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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-Q

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

For the quarterly period ended March 31, 2022

or

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

For the transition period from _____ to

Commission File 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 94560-1160	**(510) 474-0170**
(Address, including zip code, of registrant's principal executive offices)	**(Telephone number, including area code, of registrant's principal executive offices)**

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

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

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	☐
		Smaller reporting company	☐
Non-accelerated filer	☐	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 is a shell company (as defined in Rule 12b-2 of the Exchange Act of 1934). Yes ☐ No ☒

As of April 29, 2022, there were 48,656,189 shares of the registrant's Common Stock, par value $0.00001 per share, outstanding.

PROTAGONIST THERAPEUTICS, INC.
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PART I. – FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

PROTAGONIST THERAPEUTICS, INC.
Condensed Consolidated Balance Sheets
(Unaudited)
(In thousands, except share and per share data)

	March 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 98,477	$ 123,665
Marketable securities	206,812	203,235
Receivable from collaboration partner and contract asset - related party	25,150	1,566
Research and development tax incentive receivable	2,878	2,792
Prepaid expenses and other current assets	8,205	9,478
Total current assets	341,522	340,736
Property and equipment, net	2,064	1,798
Restricted cash - noncurrent	225	225
Operating lease right-of-use asset	4,485	4,936
Total assets	$ 348,296	$ 347,695
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 7,159	$ 1,600
Payable to collaboration partner - related party	380	899
Accrued expenses and other payables	32,874	37,716
Deferred revenue - related party	768	1,601
Operating lease liability - current	2,275	2,200
Total current liabilities	43,456	44,016
Operating lease liability - noncurrent	3,062	3,658
Total liabilities	46,518	47,674
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.00001 par value, 10,000,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $0.00001 par value, 90,000,000 shares authorized 48,552,102 and 47,838,330 shares issued and outstanding as of March 31, 2022 and December 31, 2021, respectively	—	—
Additional paid-in capital	732,542	709,682
Accumulated other comprehensive loss	(472)	(299)
Accumulated deficit	(430,292)	(409,362)
Total stockholders' equity	301,778	300,021
Total liabilities and stockholders' equity	$ 348,296	$ 347,695

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

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

	Three Months Ended March 31,	
	2022	2021
License and collaboration revenue - related party	$ 25,722	$ 6,189
Operating expenses:		
Research and development	36,318	24,245
General and administrative	10,515	5,965
Total operating expenses	46,833	30,210
Loss from operations	(21,111)	(24,021)
Interest income	168	102
Other income (expense), net	13	(79)
Net loss	$ (20,930)	$ (23,998)
Net loss per share, basic and diluted	$ (0.43)	$ (0.54)
Weighted-average shares used to compute net loss per share, basic and diluted	48,752,548	44,224,169

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

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

	Three Months Ended March 31,	
	2022	2021
Net loss	$ (20,930)	$ (23,998)
Other comprehensive loss:		
Gain (loss) on translation of foreign operations	95	(33)
Unrealized loss on marketable securities	(268)	(28)
Comprehensive loss	$ (21,103)	$ (24,059)

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

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

Three months ended March 31, 2022	Common Stock Shares	Common Stock Amount	Additional Paid-In Capital	Accumulated Other Comprehensive (Loss) Gain	Accumulated Deficit	Total Stockholders' Equity
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	299,131	—	2,558	—	—	2,558
Shares withheld for net settlement of tax withholding upon vesting of restricted stock units	(7,726)	—	(186)	—	—	(186)
Stock-based compensation expense	—	—	5,935	—	—	5,935
Other comprehensive loss	—	—	—	(173)	—	(173)
Net loss	—	—	—	—	(20,930)	(20,930)
Balance at March 31, 2022	48,552,102	$ —	$ 732,542	$ (472)	$ (430,292)	$ 301,778

Three months ended March 31, 2021	Common Stock Shares	Common Stock Amount	Additional Paid-In Capital	Accumulated Other Comprehensive (Loss) Gain	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2020	43,745,465	$ —	$ 563,389	$ 28	$ (283,811)	$ 279,606
Issuance of common stock under equity incentive and employee stock purchase plans	200,841	—	1,316	—	—	1,316
Shares withheld for net settlement of tax withholding upon vesting of restricted stock units	(7,060)	—	(189)	—	—	(189)
Stock-based compensation expense	—	—	2,660	—	—	2,660
Other comprehensive loss	—	—	—	(61)	—	(61)
Net loss	—	—	—	—	(23,998)	(23,998)
Balance at March 31, 2021	43,939,246	$ —	$ 567,176	$ (33)	$ (307,809)	$ 259,334

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

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

	Three Months Ended March 31,	
	2022	2021
Cash Flows from Operating Activities		
Net loss	$ (20,930)	$ (23,998)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	5,935	2,660
Operating lease right-of-use asset amortization	584	444
Net amortization of premium on marketable securities	358	348
Depreciation	249	180
Changes in operating assets and liabilities:		
Research and development tax incentive receivable	—	(751)
Receivable from collaboration partner - related party	(23,584)	(1,570)
Prepaid expenses and other assets	1,279	57
Accounts payable	5,559	(344)
Payable to collaboration partner - related party	(519)	4,091
Accrued expenses and other payables	(5,110)	(673)
Deferred revenue - related party	(833)	(8,709)
Operating lease liability	(654)	(491)
Net cash used in operating activities	(37,666)	(28,756)
Cash Flows from Investing Activities		
Purchase of marketable securities	(55,832)	(87,205)
Proceeds from maturities of marketable securities	51,629	80,552
Purchases of property and equipment	(273)	(140)
Net cash used in investing activities	(4,476)	(6,793)
Cash Flows from Financing Activities		
Proceeds from at-the-market offering, net of issuance costs	14,553	—
Proceeds from issuance of common stock upon exercise of stock options and purchases under employee stock purchase plan	2,558	1,316
Tax withholding payments related to net settlement of restricted stock units	(186)	(189)
Issuance costs related to prior common stock offering	—	(148)
Net cash provided by financing activities	16,925	979
Effect of exchange rate changes on cash, cash equivalents and restricted cash	29	(23)
Net decrease in cash, cash equivalents and restricted cash	(25,188)	(34,593)
Cash, cash equivalents and restricted cash, beginning of period	123,890	117,818
Cash, cash equivalents and restricted cash, end of period	$ 98,702	$ 83,225
Supplemental Disclosure of Non-Cash Financing and Investing Information:		
Purchases of property and equipment in accounts payable and accrued liabilities	$ 235	$ 97
Issuance costs related to common stock offering included in accrued liabilities and other payables	$ 25	$ 58
Issuance costs related to common stock offering included in accrued liabilities and other payables at the end of the previous year	$ —	$ 205

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

PROTAGONIST THERAPEUTICS, INC.
Notes to Unaudited Condensed Consolidated Financial Statements

Note 1. Organization and Description of Business

Protagonist Therapeutics, Inc. (the "Company") is headquartered in Newark, California. The Company is a biopharmaceutical company with multiple peptide-based new chemical entities in different stages of clinical development, all derived from the Company's proprietary technology platform. Protagonist Pty Limited ("Protagonist Australia") is a wholly-owned subsidiary of the Company and is located in Brisbane, Queensland, Australia.

Operating segments are components of an enterprise for which separate financial information is available and is evaluated regularly by the Company's chief operating decision maker in deciding how to allocate resources and assessing performance. The Company operates and manages its business as one operating segment. The Company's Chief Executive Officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for allocating and evaluating financial performance.

Liquidity

As of March 31, 2022, the Company had cash, cash equivalents and marketable securities of $305.3 million. The Company has incurred net losses from operations since inception and had an accumulated deficit of $430.3 million as of March 31, 2022. The Company's ultimate success depends upon the outcome of its research and development and collaboration activities. The Company expects to incur additional losses in the future and anticipates the 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.

Risks and Uncertainties

The Company is subject to risks and uncertainties as a result of the ongoing COVID-19 pandemic. The impact of the COVID-19 pandemic on the Company's activities depends on a number of factors, including, but not limited to, the duration and severity of the pandemic, including the severity of any additional periods of increases or spikes in the number of cases in the areas the Company and its suppliers operate and areas where the Company's clinical trial sites are located; the development and spread of COVID-19 variants, the timing, extent, effectiveness and durability of COVID-19 vaccine programs or other treatments; and new or continuing travel and other restrictions and public health measures. The Company has experienced delays in its existing and planned clinical trials due to the worldwide impacts of the pandemic. The Company's future results of operations and liquidity could be adversely impacted by further delays in existing and planned clinical trials, continued difficulty in recruiting patients for these clinical trials, delays in manufacturing and collaboration activities, supply chain disruptions, and the ongoing impact on its operating activities and employees. The extent of the impact of the COVID-19 pandemic remains difficult to predict as this event is ongoing and information continues to evolve. Capital markets and economies worldwide have been negatively impacted and may be further impacted in the future. Such economic disruption could have a material adverse effect on the Company's business. As of the date of issuance of these condensed consolidated financial statements, the extent to which the COVID-19 pandemic may materially impact the Company's future financial condition, liquidity or results of operations remains uncertain.

Note 2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the United States ("GAAP") and applicable rules and regulations of the SEC regarding interim financial reporting. As permitted under those rules, certain footnotes or other financial information that are normally required by GAAP have been condensed or omitted, and accordingly the condensed consolidated balance sheet as of March 31, 2022 has been derived from the Company's audited consolidated financial

statements at that date but does not include all of the information required by GAAP for complete consolidated financial statements. These unaudited interim condensed consolidated financial statements have been prepared on the same basis as the Company's annual consolidated financial statements and, in the opinion of management, reflect all adjustments (consisting of normal recurring adjustments) that are necessary for a fair presentation of the Company's condensed consolidated financial statements. The results of operations for the three months ended March 31, 2022 are not necessarily indicative of the results to be expected for the year ending December 31, 2022 or for any other interim period or for any other future year.

The accompanying condensed consolidated financial statements and related financial information should be read in conjunction with the audited consolidated financial statements and the related notes thereto for the year ended December 31, 2021 included in the Company's Annual Report on Form 10-K, filed with the SEC on February 28, 2022.

Principles of Consolidation

The accompanying unaudited interim condensed consolidated financial statements include the accounts of the Company and its wholly owned subsidiary. All intercompany transactions and balances have been eliminated upon consolidation.

Use of Estimates

The preparation of the condensed 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 condensed 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 actual costs incurred versus total estimated costs of the Company's deliverables to determine percentage of completion in addition to the application and estimates of potential revenue constraints in the determination of the transaction price under its license and collaboration agreements. 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.

Due to the ongoing COVID-19 pandemic and military conflict between Ukraine and Russia, there has been uncertainty and disruption in the global economy and financial markets. 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 date of issuance of this report. 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.

Cash as Reported in Condensed Consolidated Statements of Cash Flows

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

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

	March 31,	
	2022	2021
Cash and cash equivalents	$ 98,477	$ 83,000
Restricted cash - noncurrent	225	225
Total cash reported on condensed consolidated statements of cash flows	$ 98,702	$ 83,225

Significant Accounting Policies

There have been no material changes to the Company's significant accounting policies during the three months ended March 31, 2022 as compared to those disclosed in Note 2. Significant Accounting Policies included in our Annual Report on Form 10-K for the year ended December 31, 2021.

Recently Issued Accounting Pronouncements Not Yet Adopted as of March 31, 2022

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses (Topic 326)*, which is intended to provide financial statement users with more useful information about expected credit losses on financial assets held by a reporting entity at each reporting date. The new standard replaces the existing incurred loss impairment methodology with a methodology that requires consideration of a broader range of reasonable and supportable forward-looking information to estimate all expected credit losses. This guidance was originally effective for fiscal years and interim periods within those years beginning after December 15, 2019, with early adoption permitted for fiscal years and interim periods within those years beginning after December 15, 2018. In November 2019, the FASB issued ASU No. 2019-10, *Financial Instruments – Credit Losses (Topic 326), Derivatives and Hedging (Topic 815), and Leases (Topic 842): Effective Dates*, which amended the mandatory effective date of ASU No. 2016-13 for smaller reporting companies. Based on the Company's status as a smaller reporting company as of November 15, 2019, ASU 2016-13 is effective for the Company for fiscal years and interim periods beginning after December 15, 2022. The Company is currently evaluating the impact of this new guidance on its condensed consolidated financial statements and disclosures.

