stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in the composition of our board and management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Symbol and Listing

Our Common Stock is listed on The Nasdaq Global Market under the symbol “PTGX.”

Transfer Agent and Registrar

The transfer agent and registrar for our Common Stock is Equiniti Trust Company, LLC. The transfer agent and registrar’s address is 48 Wall Street, Floor 23, New York, New York 10005. Telephone number is (800) 468-9716.

[***] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE IT IS BOTH (i) NOT MATERIAL AND (ii) IS THE TYPE THAT THE REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.

Exhibit 10.28

AMENDMENT 1 TO AMENDED AND RESTATED LICENSE AND COLLABORATION AGREEMENT BY AND BETWEEN JANSSEN BIOTECH, INC. AND PROTAGONIST THERAPEUTICS, INC

Reference is made to the Amended and Restated License and Collaboration Agreement of July 27, 2021 ("the **Agreement**") by and between the Janssen Biotech, Inc. (hereafter "**Janssen**"), and Protagonist Therapeutics, Inc. (hereafter "**Protagonist**"), or individually as "Party" or collectively as "Parties." This Amendment is effective as of November 14, 2024 between Janssen and Protagonist.

In general, the Parties agreed to amend the Milestone Events D, E, and L under section 7.3.

NOW THEREFORE, for valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties hereby agree to amend Section 7.3 as follows:

7.3. **Development and Approval Milestones**.

7.3.1. **Development and Approval Milestone Events**. Janssen will notify Protagonist in writing within [***] after the first achievement by Janssen or any of its Affiliates or sublicensees of any of the milestone events set forth in the table below (each, a "**Milestone Event**"). In consideration of the rights and licenses granted to Janssen hereunder, Janssen shall pay to Protagonist the applicable milestone payment set forth in the table below (each, a "**Milestone Payment**") within [***] after receipt of an invoice from Protagonist with respect to achievement of each Milestone Event that occurs prior to or on the date of database lock for the PTG-200 Phase 2A Clinical Trial and [***] after receipt of an invoice from Protagonist with respect to achievement of each Milestone Event that occurs after such date.

Milestone Event	**Milestone Payment for Initial Product**	**Milestone Payment for 2nd Generation Product**
A. [Intentionally omitted]	[Intentionally omitted]	[Intentionally omitted]
B. Completion of first Phase 1 Clinical Trial of a 2nd Generation Product (i.e., database lock)	N/A	US$7,500,000
B-1. Dosing of 3rd patient in first Phase 2B Clinical Trial of the Initial Product for CD	US$50,000,000	N/A
C. Dosing of 3rd patient in first Phase 2 Clinical Trial of a 2nd Generation Product for any Indication	N/A	US$25,000,000

C-1. Dosing of 3rd patient in first Phase 3 Clinical Trial of the Initial Product or any 2nd Generation Product for any Indication	US$50,000,000 (payable one time only, upon the first occurrence with respect to the Initial Product or any 2nd Generation Product)	
D. Phase 3 Clinical Trial of a Licensed Product for any Indication Meets primary clinical endpoint	US$[***]	US$115,000,000 US$165,000,000
E. Acceptance of filing of an NDA or BLA by the FDA for use of a Licensed Product in any Indication[Intentionally omitted]	US$35,000,000 [Intentionally omitted]	US$35,000,000 [Intentionally omitted]
F. Receipt of Marketing Approval of a Licensed Product for any Indication	US$[***]	US$50,000,000
G. [***]	US$[***]	N/A
H. [***]	US$[***]	N/A
I. Acceptance of filing of an NDA or BLA by the FDA for use of a Licensed Product in a Second Indication	US$[***]	US$25,000,000
J. Receipt of Marketing Approval of a Licensed Product for a Second Indication	US$[***]	US$45,000,000
K. Dosing of 3rd patient in first Phase 2 Clinical Trial of a Licensed Product for a Second Indication	US$[***]	US$10,000,000
L. Dosing of 3rd patient in first Phase 3 Clinical Trial of a Licensed Product for a Second Indication[Intentionally omitted]	US$15,000,000 [Intentionally omitted]	US$15,000,000 [Intentionally omitted]
M. [***]	US$[***]	US$[***]
N. [***]	US$[***]	US$[***]

7.3.2. **Milestone Rules**.