Note 3. License and Collaboration Agreement

Agreement Terms

On July 27, 2021, the Company entered into an amended and restated License and Collaboration Agreement ("Restated Agreement") with Janssen Biotech, Inc., a Pennsylvania corporation ("Janssen"). The Restated Agreement amends and restates the License and Collaboration Agreement, dated May 26, 2017, by and between the Company and Janssen (as amended by the First Amendment thereto, effective May 7, 2019, the "Original Agreement"). Janssen is a related party to the Company as Johnson & Johnson Innovation - JJDC, Inc., a significant stockholder of the Company, and Janssen are both subsidiaries of Johnson & Johnson. The Original Agreement became effective on July 13, 2017. Upon the effectiveness of the Original Agreement, the Company received a non-refundable, upfront cash payment of $50.0 million from Janssen. Upon the effectiveness of the First Amendment, the Company received a $25.0 million payment from Janssen in 2019. The Company also received a $5.0 million payment triggered by the successful nomination of a second-generation oral Interleukin ("IL")-23 receptor antagonist development compound ("second-generation compound") during the first quarter of 2020 and a $7.5 million payment triggered by the completion of data collection activities for the first Phase 1 clinical trial of a second-generation compound during the fourth quarter of 2021. In March 2022, the Company became eligible to receive a $25.0 million milestone payment in connection with the dosing of the third patient in the first Phase 2 clinical trial for a second-generation compound.

The Restated Agreement relates to the development, manufacture and commercialization of oral IL-23 receptor antagonist drug candidates. The candidates nominated for initial development pursuant to the Restated Agreement include PTG-200 (JN-67864238), PN-232 (JNJ-75105186) and PN-235 (JNJ-77242113). PTG-200 is an oral IL-23 receptor antagonist that was in Phase 2a development for the treatment of Crohn's disease ("CD"). During the fourth quarter of 2021, following a pre-specified interim analysis criteria, a portfolio decision was made by Janssen to stop further development of both PTG-200 and PN-232 in favor of advancing PN-235, based on its superior potency and overall pharmacokinetic and pharmacodynamic profile. Janssen is primarily responsible for the conduct of all future trials, including these anticipated Phase 2 trials, and the Company is primarily responsible for the conduct of the second-generation Phase 1 trials.

Pursuant to the Restated Agreement, the parties have:

- amended development milestones to reflect Janssen's expected development of collaboration compounds for multiple indications in the IL-23 pathway;

- limited the Company's further development and related expense obligations under the Restated Agreement to the PTG-200 Phase 2a trial and the ongoing Phase 1 trials in PN-232 and PN-235; Janssen is responsible for all other future development and related expenses under the Restated Agreement; and

- concluded the parties' two-year research collaboration, while enabling Janssen to continue conducting additional research through July 2024 on compounds developed pursuant to the Original Agreement.

The Restated Agreement enables Janssen to develop collaboration compounds for multiple indications. Under the Restated Agreement, Janssen is required to use commercially reasonable efforts to develop at least one collaboration compound for at least two indications.

The Company's development cost obligations in the Original Agreement for the period following the effective date of the Original Agreement were as follows: (a) up to $20.0 million of costs related to up to three Phase 1 trials of second-generation compounds; (b) up to $20.0 million of costs related to Phase 2a and 2b costs for PTG-200 (i.e., 20% of the first $100.0 million in costs); and (c) up to $25.0 million in costs related to up to two Phase 2 trials evaluating second-generation compounds.

The Company's continuing development expense obligations under the Restated Agreement are as follows: (a) the Company funded 20% of the costs related to the Phase 2a trial evaluating PTG-200 for the treatment of CD (subject to a $20.0 million cap); (b) the Company was responsible for 50% of agreed-upon costs related to the ongoing Phase 1 trial evaluating PN-235 incurred through January 4, 2021; and (c) the Company was responsible for 100% of agreed-upon costs related to the Phase 1 trial evaluating PN-232.

Certain of the Company's previous development expense obligations under the Original Agreement were limited or eliminated as follows: (a) the Company's previous $25.0 million obligation for 20% of costs related to Phase 2 trials for second-generation products was eliminated; (b) the Company's previous $5.0 million obligation for 50% of the costs of a potential third Phase 1 trial evaluating a second-generation compound was eliminated; and (c) the Company had no obligation to fund any portion of any Phase 2b or other trial evaluating PTG-200 beyond the Phase 2a trial in CD.

One milestone for second-generation Phase 2 development was reduced from $50.0 million to $25.0 million in the Restated Agreement; otherwise, the various milestone payment amounts in the Restated Agreement remain substantially the same as in the Original Agreement. To reflect parallel development of multiple indications in the IL-23 pathway, milestone payments under the Restated Agreement generally now correspond to the achievement of specified milestones in: (a) any initial indication (rather than CD, as in the Original Agreement); (b) any second indication (rather than ulcerative colitis ("UC"), as in the Original Agreement); and (c) any third indication. With respect to second-generation compounds, milestone payments for second and third indications may be triggered by any second-generation compound (i.e., not necessarily the second-generation compound that triggered the initial payment for any indication, or the payment for a second indication). In addition, the opt-in payments contemplated by the Original Agreement related to the scope of Janssen's license rights have been converted into development milestones in the Restated Agreement.

Upcoming potential development milestones for second-generation compounds include:

- $10.0 million for dosing of the third patient in the first Phase 2 clinical trial for any second-generation compound for a second indication (i.e., an indication different than the indication which triggered the $25.0 million milestone described above);

- $50.0 million for dosing of the third patient in a Phase 3 clinical trial for a second-generation compound for any indication;

- $15.0 million for dosing of the third patient in a Phase 3 clinical trial for a second-generation compound for a second indication; and

- $115.0 million for a Phase 3 clinical trial for a second-generation compound for any indication meeting its primary clinical endpoint.

Development milestones for PTG-200 were unchanged under the Restated Amendment, except that milestone achievement is generally no longer indication-specific.

Pursuant to the Restated Agreement, the Company remains eligible to receive tiered royalties on net product sales at percentages ranging from mid-single digits to ten percent. The sales milestone payments in the Original Agreement also remain the same in the Restated Agreement.

Pursuant to both the Original and Restated Agreements, payments to the Company for research and development services are generally billed and collected as services are performed or assets are delivered, including research activities and Phase 1 and Phase 2 development activities. Janssen bills the Company for its share of the PTG-200 Phase 2a development costs as expenses are incurred by Janssen. Milestone payments are received after the related milestones are achieved.

Janssen retains exclusive, worldwide rights to develop and commercialize IL-23 receptor antagonist compounds derived from the research collaboration conducted under the Original Agreement, or Janssen's further research under the Restated Agreement. Any further research and development will be conducted by Janssen. The Company will have the right to co-detail (for CD and UC indications) up to two of the IL-23 receptor antagonist compounds under the collaboration in the U.S. market.

The Restated Agreement remains in effect until the royalty obligations cease following patent and regulatory expiry, unless terminated earlier. Upon a termination of the Restated Agreement, all rights revert back to the Company, and in certain circumstances, if such termination occurs during ongoing clinical trials, Janssen would, if requested, provide certain financial and operational support to the Company for the completion of such trials.

Revenue Recognition

The Restated Agreement contains a single performance obligation for the development license; Phase 1 development services for PTG-200, PN-232 and PN-235; the Company's services associated with Phase 2a development for PTG-200 in CD; the initial year of second-generation compound research services; and all other such services that the Company may perform at the request of Janssen to support the development of PTG-200 through Phase 2a and PN-232 and PN-235 through Phase 1. Under the Restated Agreement, development services performed by the Company for PTG-200 beyond Phase 2a and PN-232 and PN-235 beyond Phase 1 are no longer required.

The Company determined that the license was not distinct from the revised development services within the context of the agreement because the revised development services did not change the utility of the intellectual property. The Company also concluded that the remaining development services are not distinct from the partially delivered combined promise comprised under the agreement prior to the Restated Agreement of the development license and PTG-200, PN-232 and PN-235 services, including compound supply and other services. Therefore, the Restated Agreement is treated as if it were part of the Original Agreement. The Restated Agreement was accounted for as if it were a modification of services under the Original Agreement by applying a cumulative catch-up adjustment to revenue. As of the effective date of the Restated Agreement, the Company calculated the adjusted cumulative revenue under the Restated Agreement with primary updates to the transaction price, including the release of and update of prior constraints and fewer remaining services to be provided, resulting in a cumulative adjustment that increased revenue by $8.0 million for the year ended December 31, 2021.

The contract duration is defined as the period in which parties to the contract have present enforceable rights and obligations. For revenue recognition purposes, the duration of the Restated Agreement for the identified single initial performance obligations began on the Original Agreement effective date of July 13, 2017 and will end upon the

later of the end of Phase 2a for PTG-200 in CD or the completion of a Phase 1 clinical trial for either PN-232 or PN-235. Final activities related to these trials are expected to be completed in 2022.

The Company uses the most likely amount method to estimate variable consideration included in the transaction price. Variable consideration after the effective date of the Restated Agreement consists of future milestone payments and cost sharing payments for agreed upon services offset by development costs reimbursable to Janssen. Cost sharing payments from Janssen relate to the agreed upon services for development activities that the Company performs within the duration of the contract are included in the transaction price at the Company's share of the estimated budgeted costs for these activities, including primarily internal full-time equivalent effort and third-party contract costs. Cost sharing payments to Janssen related to agreed-upon services for activities that Janssen performs within the duration of the contract are not a distinct service that Janssen transfers to the Company. Therefore, the consideration payable to Janssen is accounted for as a reduction in the transaction price.

The transaction price of the initial performance obligation under the Restated Agreement was $131.5 million as of March 31, 2022, an increase of $25.0 million from the transaction price of $106.5 million as of December 31, 2021. In order to determine the transaction price, the Company evaluated all payments to be received during the duration of the contract, net of development costs reimbursement expected to be payable to Janssen. The transaction price as of March 31, 2022 includes $87.5 million of nonrefundable payments received to date, the $25.0 million milestone payment receivable following dosing of the third patient in the Phase 2b clinical trial of PN-235, $17.9 million of reimbursement from Janssen for services performed for IL-23 receptor antagonist compound research costs and other services, and estimated variable consideration consisting of $8.2 million of development cost reimbursement receivable from Janssen, partially offset by $7.1 million of net cost reimbursement due to Janssen for services performed. The Company concluded that the variable consideration constraint is appropriately reflected in the estimated transaction as of March 31, 2022, and that the achievement of future milestones is subject to additional development and/or regulatory uncertainty and therefore it is not probable at March 31, 2022 that a material reversal of such revenues would not occur. Janssen also opted in for certain additional services to be performed by the Company that are outside the initial performance obligation. Revenue for these additional services is recognized as these services are performed.

The Company re-evaluates the transaction price, including variable consideration, at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur. The Company and Janssen make quarterly cost sharing payments to one another in amounts necessary to ensure that each party bears its contractual share of the overall shared costs incurred.

The Company utilizes a cost-based input method to measure proportional performance and to calculate the corresponding amount of revenue to recognize. In applying the cost-based input methods of revenue recognition, the Company uses actual costs incurred relative to expected costs to fulfill the combined performance obligation. These costs consist primarily of internal full-time equivalent effort and third-party contract costs. Revenue will be recognized based on actual costs incurred as a percentage of total estimated costs as the Company completes its performance obligations. A cost-based input method of revenue recognition requires management to make estimates of costs to complete the Company's performance obligations. The Company believes this is the best measure of progress because other measures do not reflect how the Company transfers its performance obligation to Janssen. In making such estimates, significant judgment is required to evaluate assumptions related to cost estimates. The cumulative effect of revisions to estimated costs to complete the Company's performance obligations will be recorded in the period in which changes are identified and amounts can be reasonably estimated. A significant change in these assumptions and estimates could have a material impact on the timing and amount of revenue recognized in future periods.

For the three months ended March 31, 2022 and 2021, the Company recognized license and collaboration revenue of $25.7 million and $5.6 million, respectively, which was primarily related to the transaction price under the Restated Agreement recognized based on proportional performance. In addition, the Company recognized $0.6 million in revenue for the three months ended March 31, 2021 related to additional services provided by the Company under the agreement. No such revenue related to additional services provided by the Company was recognized for the three months ended March 31, 2022.

The following tables present changes in the Company's contract assets and liabilities during the periods presented (in thousands):

Three Months Ended March 31, 2022	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Contract assets:				
Receivable from collaboration partner - related party	$ 1,566	$ 25,150	$ (1,566)	$ 25,150
Contract liabilities:				
Deferred revenue - related party	$ 1,601	$ 25,658	$ (26,491)	$ 768
Payable to collaboration partner - related party	$ 899	$ 330	$ (849)	$ 380

Three Months Ended March 31, 2021	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Contract assets:				
Receivable from collaboration partner - related party	$ 2,426	$ 1,570	$ —	$ 3,996
Contract liabilities:				
Deferred revenue - related party	$ 14,477	$ 1,017	$ (9,726)	$ 5,768
Payable to collaboration partner - related party	$ 2,732	$ 4,091	$ —	$ 6,823

During the three months ended March 31, 2022 and 2021, the Company recognized revenue of $13,000 and $1.1 million, respectively, from amounts included in the deferred revenue contract liability balance at the beginning of each period.

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 table presents the fair value of the Company's financial assets determined using the inputs defined above (in thousands).

	March 31, 2022			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 35,422	$ —	$ —	$ 35,422
Commercial paper	—	138,084	—	138,084
Corporate debt securities	—	45,350	—	45,350
U.S. Treasury and agency securities	—	77,648	—	77,648
Supranational and sovereign government securities	—	3,000	—	3,000
Total financial assets carried at fair value	$ 35,422	$ 264,082	$ —	$ 299,504

	December 31, 2021			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 39,854	$ —	$ —	$ 39,854
Commercial paper	—	157,141	—	157,141
Corporate debt securities	—	75,548	—	75,548
U.S. Treasury and agency securities		40,017	—	40,017
Supranational and sovereign government securities	—	6,010	—	6,010
Total financial assets carried at fair value	$ 39,854	$ 278,716	$ —	$ 318,570

The Company's commercial paper, corporate debt securities, U.S. Treasury and agency securities, including U.S. Treasury bills, and supranational and sovereign government 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 our 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):

	March 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	$ 35,422	$ —	$ —	$ 35,422
Commercial paper	138,123	1	(40)	138,084
Corporate debt securities	45,455	—	(105)	45,350
U.S. Treasury and agency securities	77,915	1	(268)	77,648
Supranational and sovereign government securities	3,000	—	—	3,000
Total cash equivalents and marketable securities	$ 299,915	$ 2	$ (413)	$ 299,504
Classified as:				
Cash equivalents				$ 92,692
Marketable securities - current				206,812
Total cash equivalents and marketable securities				$ 299,504

	December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	$ 39,854	$ —	$ —	$ 39,854
Commercial paper	157,157	—	(16)	157,141
Corporate debt securities	75,598	—	(50)	75,548
U.S. Treasury and agency securities	40,093	—	(76)	40,017
Supranational and sovereign government securities	6,011	—	(1)	6,010
Total cash equivalents and marketable securities	$ 318,713	$ —	$ (143)	$ 318,570
Classified as:				
Cash equivalents				$ 115,335
Marketable securities - current				203,235
Total cash equivalents and marketable securities				$ 318,570

Marketable securities – current of $206.8 million and $203.2 million held at March 31, 2022 and December 31, 2021, respectively, had contractual maturities of less than one year. 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 realized gains or realized losses on marketable securities for the periods presented. Factors considered in determining whether a loss is temporary include the length of time and extent to which the fair value has been less than the amortized cost basis and whether the Company intends to sell the security or whether it is more likely than not that the Company would be required to sell the security before recovery of the amortized cost basis.

Note 6. Balance Sheet Components

Prepaid Expenses and Other Current Assets

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

	March 31, 2022	December 31, 2021
Prepaid clinical and research related expenses	$ 4,579	$ 5,242
Prepaid insurance	1,429	1,746
Other prepaid expenses	1,721	1,515
Other receivable	476	975
Prepaid expenses and other current assets	$ 8,205	$ 9,478

Property and Equipment, Net

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

	March 31, 2022	December 31, 2021
Laboratory equipment	$ 4,619	$ 4,156
Furniture and computer equipment	1,072	1,023
Leasehold improvements	898	877
Total property and equipment	6,589	6,056
Less: accumulated depreciation	(4,525)	(4,258)
Property and equipment, net	$ 2,064	$ 1,798

Accrued Expenses and Other Payables

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

	March 31, 2022	December 31, 2021
Accrued clinical and research related expenses	$ 27,514	$ 27,950
Accrued employee related expenses	2,643	7,125
Accrued professional service fees	1,063	734
Accrued collaboration payments	1,500	1,500
Other	154	407
Total accrued expenses and other payables	$ 32,874	$ 37,716

Note 7. Research Collaboration and License Agreement

The Company and Zealand Pharma A/S ("Zealand") entered into a collaboration agreement in June 2012. In October 2013, Zealand abandoned the collaboration, and the collaboration agreement was terminated in 2014. The agreement provides for certain post-termination payment obligations to Zealand with respect to compounds related to the collaboration that meet specified conditions set forth in the collaboration agreement and which the Company elects to further develop following Zealand's abandonment of the collaboration. The Company has the right, but not the obligation, to further develop and commercialize such compounds. The agreement provides for payments to Zealand for the achievement of certain development, regulatory and sales milestone events that occur prior to a partnering arrangement related to such compounds between the Company and a third party.

The Company previously determined that rusfertide is a compound for which the post-termination payments described above are required under the collaboration agreement and has made three development milestone payments for an aggregate amount of $1.0 million under the agreement. However, upon reevaluation, the Company concluded in 2019 that rusfertide is not a compound requiring post-termination payments under the agreement and initiated an arbitration proceeding in January 2020. On August 4, 2021, the Company and Zealand agreed to resolve the dispute and entered into an Arbitration Resolution Agreement.

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 research and development expense was recorded under the Zealand collaboration agreement for the three months ended March 31, 2022 or March 31, 2021.

Note 8. Research and Development Tax Incentive

The Company did not recognize any research and development cash tax incentive from Australian Tax Office ("ATO") during the three months ended March 31, 2022. During the three months ended March 31, 2021, the Company recognized AUD 1.0 million ($0.8 million) as a reduction of research and development expenses in connection with the research and development cash tax incentive from the ATO. As of March 31, 2022 and December 31, 2021, the research and development cash tax incentive receivable was AUD 3.8 million ($2.9 million) and AUD 3.8 million ($2.8 million), respectively.

Note 9. Commitments and Contingencies

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.

On January 23, 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.

On August 4, 2021, the Company and Zealand agreed to resolve the dispute and reached an Arbitration Resolution Agreement. Under the Arbitration Resolution Agreement, (1) the Company is required to make an additional payment of $1.5 million to Zealand in August 2022 with respect to rusfertide, (2) all development milestones with respect of rusfertide were reduced by 50%, except that the Company agreed to pay in full within two (2) business days after the effective date of the Agreement (and timely paid): (i) a $1.0 million milestone for initiation of a Phase 2b clinical trial; and (ii) a $1.5 million milestone for initiation of a Phase 3 clinical trial; (3) the royalty rates payable by the Company on net sales of rusfertide were reduced by 50%; (4) all sales milestone payments on net sales of rusfertide were reduced by 50%; (5) the parties agreed that each party will retain all payments previously made by the other party in connection with the original collaboration agreement; and (6) the parties released claims related to the original collaboration agreement, the abandonment agreement and the arbitration. In addition to the payments specified in items (1) and (2) above, the Company may also be required to pay Zealand up to $2.75 million in future development milestone payments relating to rusfertide. Those payments include up to $1.0 million in the aggregate for registrational proposals and up to $1.75 million in the aggregate for commercial launch in the three geographic territories specified in the original collaboration agreement.

The Company considered the outcome of these arbitration proceedings as being related to its research and development project; therefore, payments or milestone payments were recorded as research and development expenses. As a result, no related legal accruals were recognized as of March 31, 2022.

Note 10. Stockholders' Equity

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 is exercisable from August 8, 2018 through August 8, 2023. Warrants to purchase 1,375,000 shares of the Company's common stock have an exercise price of $10.00 per share and Warrants to purchase 1,375,000 shares of the Company's common stock have an exercise price of $15.00 per share. The exercise price and number of shares of common stock issuable upon the exercise of the Warrants (the "Warrant Shares") are subject to adjustment in the event of any stock dividends and splits, reverse stock split, recapitalization, reorganization or similar transaction, as described in the Warrants. Under certain circumstances, the Warrants may be exercisable on a "cashless" basis. In connection with the issuance and sale of the common stock and Warrants, the Company granted the Investors certain registration rights with respect to the Warrants and the Warrant Shares. The common stock and warrants are classified as equity in accordance with Accounting Standards Codification Topic 480, Distinguishing Liabilities from Equity ("ASC 480"), and the net proceeds from the transaction were recorded as a credit to additional paid-in capital. As of March 31, 2022, none of the Warrants have been exercised.

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 will expire ten years from the date of issuance. The Exchange Warrants are exercisable at any time prior to expiration except that the Exchange Warrants cannot 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 are classified as equity in accordance with ASC 480*,* and fair value of the Exchange Warrants was recorded as a credit to additional paid-in capital and is not subject to remeasurement. The Company determined that the fair value of the Exchange Warrants is substantially similar to the fair value of the retired shares on the issuance date due to the negligible exercise price for the Exchange Warrants. As of March 31, 2022, 400,000 of the Exchange Warrants remain unexercised.

In October 2019, the Company filed a registration statement on Form S-3 (File No. 333-234414) that was declared effective as of November 22, 2019 and permits the offering, issuance, and sale by the Company of up to a maximum aggregate offering price of $250.0 million of its common stock, preferred stock, debt securities and warrants (the "2019 Form S-3"). Up to a maximum of $75.0 million of the maximum aggregate offering price of $250.0 million may be issued and sold pursuant to an at-the market ("ATM") financing facility under a sales agreement entered into by the Company on November 27, 2019 (the "2019 Sales Agreement"). In January 2022, the Company sold 422,367 shares of its common stock under its ATM financing facility pursuant to the 2019 Sales Agreement for net proceeds of $14.6 million, after deducting issuance costs. As of March 31, 2022, a total of $79.3 million of securities remained available for sale under the 2019 Form S-3, $17.0 million of which remained available for sale under the ATM financing facility. The 2019 Form S-3 expires in October 2022.

In December 2020, the Company filed an automatic registration statement on Form S-3ASR and an accompanying prospectus (File No. 333-251254). In June 2021, pursuant to this Form S-3ASR, the Company completed an underwritten public offering of 3,046,358 shares of its common stock at a public offering price of $37.75 per share and issued an additional 456,953 shares of common stock at a price of $37.75 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 $123.8 million. The Form S-3ASR expires in December 2023.

Note 11. Equity Plans

Equity Incentive Plan

In July 2016, the Company's board of directors and stockholders approved the Company's 2016 Equity Incentive Plan (the "2016 Plan") to replace the 2007 Stock Option Plan. The 2016 Plan is administered by the board of directors, or a committee appointed by the board of directors, 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 2016 Plan expire no later than ten years from the date of grant. As of March 31, 2022, 1,095,340 shares were available for issuance under the 2016 Plan.