(a) Each Milestone Payment shall be payable only once, even if the corresponding Milestone Event occurs more than once or with respect to more than one Licensed Product of the applicable type (*i.e.*, if a Milestone Event occurs with respect to more than one Initial Product or a Milestone Event occurs with respect to more than one 2nd Generation Product). Each Milestone Payment shall be nonrefundable and non-creditable.

(b) The Milestone Payment for Milestone Event C-1 shall be payable one time only, upon the first occurrence of Milestone Event C-1 with respect to the Initial Product or any 2nd Generation Product. For example, if Milestone Event C-1 occurs for the Initial Product before the dosing of the 3rd patient in a Phase 3 Clinical Trial of a 2nd Generation Product for any Indication, then (x) the Milestone Payment for Milestone Event C-1 will be payable for occurrence of Milestone Event C-1 for the Initial Product, and (y) dosing of the 3rd patient in a Phase 3 Clinical Trial of a 2nd Generation Product will not cause any obligation to pay the Milestone Payment for Milestone Event C-1 a second time.

(c) For purposes of Milestone Event D, a Phase 3 Clinical Trial of a Licensed Product for an Indication will be deemed to meet its primary clinical endpoint on the first date when all of the following have occurred:

(1) The statistical analysis of the data from such trial is complete;

(2) The top-line results from such trial have become available to Janssen; and

(3) The top-line results demonstrate that the primary clinical endpoint (as described in the protocol for such trial) is formally statistically significant, where "statistically significant" is defined as achieving a prespecified level of significance value using the procedure defined in the protocol and statistical analysis plan for such trial.

7.3.3. [***].

7.3.4. **Definition of Second Indication**. A "**Second Indication**" means:

(a) [***];

(b) with respect to a 2nd Generation Product,

(1) [***];

(2) as used in Milestone Event J, an Indication other than the Indication with respect to which Milestone Event F occurred for a 2nd Generation Product; and

(3) as used in Milestone Event K, an Indication other than the Indication with respect to which Milestone Event C occurred for a 2nd Generation Product; and

(4) as used in Milestone Event L, either: (x) if Milestone Event C-1 occurs for a 2nd Generation Product before the dosing of the 3rd patient in a Phase 3 Clinical Trial of the Initial Product, an Indication other than the Indication with respect to which Milestone Event C-1 occurred or (y) if Milestone Event C-1 occurs for the Initial Product before the dosing of the 3rd patient in a Phase 3 Clinical Trial of a 2nd Generation Product, an Indication with respect to which Milestone Event C-1 occurred.

7.3.5. [***].

7.3.6. **Skipped Milestones**. With respect to the Milestone Events set forth in the table above in Section 7.3.1 and subject to Section 7.3.2, if for any reason:

(a) Milestone Event B does not occur for a 2nd Generation Product before the occurrence of Milestone Event C for a 2nd Generation Product, then Milestone Event B shall be deemed to occur for a 2nd Generation Product concurrently with the occurrence of Milestone Event C;

(b) Milestone Event C does not occur for a 2nd Generation Product before the occurrence of Milestone Event C-1 for a 2nd Generation Product, then Milestone Event C shall be deemed to occur for a 2nd Generation Product concurrently with the occurrence of Milestone Event C-1 for a 2nd Generation Product; and

(c) Milestone Event C does not occur for a 2nd Generation Product before the occurrence of Milestone Event D for a 2nd Generation Product, then Milestone Event C shall be deemed to occur for a 2nd Generation Product concurrently with the occurrence of Milestone Event D;.

[***]

(e) Milestone Event K for the Initial Product or a 2nd Generation Product, respectively, does not occur before the occurrence of Milestone Event L for the Initial Product or a 2nd Generation Product, respectively, then Milestone Event K shall be deemed to occur for the applicable product concurrently with the occurrence of Milestone Event L for the applicable product; and

[***]

Except as otherwise expressly provided herein, the Agreement shall remain in full force and effect without any amendments or modifications.

IN WITNESS WHEREOF, the Parties have caused this Amendment to be executed by their duly authorized representative, effective as of the date above written.

Parties explicitly agree to execute this Agreement by way of an electronic signature, and agree this shall constitute a valid and enforceable agreement between the parties. The present Agreement is made in pdf-version which is signed electronically by each party.