Inducement Plan

In May 2018, the Company's board of directors approved the 2018 Inducement Plan, as subsequently amended. The 2018 Inducement Plan is a non-stockholder approved stock plan, under which the Company 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 of directors 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. As of March 31, 2022, 743,125 shares were available for issuance under the Amended and Restated 2018 Inducement Plan.

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, 2021	5,890,540	$ 17.66	7.47	$ 102.7
Options granted	1,122,100	28.85		
Options exercised	(165,488)	11.68		
Options forfeited	(37,542)	39.04		
Balances at March 31, 2022	6,809,610	$ 19.53	7.37	$ 46.0
Options exercisable – March 31, 2022	3,349,241	$ 13.59	6.05	$ 34.5
Options vested and expected to vest – March 31, 2022	6,809,610	$ 19.53	7.37	$ 46.0

(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 March 31, 2022. The calculation excludes options with an exercise price higher than the closing price of the Company's common stock on March 31, 2022.

The estimated weighted-average grant-date fair value of common stock underlying options granted to employees during the three months ended March 31, 2022 was $22.56 per share.

Stock Options Valuation Assumptions

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

	Three Months Ended March 31,	
	2022	2021
Expected term (in years)	5.27- 6.08	5.27- 6.08
Expected volatility	97.1% - 98.2%	89.8% - 90.2%
Risk-free interest rate	1.64% - 2.13%	0.11% - 0.97%
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—For the year ended December 31, 2021, the Company's expected volatility was estimated based upon a mix of 50% of the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants and 50% of the volatility of the Company's stock price since its initial public offering in August 2016. Beginning January 1, 2022, the Company's expected volatility is 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 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.

Restricted Stock Units

Restricted stock unit 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, 2021	405,972	$ 20.13
Granted	312,550	28.73
Vested	(104,712)	14.73
Forfeited	(7,000)	28.73
Unvested RSUs at March 31, 2022	606,810	$ 24.61

Performance Stock Units

Performance stock unit ("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, 2021	105,500	$ 23.57
Granted	—	—
Vested	—	—
Forfeited	—	—
Unvested PSUs at March 31, 2022	105,500	$ 23.57

The terms of the unvested 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 expire on February 28, 2026 if the performance objectives are not achieved. The PSUs will vest, if at all, upon certification by the Compensation Committee of the Company's Board of Directors 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 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. The total fair value of outstanding PSUs as of March 31, 2022 was $2.5 million. As of March 31, 2022, the achievement of the related performance objective was deemed not probable and, accordingly, no stock-based compensation for the PSUs has been recognized as expense as of March 31, 2022.

Employee Stock Purchase Plan

The 2016 Employee Stock Purchase Plan ("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 three months ended March 31, 2022, a total of 28,931 shares of common stock were issued under the 2016 ESPP, and 1,285,068 shares remain available for issuance as of March 31, 2022.

Stock-Based Compensation

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

	Three Months Ended March 31,	
	2022	2021
Research and development	$ 3,326	$ 1,475
General and administrative	2,609	1,185
Total stock-based compensation expense	$ 5,935	$ 2,660

As of March 31, 2022, total unrecognized stock-based compensation expense was approximately $73.6 million, which the Company expects to recognize over a weighted-average period of approximately 2.9 years.

Note 12. Net Loss per Share

As the Company had net losses for the three months ended March 31, 2022 and 2021, all potential weighted average dilutive common shares were determined to be anti-dilutive. The following table sets forth the computation of basic and diluted net loss per share (in thousands, except share and per share data):

	Three Months Ended March 31,	
	2022	2021
Numerator:		
Net loss	$ (20,930)	$ (23,998)
Denominator:		
Weighted-average shares used to compute net loss per common share, basic and diluted	48,752,548	44,224,169
Net loss per share, basic and diluted	$ (0.43)	$ (0.54)

The following outstanding shares of potentially dilutive securities have been excluded from diluted net loss per share computations for the periods presented because their inclusion would be anti-dilutive:

	March 31,	
	2022	2021
Options to purchase common stock	6,809,610	5,698,164
Common stock warrants	2,750,000	2,750,000
Restricted stock units	606,810	448,380
Performance stock units	105,500	110,500
ESPP shares	19,762	16,778
Total	10,291,682	9,023,822

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our Unaudited Condensed Consolidated Financial Statements and related notes included in Part I, Item 1 of this quarterly report (this "Quarterly Report") on Form 10-Q and with our Audited Consolidated Financial Statements and related notes thereto for the year ended December 31, 2021, included in our Annual Report on Form 10-K filed with the Securities and Exchange Commission ("SEC") on February 28, 2022.

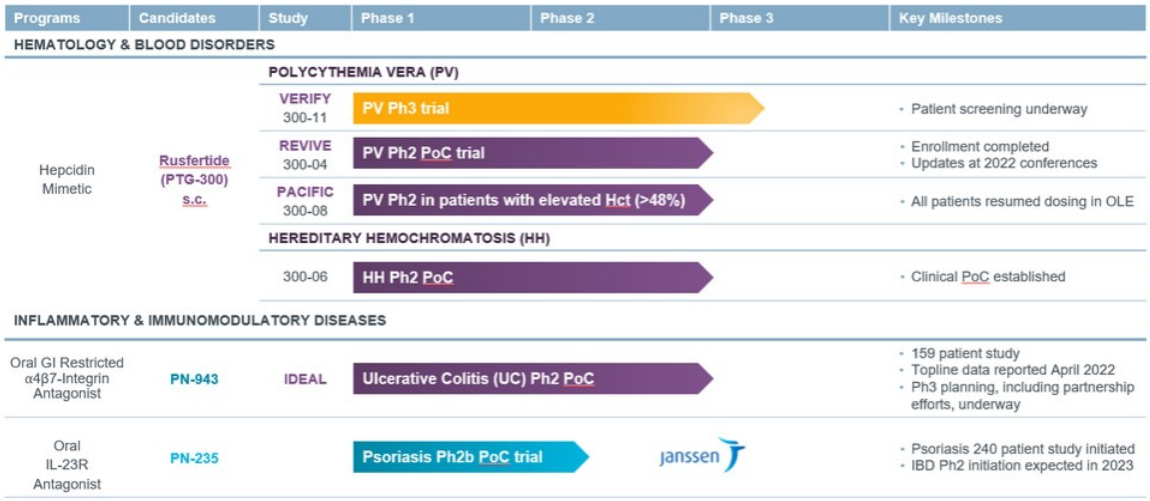
Forward-Looking Statements

This Quarterly Report contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "anticipates," "believes," "could," "estimates," "expects," "forecasts," "intends," "may," "plans," "potential," "predicts," "projects," "should," "targets," "will," "would," 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. In particular, statements, whether expressed or implied, concerning, among other things, the potential for our programs, the timing of our clinical trials, the potential for eventual regulatory approval and commercialization of our product candidates and our potential receipt of milestone payments and royalties under our collaboration agreements, the timing and amount of potential payments that we may be required to make to collaboration partners; future operating results or the ability to generate sales, income or cash flow, and the impact of the ongoing COVID-19 pandemic are forward-looking statements. They involve risks, uncertainties and assumptions that are beyond our ability to control or predict, including those discussed in Part II, Item 1A, of this Quarterly Report. While we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. 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 Quarterly 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, even if new information becomes available in the future. "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.

Overview

We are a biopharmaceutical company with multiple peptide-based new chemical entities in different stages of development, all derived from the Company's proprietary discovery technology platform. Our clinical programs fall into two broad categories of diseases; (i) hematology and blood disorders, and (ii) inflammatory and immunomodulatory diseases.

Our Product Pipeline



Our most advanced clinical asset, rusfertide (generic name for PTG-300), is an injectable hepcidin mimetic in development for the potential treatment of erythrocytosis, iron overload and other blood disorders. Hepcidin is a key hormone in regulating iron equilibrium and is critical to the proper development of red blood cells. Rusfertide mimics the effect of the natural hormone hepcidin, but with greater potency, solubility and stability. We initiated REVIVE, a Phase 2 proof of concept ("POC") trial in the blood disorder polycythemia vera ("PV"), in the third quarter of 2019. We completed enrollment of patients in the ongoing REVIVE Phase 2 clinical trial of rusfertide in PV in the first quarter of 2022 with a target of approximately 50 patients to be enrolled through the end of the randomization portion of the trial. We initiated a Phase 2 POC trial in hereditary hemochromatosis ("HH") in January 2020, which was completed during the fourth quarter of 2021. During the first quarter of 2021, we initiated PACIFIC, another Phase 2 trial for rusfertide in up to 20 patients diagnosed with PV and with routinely elevated hematocrit levels (>48%). Data from these trials presented at medical conferences in 2021 provided evidence regarding the potential of rusfertide for managing hematocrit, reducing thrombotic risk and improving iron deficiency symptoms. Rusfertide has a unique mechanism of action in the potential treatment of PV, which may enable it to specifically decrease and maintain hematocrit levels within the range of recommended clinical guidelines without causing the iron deficiency that can occur with frequent phlebotomy.

On September 16, 2021, the U.S. Food and Drug Administration ("FDA") placed a clinical hold on our rusfertide clinical trials following our submission to the FDA of findings in a 26-week rasH2 transgenic mouse carcinogenicity study. In October 2021, we submitted a Complete Response to the FDA related to the clinical hold, and the FDA removed the clinical hold on October 8, 2021. In our Complete Response, we provided the individual patient clinical safety reports the FDA requested for human cancers observed in rusfertide clinical trials, updated the investigator brochure and patient informed consent forms for ongoing rusfertide trials, proposed new safety and stopping rules in trial protocols for our ongoing rusfertide clinical trials, and performed a comprehensive review of our rusfertide safety database. Dosing of patients and enrollment in ongoing clinical trials with rusfertide resumed in the fourth quarter of 2021.

Based on ongoing end of Phase 2 feedback provided by the FDA's Division of Nonmalignant Hematology and written comments from the European Medicines Agency ("EMA"), we activated sites and initiated patient screening for VERIFY, a global Phase 3 clinical trial of rusfertide in PV, in the first quarter of 2022. Patient enrollment in VERIFY is expected to be completed in the first half of 2023.

The FDA granted orphan drug designation for rusfertide for the treatment of PV in June 2020, and Fast Track designation for rusfertide for the treatment of PV in December 2020. The EMA granted orphan drug designation for rusfertide for treatment of PV in October 2020. The FDA granted Breakthrough Therapy Designation for rusfertide for the treatment of PV in June 2021. In April 2022, we received a letter from the FDA indicating the FDA's intent to rescind Breakthrough Therapy Designation for rusfertide in PV. We submitted a meeting request to the FDA, along with a briefing document articulating why we believe rusfertide continues to warrant Breakthrough Therapy Designation. The FDA letter does not relate to the rusfertide Fast Track Designation, which remains active.

Our alpha-4-beta-7 ("α4β7") antagonist PN-943 and our Interleukin-23 receptor ("IL-23R") antagonist compound PN-235 are orally delivered investigational drugs that are designed to block biological pathways currently targeted by marketed injectable antibody drugs. Our orally stable peptide approach may offer a targeted therapeutic approach for GI and systemic compartments as needed. We believe that, compared to antibody drugs, these product candidates have the potential to provide improved safety due to minimal exposure in the blood, increased convenience and compliance due to oral delivery, and the opportunity for the earlier introduction of targeted oral therapy.