Protagonist Therapeutics, Inc.	**Janssen Biotech, Inc.**
By: /s/ Dinesh Patel	By: /s/ Kevin Hamill
Name: Dinesh Patel	Name: Kevin Hamill

Title: President & CEO

Date: November 13, 2024

Title: President

Date: November 14, 2024

Exhibit 19.1

INSIDER TRADING AND TRADING WINDOW POLICY

Frequently Asked Questions

1. ***What is insider trading?***

A: Insider trading is the buying or selling of stocks, bonds, futures, or other securities by someone in possession of material, non-public information. Insider trading also includes trading in derivative securities (puts and calls), the price of which is linked to the underlying price of a company's stock. It does not matter how many shares you buy or sell, or whether the information has an effect on the stock price— if you have material, non-public information and you trade, you have broken the law.

2. ***Why is insider trading illegal?***

A: If company insiders are able to use their confidential knowledge to their financial advantage, other investors would not have confidence in the fairness and integrity of the marketplace. Requiring those who have such information to disclose (the information to the public) or abstain (from trading) ensures an even playing field.

3. ***What is material, non-public information?***

A: Information is material if it would influence a reasonable investor to buy or sell a stock,bond or other security or if it would influence the price that a reasonable investor would pay for a stock, bond or other security. This could mean many things, including but not limited to, financial results, merger or acquisition news, regulatory approval, clinical data and other drug candidate developments, drug commercialization developments, licensing, joint venture and other collaboration developments, litigation filings or results, governmental actions or key personnel hires or departures. Either positive or negative information may be material. Information is non-public if it has not yet been released and disseminated to the public.

4. ***Who can be guilty of insider trading?***

A: Anyone who buys or sells a security while in possession of material, non-public information. It does not matter if you are not an executive officer or director, or even if you do not work at Protagonist — if you know something material about the value of a security that not everyone else does, regardless of who you are, you can be found guilty of insider trading.

5. ***Does Protagonist have an insider trading policy?***

A: Yes. The policy is attached to this FAQ.

6. ***What if I work in a foreign office?***

A: There is no difference. The policy and law applies to you. Because our common stock trades on a United States, or U.S., securities exchange, the insider trading laws of the U.S. apply. The U.S. Securities and Exchange Commission, or SEC, (a U.S. government agency in charge of investor protection) and the Financial Industry Regulatory Authority, or FINRA, (a private regulator that oversees U.S. exchanges) routinely investigate trading in a company's securities conducted by internationally-based individuals and firms. In addition, as a Protagonist employee, our policies apply to you no matter where in the world you work.

7. ***What if I don't buy or sell anything, but I tell someone else the information and they buy or sell?***

A: That is called "tipping." You are the "tipper" and the other person is called the "tippee". If the tippee buys or sells based on that material, non-public information, you might still be guilty of insider trading. In fact, if you tell family members who tell others and those people then trade on the information, those family members might be guilty of insider trading too. As a result, you may not discuss material, non-public information about Protagonist with anyone outside Protagonist, including spouses, family members, friends, or business associates. This includes anonymous discussion on the Internet about Protagonist or companies with which Protagonist does business.

8. ***What if I don't tell them the information itself; I just tell them whether they should buy or sell?***

A: That is still tipping, and you can still be found guilty of insider trading. According to our policies, you may never recommend to another person that they buy, hold or sell our common stock or any derivative security related to our common stock.

9. ***What are the penalties if I trade on inside information, or tip off someone else?***

A: Anyone found liable in a civil case for trading on inside information may need to pay the U.S. government an amount equal to any profit made or any loss avoided and may also face apenalty of up to three times this amount. Persons found liable for tipping inside information, even if they did not trade themselves, may face a penalty of up to three times the amount of any profit gained or loss avoided by everyone in the chain of tippees. In addition, anyone convicted of criminal insider trading can face prison terms and additional fines.

10. ***What is "loss avoided"?***

A: If you sell a common stock or a related derivative security (such as publicly traded call or put options) before negative news is publicly announced, and as a result of the announcement the stock price declines, you have avoided the loss caused by the negative news.

11. ***Am I restricted from trading securities of any companies except Protagonist (for example a customer or competitor of Protagonist)?***

A: Yes. U.S. insider trading laws restrict everyone from trading in a company's securities based on material non-public information about that company, regardless of whether the person is directly connected with that company. Therefore, if you obtain material non-public information about another company, you should not trade in that company's securities. You should be particularly conscious of this restriction if, through your position at Protagonist, you sometimes obtain sensitive, material information about other companies and their business dealings with Protagonist.

12. ***So if I do not trade Protagonist securities when I have material non-public information, and I don't "tip" other people, I am in the clear, right?***

A: Not necessarily. Even if you do not violate U.S. law, you may still violate our policies. Our policies are stricter than the law requires, so that we and our employees can avoid even the appearance of wrongdoing. Therefore, please review the entire policy carefully.

13. ***So when can I buy or sell my Protagonist securities?***

A: According to our policies, if you have material, non-public information, you may not buy or sell our common stock until the second trading day after that information is released or announced to the public. At that point, the information is considered public. **Even if you do not have material, non-public information, you may not trade in our common stock during any trading "blackout" period.** (trading blackout periods may be announced by email.)

14. ***What steps do I need to follow before engaging in any transaction in Protagonist securities if I am an officer, director or employee of Protagonist?***

A: According to our policies, all officers, directors and employees must obtain pre-clearance of any transaction from the Company's Clearing Officer (the General Counsel or Chief Financial Officer), at least two business days in advance of the proposed transaction. The Clearing Officer will then determine whether the transaction may proceed and, if required, will coordinate Protagonist's assistance in complying with the reporting requirements under Section 16(a) of the Exchange Act, if any. Pre-cleared transactions not completed within three trading days of pre-clearance shall require new pre-clearance under the provisions of this paragraph. Protagonist may, at its discretion, shorten such period of time.

15. ***If I have an open order to buy or sell Protagonist securities on the date the trading windowcloses, my broker will cancel the open order and won 't execute the trade, right?***

A: No. If you have any open orders at the time the trading window closes, it is your responsibility to cancel these orders with your broker. If you have an open order and it executes after the trading window closes, it is a violation of our insider trading policy and may also be a violation of the insider trading laws.

16. ***Am I allowed to trade derivative securities of Protagonist? Or short Protagonist common stock?***

A: No. Under our policies, you may not trade in derivative securities related to our common stock, which includes, but is not limited, to publicly traded call and put options. In addition, under our policies, you may not engage in short selling of our common stock at any time.

"Derivative securities" are securities other than common stock that are speculative in nature because they permit a person to leverage his or her investment using a relatively small amount of money. Examples of derivative securities include (but are not limited to) "put options" and "call options". These are different from employee stock options, which are not derivative securities.

"Short selling" is profiting when you expect the price of the stock to decline, and includes transactions in which you borrow stock from a broker, sell it, and eventually buy it back on the market to return the borrowed shares to the broker. Profit is made through the expectation that the stock price will decrease during the period of borrowing.

17. ***Why does Protagonist prohibit trading in derivative securities and short selling?***

A: Many companies with volatile stock prices have adopted such policies because of the temptation it represents to try to benefit from a relatively low-cost method of trading on short term swings in stock prices (without actually holding the underlying common stock) and encourages speculative trading. For this reason, we have decided to prohibit employees from such trading. As we are dedicated to building stockholder value, short selling our common stock is adverse to our stated values and would not be received well by our stockholders.

18. ***Can I purchase Protagonist securities on margin or hold them in a margin account?***

A: Under our policies, you may not purchase our common stock on margin or hold it in a margin account at any time.

"Purchasing on margin" is the use of borrowed money from a brokerage firm to purchase our securities. Holding our securities in a margin account includes holding the securities in an account in which the shares can be sold to pay a loan to the brokerage firm.

19. ***Why does Protagonist prohibit me from purchasing Protagonist securities on margin or holding them in a margin account?***

A: Margin loans are subject to a margin call whether or not you possess insider information atthe time of the call. If your margin call were called at a time when you had insider information and you could not or did not supply other collateral, you and Protagonist could be subject to litigation based on your insider trading activities: the sale of the stock (through the margin call) when you possessed material non-public information. The sale would be attributed to you, even though the lender made the ultimate determination to sell. The SEC takes the view that you made the determination to not supply the additional collateral and you are therefore responsible for the sale.

20. ***Can I exercise stock options during a trading blackout period or when I possess material non-public information?***

A: Yes. You may exercise the option and receive shares, but you may not sell the shares (even to pay the exercise price or any taxes due) or otherwise settle the option during a trading blackout period or any time that you have material, non-public information. Also note that if you choose to exercise and hold the shares, you will be responsible at that time for the exercise price and any taxes due.