PN-943 is an investigational, orally delivered, gut-restricted α4β7 specific integrin antagonist for inflammatory bowel disease ("IBD"). We submitted a U.S. Investigational New Drug application with the FDA for PN-943 in December 2019, which took effect in January 2020. During the second quarter of 2020 we initiated IDEAL, a 159 patient Phase 2 trial evaluating the safety, tolerability and efficacy of PN-943 in patients with moderate to severe UC. This trial includes a 12-week induction period and a 40-week extended treatment period. Enrollment in IDEAL was completed during the first quarter of 2022. Patients were randomized to either twice daily ("BID") with 150 mg or 450 mg PN-943, or placebo, for 12 weeks and analyzed for outcome measures. Topline data from the 12-week induction period reported in April 2022 demonstrated that while the higher 450 mg BID dose arm did not meet the prespecified primary endpoint, the lower 150 mg BID dose arm achieved 27.5% clinical remission with a delta of 13% versus placebo, with strong concordance across several key proxies including histological and endoscopic endpoints for efficacy. Consistent with the goals of a Phase 2 study and based on the safety and efficacy data from the 150 mg BID arm, IDEAL achieved clinical POC and validation for an oral, gut-restricted approach for UC via blockade of the α4β7 pathway. We are currently finalizing the study design for a registrational Phase 3 trial anchored around the 150 mg BID dose of PN-943, pending regulatory guidance. We intend to pursue further clinical development in collaboration with a large pharmaceutical partner or through a structured financing arrangement.

In May 2017, we entered into a worldwide license and collaboration agreement with Janssen Biotech, Inc. ("Janssen"), a Johnson & Johnson company, to co-develop and co-detail our IL-23R antagonist compounds, including PTG-200 (JNJ-67864238) and certain related compounds for all indications, including IBD. PTG-200 was a first-generation investigational, orally delivered, IL-23R antagonist for the treatment of IBD. The agreement with Janssen was amended in May 2019 to expand the collaboration by supporting efforts towards second-generation IL-23R antagonists; and in July 2021 to, among other things, enable Janssen to independently research and develop collaboration compounds for multiple indications in the IL-23 pathway and further align our financial interests.

In October 2020, we and Janssen announced the selection of two second-generation IL23-R antagonists for advancement into clinical development, PN-232 (JNJ-75105186) and PN-235 (JNJ-77242113). During the fourth quarter of 2021, following a pre-specified interim analysis criteria, a portfolio decision was made by Janssen to stop further development of both PTG-200 and PN-232 favor of advancing PN-235, based on its superior potency and overall pharmacokinetic and pharmacodynamic profile. A PN-235 Phase 1 trial was completed in the fourth quarter of 2021. Janssen initiated FRONTIER 1, a 240-patient Phase 2b clinical trial of PN-235 in moderate-to-severe plaque psoriasis, in February 2022 and is expected to initiate a separate Phase 2 trial of PN-235 in IBD in 2023.

During the fourth quarter of 2021, we received a $7.5 million milestone payment from Janssen triggered by the completion of data collection for PN-235 Phase 1 activities. In March 2022, we became eligible to receive a $25.0

million milestone payment in connection with the dosing of a third patient in FRONTIER 1, which we received in April 2022. We will be eligible to receive a $10.0 million milestone payment in connection with the dosing of a third patient in the second Phase 2 trial of a second-generation candidate. We remain eligible for up to approximately $875.0 million in development-related milestone payments, in addition to the $112.5 million in milestone payments already earned.

Our 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 in an effort to overcome 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. We continue to use our peptide technology platform to discover product candidates against targets in disease areas with significant unmet medical needs.

COVID-19 Business Impact

We are subject to risks and uncertainties as a result of the ongoing COVID-19 pandemic. The severity of the impact of the COVID-19 pandemic on our activities depends on a number of factors, including, but not limited to, the duration and severity of the pandemic, including the severity of any additional periods of increases or spikes in the number of cases in the areas we and our suppliers operate and areas where our clinical trial sites are located; the development and spread of COVID-19 variants, the timing, extent, effectiveness and durability of COVID-19 vaccine programs or other treatments; and new or continuing travel and other restrictions and public health measures. We have experienced delays in our existing and planned clinical trials due to the worldwide impacts of the pandemic. Our future results of operations and liquidity could be adversely impacted by further delays in existing and planned clinical trials, continued difficulty in recruiting patients for these clinical trials, delays in manufacturing and collaboration activities, supply chain disruptions, and the ongoing impact on our operating activities and employees. The extent of the impact of the COVID-19 pandemic remains difficult to predict as this event is ongoing and information continues to evolve. Capital markets and economies worldwide have been negatively impacted and may be further impacted in the future. Such economic disruption could have a material adverse effect on our business. As of the date of issuance of these condensed consolidated financial statements, the extent to which the COVID-19 pandemic may materially impact our future financial condition, liquidity or results of operations remains uncertain.

Operations

We have incurred net losses in each year since inception and we do not anticipate achieving sustained profitability in the foreseeable future. Our net loss was $20.9 million and $24.0 million for the three months ended March 31, 2022 and 2021, respectively. As of March 31, 2022, we had an accumulated deficit of $430.3 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, development and other expenses related to our ongoing operations, product development, and pre-commercialization activities. As a result, we expect to continue to incur losses in the future as we continue our development of, and seek regulatory approval for, our product candidates.

Janssen License and Collaboration Agreement

On July 27, 2021, we entered into an amended and restated License and Collaboration Agreement ("Restated Agreement") with Janssen. The Restated Agreement amends and restates the License and Collaboration Agreement, dated May 26, 2017, by and between us and Janssen (as amended by the First Amendment thereto, effective May 7, 2019, the "Original Agreement"). Janssen is a related party to us as Johnson & Johnson Innovation - JJDC, Inc., a significant stockholder of ours, and Janssen are both subsidiaries of Johnson & Johnson. The Original Agreement became effective on July 13, 2017. Upon the effectiveness of the Original Agreement, we received a non-refundable, upfront cash payment of $50.0 million from Janssen. Upon the effectiveness of the First Amendment, we received a $25.0 million payment from Janssen in 2019. We also received a $5.0 million payment triggered by the successful nomination of a second-generation IL-23R antagonist development compound during the first quarter of 2020. In the

fourth quarter of 2021, we received a $7.5 million milestone payment from Janssen triggered by completion of the data collection for PN-235 Phase 1 activities. In April 2022, we received a $25.0 million milestone payment in connection with the initiation of the first Phase 2 trial of a second-generation candidate. See Note 3 to the condensed consolidated financial statements included elsewhere in this report for additional information.

Critical Accounting Polices and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our unaudited condensed consolidated financial statements, which have been prepared in accordance with United States generally accepted accounting principles. The preparation of these unaudited condensed 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 unaudited condensed consolidated financial statements, as well as the reported revenue generated, and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources.

There have been no material changes to our critical accounting policies during the three months ended March 31, 2022, as compared to those disclosed in *"Management's Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Estimates"* in our Annual Report for the year ended December 31, 2021 filed with the SEC on February 28, 2022.

Components of Our Results of Operations

License and Collaboration Revenue

Our license and collaboration revenue is derived from payments we receive under the Janssen License and Collaboration Agreement. See Note 3 to the condensed consolidated financial statements included elsewhere in this report 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, non-clinical and clinical studies;

- costs related to production of clinical supplies and non-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 other supplies.

We recognize the funds from grants under government programs as a reduction of research and development expenses when the related research costs are incurred. In addition, we recognize the funds related to our Australian research and development refundable cash tax incentive that are not subject to refund provisions as a reduction of research and development expenses. The research and development tax incentives are recognized when there is reasonable assurance that the incentives 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 taxable credit in the form of a non-cash tax incentive.

We allocate direct costs 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 clinical expenses are incurred for our early-stage research and drug discovery projects, 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.

The following table summarizes our research and development expenses incurred during the periods indicated:

	Three Months Ended March 31,	
	2022	2021
	(Dollars in thousands)	
Clinical and development expense — PN-943	$ 15,741	$ 7,724
Clinical and development expense — rusfertide (PTG-300)	13,377	10,079
Clinical and development expense — PN-235	221	1,799
Clinical and development expense — PN-232	68	—
Clinical and development expense — PTG-200	(6)	1
Clinical and development expense — PTG-100	190	109
Pre-clinical and drug discovery research expense	6,727	5,361
Grants and tax incentives expense reimbursement, net	—	(828)
Total research and development expenses	$ 36,318	$ 24,245

We expect our research and development expenses will increase as we progress our product candidates into later stage clinical trials, add to the number of ongoing clinical trials, advance our discovery research projects into the pre-clinical stage and continue our early-stage research and prepare for the commercialization of our product candidates. The process of conducting research, identifying potential product candidates and conducting pre-clinical 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 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, 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 supplies. We expect to continue to incur expenses to support our continued operations as a public company, including expenses related to existing and future compliance with rules and regulations of the SEC and those of the national securities exchange on which our securities are traded, insurance expenses, investor relations, 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 Three Months Ended March 31, 2022 and 2021

	Three Months Ended March 31,		Dollar Change	% Change
	2022	2021		
	(Dollars in thousands)			
License and collaboration revenue - related party	$ 25,722	$ 6,189	$ 19,533	316
Operating expenses:				
Research and development [1]	36,318	24,245	12,073	50
General and administrative [2]	10,515	5,965	4,550	76
Total operating expenses	46,833	30,210	16,623	55
Loss from operations	(21,111)	(24,021)	2,910	(12)
Interest income	168	102	66	65
Other income (expense), net	13	(79)	92	(116)
Net loss	$ (20,930)	$ (23,998)	$ 3,068	(13)

(1) Includes $3.3 million and $1.5 million of non-cash stock-based compensation expense for the three months ended March 31, 2022 and 2021, respectively.

(2) Includes $2.6 million and $1.2 million of non-cash stock-based compensation expense for the three months ended March 31, 2022 and 2021, respectively.

License and Collaboration Revenue

License and collaboration revenue increased $19.5 million, or 316%, from $6.2 million for the three months ended March 31, 2021 to $25.7 million for the three months ended March 31, 2022. The increase in revenue was primarily due to an increase in transaction price and proportional performance resulting from the $25.0 million milestone payment we became eligible to receive in March 2022 upon the dosing of the third patient in the Janssen Phase 2b FRONTIER 1 trial of PN-235 for moderate-to-severe plaque psoriasis.

We determined that the transaction price of the initial performance obligation under the Restated Janssen License and Collaboration Agreement was $131.5 million as of March 31, 2022, an increase of $25.0 million from the transaction price of $106.5 million as of December 31, 2021. In order to determine the transaction price, we evaluated all payments to be received during the duration of the contract, net of development costs reimbursement expected to be payable to Janssen. The transaction price as of March 31, 2022 includes $87.5 million of nonrefundable payments received to date, the $25.0 million milestone payment receivable following the dosing of the third patient in the Phase 2b FRONTIER 1 clinical trial of PN-235, $17.9 million of reimbursement from Janssen for services performed for IL-23 receptor antagonist compound research costs and other services, and estimated variable consideration consisting of $8.2 million of development cost reimbursement receivable from Janssen, partially offset by $7.1 million of net cost reimbursement due to Janssen for services performed. The increase in transaction price from December 31, 2021 to March 31, 2022 was due primarily to the $25.0 million milestone payment we became eligible to receive in March 2022 upon the dosing of the third patient in the Janssen Phase 2b FRONTIER 1 trial for moderate-to-severe plaque psoriasis. We re-evaluate the transaction price each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Research and Development Expenses

	Three Months Ended March 31,		Dollar	%
	2022	2021	Change	Change
	(Dollars in thousands)			
Clinical and development expense — PN-943	$ 15,741	$ 7,724	$ 8,017	104
Clinical and development expense — rusfertide (PTG-300)	13,377	10,079	3,298	33
Clinical and development expense — PN-235	221	1,799	(1,578)	(88)
Clinical and development expense — PN-232	68	—	68	*
Clinical and development expense — PTG-200	(6)	1	(7)	*
Clinical and development expense — PTG-100	190	109	81	74
Pre-clinical and drug discovery research expense	6,727	5,361	1,366	25
Grants and tax incentives expense reimbursement, net	—	(828)	828	(100)
Total research and development expenses	$ 36,318	$ 24,245	$ 12,073	50

*Percentage not meaningful

Research and development expenses increased $12.1 million, or 50%, from $24.2 million for the three months ended March 31, 2021 to $36.3 million for the three months ended March 31, 2022. The increase was primarily due to an increase of $8.0 million in PN-943 contract manufacturing costs and clinical expenses related to the Phase 2 IDEAL trial in UC initiated in 2020, an increase of $3.3 million in rusfertide clinical and contract manufacturing expenses for VERIFY, the global Phase 3 clinical trial in PV initiated in the first quarter of 2022, an increase of $1.4 million in pre-clinical and drug discovery research expenses, and a decrease of $0.8 million in Australia research and tax incentive expense reimbursement. These increases were partially offset by a decrease of $1.6 million in clinical and development expenses for the PN-235 Phase 1 trial under the Janssen License and Collaboration agreement, which was completed in the fourth quarter of 2021.