21. ***Am I subject to the trading blackout period if I am no longer an employee of Protagonist?***

A: It depends. If your employment with Protagonist ends on a day that the trading window is closed, you will be subject to the trading blackout period then in effect. If your employment with Protagonist ends on a day that the trading window is open, you will not be subject to the next trading blackout period. However, even if you are not subject to our trading blackout period after you leave Protagonist, you should not trade in Protagonist securities if you possess material non-public information. That restriction stays with you as long as the information you possess is material and not released by Protagonist.

22. ***Can I gift stock while I possess material non-public information or during a trading blackout period?***

A: Because of the potential for the appearance of impropriety, you may not make gifts, whether to charities, to a trust or otherwise, of our common stock when you possess material non-public information or during a trading blackout period.

23. ***What if I purchased publicly traded options or other derivative securities before I became a Protagonist employee (or contractor or consultant)?***

A: The same rules apply as for employee stock options. You may exercise the publicly traded options at any time, but you may not sell such securities during a trading blackout period or at any time that you have material, non-public information. When you become a Protagonist employee, you must report to our Finance department that you hold such publicly traded options or other derivative securities.

24. ***May I own shares of a mutual fund that invests in Protagonist?***

A: Yes.

25. ***Are mutual fund shares holding Protagonist subject to the trading blackout periods?***

A: Generally no. Unless Protagonist shares constitute more than 10% of the fund, you may trade in mutual funds holding our common stock at any time.

26. ***May I use a "routine trading program" or "10b5-1 plan***

A: Yes, subject to the requirements discussed in our Insider Trading and Trading Window Policy set forth below. A routine trading program, also known as a 10b5-1 plan, allows you to set up a highly structured program with your stock broker through which you specify ahead of

time the date, price, and amount of securities to be traded. If you wish to create a 10b5-1 plan, you should contact the Finance department at least ten [10] business days in advance for approval, and the plan must be executed during an open trading window and at a time when you do not have material, non-public information.

27. ***What happens if I violate our insider trading policy?***

A: Violation of our policies may result in severe personnel action, including a memo to your personnel file and up to and including termination of your employment or other relationship with Protagonist. In addition, you may be subject to criminal and civil enforcement actions by the government.

28. ***Who should I contact if I have questions about our insider trading policy?***

A: You should contact the Company's Stock Plan Administrator, or General Counsel or Chief Financial Officer.

INSIDER TRADING AND TRADING WINDOW POLICY

Because our stock is publicly traded, you must comply with the provisions of federal and state securities laws and with our policies. During the course of your relationship with Protagonist Therapeutics, Inc. ("**the Company**"), you will learn information about us that is not publicly known. **It is illegal for you to buy or sell our stock or other securities, or the stock of companies working with the Company, on the basis of material, non-public information. It is also illegal for you to pass such information on to others who use it to buy or sell our stock.**

COVERED PERSONS

This policy applies to all directors, officers, employees, consultants and contractors of the Company. This policy also applies to all family members and anyone that lives in the household (other than household employees) of those covered by this policy and all companies controlled by those covered by this policy.

STATEMENT OF POLICY

This policy prohibits not only illegal activities, but also other trading activities that may not be illegal. These additional restrictions are designed to protect both you and us from even the appearance of improper activity. Our policy is as follows:

1. You may not trade our stock while you possess information about the Company that is both material and non-public. Material information is information that a reasonable person would consider important in deciding whether (or at what price) to buy, hold or sell our stock. For example, material information may include (but is not limited to) financial results, merger or acquisition news, regulatory approval, clinical data and other drug candidate developments, drug commercialization developments, licensing, joint venture and other collaboration developments, litigation filings or results, governmental actions or key personnel hires or departures. Non-public information is information that has not been announced publicly, such as by press release, conference call, public filing or similar means of public dissemination. You must wait until the second trading day after the information is publicly announced before you can trade. For example, if the information is publicly announced late on a Tuesday, you cannot trade until Thursday. In addition, you are not allowed to buy or sell stock during any "blackout" period announced by the Company.