We had 97 and 63 full-time equivalent research and development employees as of March 31, 2022 and 2021, respectively.

General and Administrative Expenses

General and administrative expenses increased $4.6 million, or 76%, from $6.0 million for the three months ended March 31, 2021 to $10.5 million for the three months ended March 31, 2022 primarily due to increases of $2.1 million in personnel expenses and $2.5 million in expenses to support the growth of our business and other costs. The increase in personnel expenses was primarily due to increases of $1.4 million in stock-based compensation expense and $0.7 million in wages and benefits.

We had 25 and 20 full-time equivalent general and administrative employees as of March 31, 2022 and 2021, respectively.

Interest Income

Interest income increased $0.1 million, or 65%, from $0.1 million for the three months ended March 31, 2021 to $0.2 million for the three months ended March 31, 2022. This increase was due primarily to higher yields on invested balances during a period of increasing interest rates compared to the prior year period.

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 the receipt of payments under collaboration agreements.

In October 2019, we filed a registration statement on Form S-3 (File no. 333-234414) that was declared effective as of November 22, 2019 and permits the offering, issuance, and sale by us of up to a maximum aggregate offering price of $250.0 million of our common stock, preferred stock, debt securities and warrants (the "2019 Form S-3"). Up to a maximum of $75.0 million of the maximum aggregate offering price of $250.0 million may be issued and sold pursuant to an ATM financing facility under a sales agreement we entered into on November 27, 2019 (the "2019 Sales Agreement"). In January 2022, we issued 422,367 shares of our common stock under our ATM financing facility for net proceeds of $14.6 million, after deducting issuance costs. As of March 31, 2022, a total of $79.3 million of common stock remained available for sale under the 2019 Form S-3, $17.0 million of which remained available for sale under the ATM financing facility. This Form S-3 expires in October 2022.

In December 2020, we filed an automatic registration statement on Form S-3ASR and an accompanying prospectus (File No. 333-251254). In June 2021, pursuant this S-3ASR, we completed an underwritten public offering of 3,046,358 shares of common stock at a public offering price of $37.75 per share and issued an additional 456,953 shares of common stock at a public offering price of $37.75 per share following the underwriters' exercise of their option to purchase additional shares. Net proceeds, after deducting underwriting commission and offering costs paid by us, were $123.8 million. This Form S-3ASR expires in December 2023.

We have received $112.5 million in non-refundable payments from Janssen since the inception of the Janssen License and Collaboration Agreement in 2017 through the date of this report as follows:

- Upon effectiveness of the agreement, we received a non-refundable, upfront cash payment of $50.0 million from Janssen;
- Upon effectiveness of the First Amendment, we became eligible to receive a $25.0 million payment from Janssen, which was received during the second quarter of 2019;
- In December 2019, we became eligible to receive a $5.0 million payment triggered by the successful nomination of a second-generation development compound, which was received during the first quarter of 2020;
- In October 2021, we became eligible to receive a $7.5 million milestone payment triggered by completion of the data collection for PN-235 Phase 1 activities, which was received during the fourth quarter of 2021; and
- In March 2022, we became eligible to receive a $25.0 million milestone payment in connection with the dosing of the third patient in the Phase 2b clinical trial of PN-235 in moderate-to-severe plaque psoriasis, which we received in April 2022.

We also receive payments for services provided under the collaboration agreement and we make in-kind payment reimbursements to Janssen for certain costs they have incurred based on the cost sharing terms of the agreement.

Pursuant to the amended and restated License and Collaboration Agreement with Janssen executed July 27, 2021 (the "Restated Agreement"), we will be eligible to receive clinical development, regulatory and sales milestones, if and as achieved. Upcoming potential development milestones for second-generation products include:

- $10.0 million for dosing of the third patient in the first Phase 2 clinical trial for any second-generation product for a second indication (i.e., an indication different than the indication which triggered the $25.0 million milestone described above); and

- $50.0 million for dosing of the third patient in a Phase 3 clinical trial for a second-generation compound for any indication.

Capital Requirements

As of March 31, 2022, we had $305.3 million of cash, cash equivalents and marketable securities and an accumulated deficit of $430.3 million. Our capital expenditures for the three months ended March 31, 2022 were $0.5 million. Our capital expenditures for the years ended December 31, 2021 and 2020 were $1.1 million and $0.5 million, respectively. Our primary uses of cash are to fund operating expenses, primarily our research and development expenditures, general and administrative costs and pre-commercialization costs. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses. We believe, based on our current operating plan and expected expenditures, that our existing cash, cash equivalents and marketable securities will be sufficient to meet our anticipated operating and capital expenditure requirements for at least the next 12 months from the date of this filing. We have based this estimate on assumptions that may prove to be wrong. We could utilize our available capital resources sooner than we currently expect if our planned pre-clinical and clinical trials are successful or expanded, our product candidates enter new and more advanced stages of clinical development or our newer product clinical trials advance beyond the discovery stage. We expect to require additional financing to advance our product candidates through clinical development and toward potential regulatory approval and to develop, acquire or in-license other potential product candidates. Such additional funding may come from raising additional capital, seeking access to debt, and additional collaborative or other arrangements with corporate sources, but such funding may not be available at terms acceptable to us, if at all.

We anticipate that we will need to raise substantial additional funding, the requirements of which 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 ability to obtain clinical and commercial supplies and any other product candidates we may identify and develop;

- our ability to successfully commercialize the product candidates we may identify and develop;

- the selling and marketing costs associated with our current product candidates and any other product candidates we may identify and develop, including the cost and timing of expanding our sales and marketing capabilities;

- the achievement of development, regulatory and sales milestones resulting in payments to us from Janssen under the Janssen License and Collaboration Agreement, as amended, 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 under the Janssen License and Collaboration Agreement on worldwide net sales of IL-23 receptor antagonist compounds, 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 discovery of product candidates;
- the time and cost necessary to respond to technological and market developments;
- the extent to which we may acquire or in-license other product candidates and technologies;
- costs necessary to attract, hire and retain qualified personnel;
- the costs of maintaining, expanding and protecting our intellectual property portfolio; and
- the costs of ongoing general and administrative activities to support the growth of our business.

Adequate additional funding may not be available to us on acceptable terms, or at all. 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 will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may 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.

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

Condensed Consolidated Statements of Cash Flows Data:	**Three Months Ended March 31,**	
	2022	**2021**
	(Dollars in thousands)	
Cash used in operating activities	$ (37,666)	$ (28,756)
Cash used in investing activities	$ (4,476)	$ (6,793)
Cash provided by financing activities	$ 16,925	$ 979
Stock-based compensation	$ 5,935	$ 2,660
Receivable from collaboration partner - related party	$ (23,584)	$ (1,570)
Decrease in deferred revenue - related party	$ (833)	$ (8,709)

Cash Flows from Operating Activities

Cash used in operating activities for the three months ended March 31, 2022 was $37.7 million, consisting of our net loss of $20.9 million and a net change of $23.9 million in net operating assets and liabilities, partially offset by certain non-cash items, including $5.9 million of stock-based compensation expense. The $8.9 million increase in cash flow used in operating activities during the three months ended March 31, 2022, as compared to the three months ended March 31, 2021, was primarily due to a $22.0 million increase in receivables from a collaboration partner related to the $25.0 million milestone we became eligible to receive upon the dosing of the third patient in the Janssen Phase 2

FRONTIER 1 trial of PN-943 in UC. This increase was partially offset by a $7.9 million change in decrease in deferred revenue, a $3.3 million increase in stock-based compensation expense, and a $3.1 million decrease in our net loss.

Cash Flows from Investing Activities

Cash used in investing activities for the three months ended March 31, 2022 was $4.5 million, consisting of purchases of marketable securities of $55.8 million and purchases of property and equipment of $0.3 million, partially offset by proceeds from maturities of marketable securities of $51.6 million. The $2.3 million decrease in cash used in investing activities for the three months ended March 31, 2022, as compared to the three months ended March 31, 2021, was primarily related to a decrease of $31.3 million in purchases of marketable securities, partially offset by a decrease of $28.9 million in proceeds from maturities of marketable securities. Purchases of property and equipment were primarily related to purchases of laboratory and computer equipment.

Cash Flows from Financing Activities

Cash provided by financing activities for the three months ended March 31, 2022 was $16.9 million, consisting primarily of net cash proceeds from ATM sales of $14.6 million and proceeds from the issuance of common stock upon exercise of stock options and purchases of common stock under our employee stock purchase plan of $2.6 million. The $15.9 million increase in cash provided by financing activities for the three months ended March 31, 2022, as compared to the three months ended March 31, 2021, was primarily due to a $14.6 million increase in net cash proceeds from ATM sales, and a $1.2 million increase in proceeds from issuance of common stock upon exercise of stock options and purchases of common stock under our employee stock purchase plan.

Contractual Obligations and Other Commitments

During the three months ended March 31, 2022, there were no material changes to our contractual obligations and commitments described under *Management's Discussion and Analysis of Financial Condition and Results of Operations* in our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC on February 28, 2022.

ITEM 3. 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.

We had $305.3 million and $326.9 million in cash, cash equivalents and marketable securities at March 31, 2022 and December 31, 2021, respectively. Cash and cash equivalents consist of cash, money market funds, commercial paper and government bonds. Marketable securities consist of corporate bonds, commercial paper and government bonds. A portion of our investments may be subject to interest rate risk and could fall 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 interest income by approximately $2.3 million, while an immediate 100 basis point decrease in interest rates would decrease our interest income by approximately $1.2 million.

Approximately $1.2 million and $1.1 million of our cash balance was located in Australia at March 31, 2022 and December 31, 2021, 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 our results of operations.

ITEM 4. 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 the end of the period covered by this report. Based on the evaluation of our disclosure controls and procedures, our Chief Executive Officer and Chief Financial Officer have concluded that, as of the end of the period covered by this report, our disclosure controls and procedures were effective at the reasonable assurance level.

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 the most recent fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II – OTHER INFORMATION

ITEM 1. 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 aware of any pending or threatened legal proceeding against us that we believe could have a material adverse effect on our business, operating results or financial condition.

ITEM 1A. RISK FACTORS

We have identified the following risks and uncertainties that may have a material adverse effect on our business, financial condition or results of operations. Investors should carefully consider the risks described below before making an investment decision. Our business faces significant risks and the risks described below may not be the only risks we face. If any of these risks occur, our business, results of operations or financial condition could suffer, and the market price of our common stock could decline.

Summary of Risk Factors

The following is a summary of the principal risks that could adversely affect our business, results of operations, and financial condition.

Under "**Risks Related to the COVID-19 Pandemic**" we describe risks to our business arising from the COVID-19 pandemic. The pandemic has and could continue to adversely impact our business, including our ongoing and planned clinical trials and pre-clinical and discovery research. The impacts on our business include, among others, delays to certain of our ongoing clinical trials.

Under "**Risks Related to Clinical Development**" we describe risks related to on our ongoing clinical development efforts. They include, among others, the following:

- We have no approved products and no historical product 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, order us to suspend or cease altogether further development of our product candidates.