2. You may not discuss material, non-public information about the Company with anyone outside the Company, and discussions inside the Company should be kept on a need-to-know basis. This prohibition covers spouses, family members, friends, business associates, or persons with whom we are doing business (except to the extent that such persons are covered by a non-disclosure agreement and the discussion is necessary to accomplish a business purpose of the Company).

3. You may buy or sell our stock only when the trading window period is open and when you do not possess material, non-public information about the Company. If you are a director, officer or employee of the Company, you must also receive approval prior to engaging in transactions in the Company's stock, as described in paragraph 4 below. Open trading window periods are those periods of time during which employees, contractors and consultants can, potentially, trade our stock, so long as they are not in possession of material, non-public information. At these times, the "window" is said to be "open." This window period may be closed and may not reopen if, in the judgment of the Company's General Counsel, there exists undisclosed information that would make trades by members of the Company's management and directors inappropriate. This closing of the window/prohibition on trading is commonly called, and referred to in this policy, as a "trading blackout." A trading blackout may be implemented, for example, if there is some information or development with or relating to the Company's business that merits a suspension of trading. It is important to note that the fact that a trading blackout has been imposed and/or that the window period has not reopened should itself be considered inside information. If a trading blackout has been imposed due to the existence of material non-public information, generally the window period will not re-open until the second trading day (e.g., one full trading day has elapsed) after the Company's public dissemination of the material non-public information, or until such time a determination is made that it is no longer material non-public information.

4. In addition to the requirements of paragraph 3 above, if you are a director, officer or employee of the Company, you may not may not engage in any transaction in the Company's securities, including any purchase or sale in the open market, loan, pledge, hedge or other transfer of beneficial ownership without first obtaining pre-clearance of the transaction from the Company’s Clearing Officer (the General Counsel or Chief Financial Officer), at least two business days in advance of the proposed transaction. The Clearing Officer will then determine whether the transaction may proceed and, if required, will coordinate the Company's assistance in complying with the reporting requirements under Section 16(a) of the Exchange Act, if any. Pre-cleared transactions not completed within three trading days shall require new pre-clearance under the provisions of this paragraph. The Company may, at its discretion, shorten such period of time.

5. You may not engage in transactions designed to hedge or offset any decrease in the market value of the Company’s stock or trade derivative securities of the Company at any time. Derivative securities are securities other than common stock that are speculative in nature because they permit a person to leverage his or her investment using a relatively small amount of money. Examples of derivative securities include (but are not limited to) "put options" and "call options". These are different from employee stock options, which are not derivative securities.

6. You may not engage in short-term or speculative trading (generally defined as selling Company securities within six months following a purchase). You may not engage in short selling of our securities or purchase our securities on margin or hold them in a margin account at any time. Selling short includes transactions in which you borrow stock from a broker, sell it, and eventually buy it back on the market to return the borrowed shares to the broker. Profit is made through the expectation that the stock price will decrease during the period of borrowing. Purchasing our securities on margin is the use of borrowed money from a brokerage firm to purchase our securities. Holding our securities in a margin account includes holding the securities in an account in which the shares can be sold to pay a loan to a brokerage firm.

7. You may not participate in "chat rooms" or other electronic discussion groups or contribute to blogs, bulletin boards or social media forums on the Internet concerning the activities of the Company or other companies with which the Company does business, even if you do so anonymously, unless doing so is part of your job responsibilities and you have explicit authorization from the Finance department.

8. You may never recommend to another person that he or she buy, hold or sell our stock.

9. The restrictions above also apply to transactions in the stock of other companies, to the extent you have learned material non-public information about these companies as a result of your role with the Company.

The only exceptions to this policy are specifically noted below. Trading activities that may be necessary or justifiable for independent reasons (such as the need to raise money for an emergency expenditure) or that are small transactions are **not** exempted from this policy. The insider trading laws do not recognize any mitigating circumstances and, in any event, even the appearance of an improper transaction must be avoided to preserve our reputation for adhering to the highest standards of conduct.

RULE 10B5-1 PLANS

Notwithstanding the prohibitions above, directors, officers and certain employees may establish written programs (i.e., trading plans) pursuant to Rule 10b5-l (c) of the Securities Exchange Act of 1934 which permit (a) automatic trading of our stock according to set criteria or (b) trading of our stock by an independentperson (such as an investment bank) who is not aware of material non-public information. So long as the program is properly established, trading pursuant to a program may occur even at a time outside of our "open window" or when the plan participant is aware of material non-public information. Each form of program must be reviewed and approved in advance by the Company, solely to confirm compliance with the guidelines set forth herein. The Company will not review or pre-approve the trading specifics of any program, only the form of program itself. These programs may only be established and subsequently amended during an open window and at a time when the plan participant is not aware of material non-public information.