Under "**Risks Related to our Financial Position and Capital Requirements**" we describe risks associated with our financial position and future capital requirements. They include, among others, the following:

- We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.
- We have never generated any revenue from product sales and may never be profitable.
- We expect to require substantial additional funding.
- Raising additional capital may cause dilution to our existing stockholders.

Under "**Risks Related to our Reliance on Third Parties**" we describe risks related to our reliance on third parties. They include, among others, the following:

- We rely on Janssen Biotech, Inc. ("Janssen") to continue the development of product candidates subject to our license and collaboration with Janssen, and to successfully commercialize any resulting products.
- 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.

Under "**Risks Related to Regulatory Approval**" we describe risks related to the potential regulatory approval required to market our product candidates in the United States or other jurisdictions. If we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

Under "**Risks Related to Commercialization of our Product Candidates**" we describe risks related to the commercialization of any of our product candidates that are eventually approved for marketing. We have no marketing and sales organization and may not be able to effectively market and sell any products or generate product revenue if any of our product candidates are approved for marketing. Also, if we commercialize our product candidates abroad, we will be subject to the risks of doing business outside of the United States.

Under "**Risks Related to our Business and Industry**" we describe risks related to our business in general, and to our company in the biotechnology and pharmaceutical industry. They include, among others, the following:

- We face significant competition from other biotechnology and pharmaceutical companies.
- 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.

Under "**Risks Related to our Intellectual Property**" we describe risks related to the intellectual property that is critical to the success of our business. They include, among others, the following:

- 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.

Under "**Risks Related to Ownership of our Common Stock**" we describe risks associated with owning our common stock. They include, among others, the following:

- Our stock price has been and will likely continue to be volatile and may decline, regardless of our operating performance.
- Any failure to maintain the adequacy of internal controls may adversely affect investor confidence in our company and, as a result, the value of our common stock.
- Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others or make it difficult for stockholders to replace members of our board of directors.

Risks Related to the COVID-19 Pandemic

The COVID-19 pandemic has and could continue to adversely impact our business, including our ongoing and planned clinical trials and pre-clinical and discovery research.

The extent to which the ongoing COVID-19 pandemic will continue to impact our business is uncertain and cannot be predicted. The pandemic's impact on our business will depend on a variety of factors, including the timing, extent, effectiveness and durability of vaccine programs or other treatments, new or continuing travel and other restrictions and public health measures, such as social distancing, business closures or disruptions, and the development

and spread of COVID-19 variants. The effectiveness of actions taken in the United States and other countries to contain, ameliorate the impact of and treat the disease and to address its impact, is not yet known. A number of jurisdictions, including California and other jurisdictions in the United States, have re-opened only to return to restrictions in the face of increases in new COVID-19 cases. As the COVID-19 pandemic continues, we could 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;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and trial procedures, which may impact the integrity of subject data and clinical trial endpoints;
- limitations in resources, including our employees, that would otherwise be focused on the conduct of our business or our current or planned clinical trials or pre-clinical research, including because of sickness, the desire to avoid contact with large groups of people or restrictions on movement or access to our facility as a result of government-imposed "shelter-in-place" or similar working restrictions;
- interruptions or delays in the operations of the U.S. Food and Drug Administration ("FDA") or other regulatory authorities, which may impact review and approval timelines;
- delays in manufacturing, receiving the supplies, materials and services needed to conduct clinical trials and pre-clinical research;
- changes in regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs or require us to discontinue the clinical trial altogether; and
- delays in necessary interactions with regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or furloughs of government or contractor personnel.

In addition, since March 2020, Alameda County, California, where our headquarters are located, has been subject to various "shelter-in-place" regulations and guidance related to the pandemic. While the "shelter-in-place" orders have terminated or been phased out along with the reopening of businesses in Alameda County, California, we may continue to be subject to capacity restrictions and health and safety recommendations that encourage continued social distancing and remote work, limiting or ability to return to pre-pandemic levels of activity. Our laboratory facilities currently remain open with heightened safety measures designed to minimize occupational exposure and reduce transmission of COVID-19 within our workplace. Our non-laboratory employees telecommute at least part-time, which may impact certain of our operations over the near term and long term. In addition, we may in the future resume a more restrictive remote work model due to the pandemic. These disruptions in our operations could negatively impact our business, operating results and financial condition.

Further, we may be required to develop and implement additional clinical trial policies and procedures designed to help protect trial participants from the COVID-19 virus and its variants, which may include using telemedicine visits, remote monitoring of patients and clinical sites, shipping drug product directly to patients rather than clinical sites, and measures to ensure that clinical data are collected pursuant to the trial protocol and consistent with good clinical practices ("GCPs"). Patients who miss scheduled appointments, any interruption in trial drug supply,

or other consequence that may result in incomplete data being generated during a trial as a result of the pandemic must be adequately documented and justified in accordance with FDA guidance. These additional requirements may be difficult to fulfill and may result in an incomplete data set, which could negatively impact the trial results.

While the extent of the impact of the COVID-19 pandemic on our business and financial results is uncertain, a continued and prolonged public health crisis such as the COVID-19 pandemic could have a material negative impact on our business, financial condition, and operating results.

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 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 Phase 1 and Phase 2 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 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 in registrational or pivotal clinical trials or 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 a new drug application ("NDA") from the FDA, or in any foreign countries until approval by corresponding regulatory authorities. We will need to conduct larger, more 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, for rusfertide for 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. 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 following the announcement in September 2021 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 topline data from our Phase 2 clinical trial evaluating PN-943 in ulcerative colitis.

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 expect to have 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 never conducted a Phase 3 clinical trial or submitted an NDA. As a result, we have no history or track record to rely on when entering 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. Clinical trials can be delayed for a variety of reasons, including if a clinical trial is modified, suspended or terminated by us, 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, on September 16, 2021, a full clinical hold by the FDA for the rusfertide clinical studies was triggered by a non-clinical finding in a 26-week rasH2 transgenic mouse model indicating benign and malignant subcutaneous skin tumors. On October 8, 2021, the FDA removed the full clinical hold on our rusfertide clinical studies and dosing in all clinical studies of rusfertide could be resumed. Also, in April 2022, the FDA indicated that it intends to rescind Breakthrough Therapy Designation for rusfertide in PV. For additional information, see the Risk Factor – "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 inflammatory bowel disease and in hematologic disorders that are currently ongoing, especially in Phases 2 and 3, making it highly competitive and challenging to recruit subjects. Furthermore, any negative results we may report in clinical trials of our product candidates, such as the premature termination of our Phase 2 clinical trial of PTG-100 for the treatment of moderate-to-severe UC, may make it difficult or impossible to recruit and retain patients in other 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. In addition, we are subject to risks and uncertainties as a result of the ongoing military conflict in Ukraine and Russia. A limited number of subjects were enrolled in our PN-943 Phase 2 IDEAL trial at clinical sites in Ukraine and Russia. On March 3, 2022, due to the ongoing military conflict in this region, we decided to close down our clinical sites in Ukraine and Russia. The impact of the ongoing military conflict in Ukraine and Russia on any future studies is uncertain at this time.

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, since our product candidates PN-943 and PN-235 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, on September 16, 2021 the Company's clinical studies for rusfertide were placed on a full clinical hold by the FDA. On October 8, 2021, per the FDA, the full clinical hold was lifted and dosing in all clinical studies of rusfertide could be resumed. We provided the FDA with all requested information as the basis for a Complete Response and subsequent removal of the clinical hold. In particular, we provided the requested individual patient clinical safety reports, updated the investigator brochure and patient informed consent forms, performed a comprehensive review of the most recent safety database, and included new safety and stopping rules in the study protocols. We are working closely with trial investigators and clinical trial sites to resume dosing of patients in ongoing clinical trials with rusfertide after patients have been reconsented. The clinical hold was initially triggered by a recent non-clinical finding in a 26-week rasH2 transgenic mouse model indicating benign and malignant subcutaneous skin tumors. The rasH2 signal also prompted a re-examination of the four cases of cancer observed across all rusfertide clinical trials involving over 160 patients, and a comprehensive review of the safety database, including cases of suspected unexpected serious adverse reactions. In April 2022, the FDA subsequently indicated that it intends to rescind Breakthrough Therapy Designation for rusfertide in PV.

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 focused on research programs and product candidates mainly on the development of rusfertide, PN-943 and the product candidates subject to our Janssen collaboration. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. 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 significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. We have never generated any revenue from product sales and may never be profitable.

We have incurred significant operating losses every year since inception and expect to continue to incur operating losses for the foreseeable future. As of March 31, 2022, we had an accumulated deficit of $430.3 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 at least several years, if ever, and we do not yet have any product candidates in registration or pivotal clinical trials. 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 collaboration with Janssen, 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 expect to require substantial 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 expect to require substantial 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 our Janssen License and Collaboration Agreement is terminated, we may not receive any additional fees or milestone payments under that agreement. Absent the funding support from this agreement, 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 March 31, 2022, we had cash, cash equivalents and marketable securities of $305.3 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 expect that we will need to have access to substantial 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 may seek additional funding through a combination of equity offerings, 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. 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 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 would experience additional dilution and, as a result, our stock price may decline.

Risks Related to our Reliance on Third Parties

If Janssen does not elect to continue the development of PN-235, our business and business prospects would be adversely affected.

PN-235, the product candidate in development pursuant to our Janssen collaboration, 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 Janssen License and Collaboration Agreement, Janssen 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, Janssen will generally have control over the further clinical development of PN-235 and any other second-generation compounds. Janssen's decisions with respect to such development will affect the timing and availability of potential future payments under the agreement, if any. During the fourth quarter of 2021, following a pre-specified interim analysis criteria, a portfolio decision was made by Janssen to stop further development of PTG-200, and further development of PN-232 was also discontinued during the quarter, both in favor of PN-235, a novel peptide with exceptional, low picomolar potency and with superior in vivo stability. If the Janssen License and Collaboration Agreement is terminated early, or if Janssen'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 Janssen during the term of the Janssen License and 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 Janssen regarding the development of PN-235 or other matters under the Janssen License and Collaboration Agreement, such as the interpretation of the agreement or ownership of proprietary rights. Also, after the period of collaborative development ends under the agreement, Janssen will have sole decision-making authority for product candidates resulting from the collaboration, which could lead to disputes with Janssen. Disagreements with Janssen could lead to litigation or arbitration, which would be expensive and would be time-consuming for our management and employees.

We may not be successful in obtaining or maintaining development and commercialization collaborations, any collaboration arrangements we enter into in the future may not be successful.

Other than our Janssen License and Collaboration Agreement, we have no active collaborations for any of our product candidates. Even if we establish other collaboration arrangements, any such collaboration may not ultimately be successful, which could have a negative impact on our business, results of operations, financial condition and growth prospects. If we enter into collaborations limited to certain territories, we may not maintain significant rights or control of future development and commercialization of any product candidate subject to the collaboration and potential disputes could develop in the future over the terms of the collaboration and the respective rights of the parties.

If our strategic collaborations do not result in the successful development and commercialization of product candidates or if one of our collaborators fails to act under the collaboration agreement or terminates its agreement with us, we may not receive any future research funding or milestone or royalty 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 European Medicines Agency ("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, 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 (particularly during the ongoing pandemic) and will force us to rely heavily on CROs to ensure 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 good manufacturing processes ("GMPs") required 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, the ongoing COVID-19 pandemic 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 Approval

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, 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 orphan drug designations from the FDA and/or EU 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 European Union ("EU"). 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. In order to commercialize any of our product candidates that receive marketing approval, we will have to build marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. In the event of 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. With respect to our product candidates, 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, and in the case of the Janssen License and Collaboration Agreement, we may elect to exercise our Co-Detailing Option (allows us to elect to provide up to 30% of the selling effort in the United States for any IL-23R antagonist compounds approved for commercial sale), 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.

For example, in the United States in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, (collectively, the "ACA") was enacted to increase access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and the health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The law has continued the downward pressure on pharmaceutical pricing, especially under the Medicare program, and increased the industry's regulatory burdens and operating costs.