Once the program becomes effective, it cannot be changed or deviated from except (a) with notice to and approval from the Company, (b) in full compliance with the requirements of the program guidelines and (c) at a time when the plan participant is permitted to trade in our stock under the guidelines set forth herein. Plans must specify a cooling off period of at least 30 days between plan execution and the date of the first trade under the plan.

CONSEQUENCES OF VIOLATIONS

Violations of either the insider trading laws or this policy are extremely serious matters. The U.S. Securities and Exchange Commission and the stock exchanges monitor stock trading and routinely investigate suspicious activity. The penalties for violating the insider trading laws are severe (including fines and imprisonment), and even having to respond to an investigation can result in significant legal expenses and unwanted negative publicity for both you and us.

ADDITIONAL INFORMATION AND QUESTIONS

If you have any questions about any aspect of this policy, you are encouraged to contact the Company's Stock Plan Administrator, General Counsel or Chief Executive Officer. You may also refer to the "Frequently Asked Questions" preceding this policy.

Exhibit 21.1

SUBSIDIARIES OF PROTAGONIST THERAPEUTICS, INC.

Subsidiary	Jurisdiction of Formation/Organization
Protagonist Pty Limited	Australia

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. 333-227216 and 333-266595) of Protagonist Therapeutics, Inc.,
(2) Registration Statements (Form S-8, Nos. 333-237066 and 333-263097) pertaining to the Protagonist Therapeutics, Inc. 2016 Equity Incentive Plan, the Protagonist Therapeutics, Inc. 2016 Employee Stock Purchase Plan, and the Protagonist Therapeutics, Inc. Amended and Restated 2018 Inducement Plan,
(3) Registration Statement (Form S-8, No. 333-225294) pertaining to the Protagonist Therapeutics, Inc. Amended and Restated 2018 Inducement Plan, and
(4) Registration Statements (Form S-8 Nos. 333-213120, 333-216532, 333-22 3500, 333-230213, 333-254090, 333-270573 and 333-277409) pertaining to the Protagonist Therapeutics, Inc. 2016 Equity Incentive Plan and the Protagonist Therapeutics, Inc. 2016 Employee Stock Purchase Plan;

of our reports dated February 21, 2025, with respect to the consolidated financial statements of Protagonist Therapeutics, Inc. and the effectiveness of internal control over financial reporting of Protagonist Therapeutics, Inc. included in this Annual Report (Form 10-K) of Protagonist Therapeutics, Inc. for the year ended December 31, 2024.

/s/ Ernst & Young LLP

San Mateo, California

February 21, 2025

Exhibit 31.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Dinesh V. Patel, certify that:

1. I have reviewed this Annual Report on Form 10-K of Protagonist Therapeutics, 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.

Date: February 21, 2025

/s/ Dinesh V. Patel, Ph.D.
Dinesh V. Patel, Ph.D.
President, Chief Executive Officer

Exhibit 31.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Asif Ali, certify that:

1. I have reviewed this Annual Report on Form 10-K of Protagonist Therapeutics, 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.

Date: February 21, 2025

/s/ Asif Ali
Asif Ali
Executive Vice President, Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER AND CHIEF FINANCIAL OFFICER
Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

Pursuant to Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, we, Dinesh V. Patel, President and Chief Executive Officer of Protagonist Therapeutics, Inc. (the "Company"), and Asif Ali, Executive Vice President and Chief Financial Officer of the Company, each hereby certify that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the year ended December 31, 2024 (the "Annual Report"), to which this Certification is attached as Exhibit 32.1, fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended; and

2. The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Dinesh V. Patel, Ph.D.
Date: February 21, 2025 **Dinesh V. Patel, Ph.D.**
President, Chief Executive Officer

/s/ Asif Ali
Date: February 21, 2025 **Asif Ali**
Executive Vice President, Chief Financial Officer

This certification accompanies the Form 10-K to which it relates, and is not deemed to be filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Protagonist Therapeutics, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.