There have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, former President Trump signed Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. 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 (the "Tax Act") included a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to 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, effective January 1, 2021, also eliminated the health insurance tax. Further, the Bipartisan Budget Act of 2018 (the "BBA") among other things, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court is currently reviewing this case, but it is unclear when a decision will be made. On February 10, 2021, the Biden administration withdrew the federal government's support for overturning the ACA. Although the U.S. Supreme Court has not yet ruled on the constitutionality of the ACA, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021 and will remain open until August 15, 2021. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how the Supreme Court ruling, other such litigation and the healthcare reform measures of the Biden administration will impact the ACA and our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2030 unless additional action is taken by Congress. COVID-19 relief legislation suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2021. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period in which the government may recover overpayments to providers from three to five years.

Heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. 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, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by

law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed until January 1, 2023. On November 20, 2020, the Centers for Medicare & Medicaid Services ("CMS") issued an interim final rule implementing former President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. At the state level, 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. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates, if approved.

We expect that additional state and federal healthcare reform measures will be adopted in the future, particularly in light of the new presidential administration, any of which could limit the amounts that federal and state governments will pay for healthcare therapies, which could result in reduced demand for our product candidates or additional pricing pressures. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.

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.

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.

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 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 June 2020, the FDA accepted 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. The FDA approved this application in November 2021. 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 PV and hereditary hemochromatosis (“HH”) 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.

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, Janssen or we are unable to comply with these regulations, our ability to earn potential royalties from worldwide net sales of Janssen collaboration product candidates 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 with Janssen or cause Janssen to terminate the Janssen 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. 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, and we may experience difficulties in managing this growth.

As of March 31, 2022, we had 122 full-time equivalent employees, including 97 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 breaches of data security 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 partner, and other third parties on which we rely may make them potentially vulnerable to breakdown, telecommunications and electrical failures, malicious intrusion such as ransomware and computer viruses that may result in the impairment of key business processes. Our systems are potentially vulnerable to data security breaches, by employees or others, that may expose sensitive data to unauthorized persons. Such data security breaches could lead to the loss of trade secrets or other intellectual property or could lead to the public exposure of personally identifiable information (including sensitive personal information) of our employees, collaborators, clinical trial patients, and others. A malicious intrusion, email compromise or other data security breach or privacy violation that leads to disclosure or modification of or prevents access to patient information, including personally identifiable information or protected health information, 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. If we are unable to prevent such data security breaches 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 wastes. 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, 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 fires. 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. patents covering PN-943 and PTG-200 expire in 2035, and our granted U.S. patent covering rusfertide expires in 2034. Although the life of a patent can be increased based on certain delays caused by the U.S. Patent and Trademark Office (the "PTO"), 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 of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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 IL-23R, α4β7 integrin or hepcidin mimetics, 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 Janssen or us to litigation, or otherwise preventing the commercialization of product candidates in the relevant jurisdiction(s); or
- requiring Janssen 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 collaboration with Janssen or cause Janssen to terminate the Janssen License and Collaboration Agreement.

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 also 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, 2021 through March 31, 2022, the reported sale price of our common stock has fluctuated between $12.80 and $50.54 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 obligated 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. If we have a material weakness, we would receive an adverse opinion regarding our internal control over financial reporting from our independent registered accounting firm.

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. 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.

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 of 1933, as amended, 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 of directors, 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 and in the current year, 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.

We may have additional tax liabilities.

We are regularly subject to audits by tax authorities in the jurisdictions in which we conduct business. Although we believe our tax positions are reasonable, the final outcome of tax audits and related litigation could be materially different than that reflected in our historical income tax provisions and accruals, and we could be subject to assessments of additional taxes and/or substantial fines or penalties. The resolution of any audits or litigation could have an adverse effect on our financial position and results of operations. We and our subsidiary are engaged in intercompany transactions, the terms and conditions of which may be scrutinized by tax authorities, which could result in additional tax and/or penalties becoming due.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

Recent Sales of Unregistered Securities

None.

Repurchases of Shares or of Company Equity Securities

None.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

None.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

None.

ITEM 6. EXHIBITS

EXHIBIT INDEX

Exhibit Number	Exhibit Description	Incorporation By Reference			
		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	Amended and Restated Bylaws	S-1/A	333-212476	3.2	8/1/2016
10.1+	Employment Offer Letter dated March 25, 2022 by and between the Registrant and Asif Ali				
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				
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				
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				
101.INS+	XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.				
101.SCH+	Inline XBRL Taxonomy Extension Schema Document				
101.CAL+	Inline XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF+	Inline XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB+	Inline XBRL Taxonomy Extension Labels Linkbase Document				
101.PRE+	Inline XBRL Taxonomy Extension Presentation Linkbase Document				
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				

+ Filed herewith

† Confidential treatment has been granted for a portion of this exhibit.

* This certification attached as Exhibit 32.1 that accompanies this Quarterly Report on Form 10-Q 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-Q, irrespective of any general incorporation language contained in such filing.

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: May 5, 2022

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

Date: May 5, 2022

By: /s/ Asif Ali
Asif Ali
Executive Vice President, Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 10.1

Protagonist Therapeutics Inc

7707 Gateway Blvd., Ste 140
Newark, CA 94560

United States of America

Tel + 1 510 474 0170
Fax + 1 649 649 7377

www.protagonist-inc.com

March 25, 2022

Asif Ali
[email address]
[telephone number]

Dear Asif,

On behalf of Protagonist, a biopharmaceutical company dedicated to discovering and developing peptides as novel pharmaceutical drugs, I am happy to extend to you an offer of full-time employment in our organization as **EVP, Chief Financial Officer** reporting directly to Dinesh V. Patel**,** President/Chief Executive Officer, starting on Monday, **April 18, 2022 ("Hire Date").**

Specifically, this letter will confirm in writing the terms of Protagonist's offer to you:

1. This is a salaried regular position exempt from state and federal wage and hours laws and regulations. Your annual base salary will be **$425,000.** Your base salary will be paid in accordance with the Company's normal payroll procedures and will be subject to applicable withholding required by law. Presently employees are paid on the 15th and on the last day of each month. You will be eligible for a discretionary annual bonus of up to **40%** of your salary, prorated to actual days of employment in a calendar year based on the accomplishment of corporate and personal goals. Employees that start in the fourth quarter are not eligible for a bonus for that year. You must be employed by the Company on the date on which the bonus is paid. The Company reserves the right to change your position, duties, work location, reporting relationship and compensation from time to time in its discretion.

2. As a full-time employee of the Company, promptly following commencement of your employment, which will be Monday, April 18, 2022, and as a material inducement to your employment by the Company, you will be granted by the Compensation Committee of the Board of Directors (the "Committee") an option to purchase **82,500** (eight two thousand five hundred) shares of the Company's Common Stock (the "Option") and **13,750** (thirteen thousand seven hundred fifty) Restricted Stock Units (the "RSUs") pursuant to the Protagonist Therapeutics, Inc. 2018 Inducement Plan (the "Plan"). The exercise price per share for the Option shall be equal to the Fair Market Value (as defined in the Plan) as of the date of grant of the Option (which is expected be April 18, 2022 based on your employment start date). The Option and the RSUs will be subject to the terms and conditions of the Plan and the applicable grant notices and option agreements. You will vest in 25% of the option shares after 12 months of continuous service, and the balance will vest in equal monthly installments over the next 36 months of continuous service. Your RSUs will not have an exercise or

purchase price, and will vest in four equal installments on the first four anniversaries of their grant date, subject to your continuous service to the Company.

3. You will be eligible to participate in Protagonist's employee benefits program including medical, dental, vision, life, Employee Stock Purchase Plan (ESPP) and AD&D insurance as well as participate in our 401(k) plan. The Company reserves the right to amend, add or discontinue benefits from time to time in its sole discretion.

4. As a Protagonist employee, you will be expected to abide by Company rules and policies, and sign and comply with the Proprietary Information and Inventions Agreement, which prohibits unauthorized use or disclosure of Protagonist's proprietary information.

5. In your work for the Company, you will be expected not to use or disclose any confidential or proprietary information, including trade secrets, of other companies or third parties. If you have or have had access to trade secrets or other confidential, proprietary information from your former employer or another third party, the use of such information in performing your duties at the Company is prohibited. This may include, but is not limited to, confidential or proprietary information in the form of documents, magnetic media, software, customer lists, and business plans or strategies. You will be expected to use only that information which is generally known and used by persons with training and experience comparable to your own, which is common knowledge in the industry or otherwise legally in the public domain, or which is otherwise provided or developed by the Company. During our discussions about your proposed job duties, you assured us that you would be able to perform those duties within the guidelines just described. You must also advise the Company before your employment start date of any restrictions on your ability to work for the Company, such as any covenants not to compete or solicit with any former employers. The Company reserves the right to rescind this offer should it determine that such restriction poses a legal risk to the Company.

6. In your capacity as a full-time employee of Protagonist, you will be expected to relinquish all consulting roles and obligations with other organizations. The Company expects you to devote your full business time, attention, knowledge and skills to the affairs of the Company and to your duties for the Company, and to perform those duties diligently and to the best of your ability.

7. You agree that you will not bring onto Company premises any unpublished documents or property belonging to any former employer or other person to whom you have an obligation of confidentiality.

8. Your employment will be "at will". You may terminate your employment with Protagonist at any time and for any reason whatsoever simply by notifying Protagonist. Likewise, Protagonist may terminate your employment at any time and for any reason whatsoever, with or without cause or advance notice. This at-will employment relationship cannot be changed except in a writing signed by a Company officer.

9. To ensure the rapid and economical resolution of disputes that may arise in connection with your employment with the Company, you and the Company agree that any and all disputes, claims, or causes of action, in law or equity, including but not limited to statutory claims, arising from or relating to the enforcement, breach, performance, or interpretation of this Agreement, your employment with the Company, or the termination of your employment, shall be resolved, to the fullest extent permitted by law, by final, binding and confidential arbitration in San Francisco, California conducted by JAMS or its successor, under JAMS' rules and procedures for employment disputes (which can be downloaded at http://www.jamsadr.com/rules-employment-arbitration/ or will be provided to you upon request). You acknowledge that by agreeing to this arbitration procedure, both you and the Company waive the right to resolve any such dispute through a trial by jury or judge or administrative proceeding. All claims, disputes or causes of action, by either you or the Company, must be brought in an individual capacity, and shall not be brought as a plaintiff (or claimant) or class member in any purported class or representative proceeding, nor brought in a private attorney general capacity or proceeding, nor joined or consolidated with any claims of any other person or entity. You

will have the right to be represented by legal counsel at any arbitration proceeding. The arbitrator shall: (a) have the authority to compel adequate discovery for the resolution of the dispute and to award such relief as would otherwise be permitted by law; and (b) issue a written statement signed by the arbitrator regarding the disposition of each claim and the relief, if any, awarded as to each claim, the reasons for the award, and the arbitrator's essential findings and conclusions on which the award is based. The arbitrator shall be authorized to award all relief that you or the Company would be entitled to seek in a court of law. The Company shall pay all JAMS arbitration fees in excess of the administrative fees that you would be required to pay if the dispute were decided in a court of law. Nothing in this letter agreement is intended to prevent either you or the Company from obtaining injunctive relief in court to prevent irreparable harm pending the conclusion of any such arbitration.

10. This offer is contingent upon completion of a satisfactory background check. As required by law, this offer is subject to satisfactory proof of your identity and eligibility to work in the United States.

11. This letter, together with your Proprietary Information Agreement, forms the complete and exclusive statement of your agreement with the Company concerning the subject matter hereof. The terms in this letter supersede any other representations or agreements made to you by any party, whether oral or written. The terms of this agreement cannot be changed (except with respect to those changes expressly reserved to the Company's discretion in this letter) without a written agreement signed by you and a duly authorized officer of the Company. This agreement is to be governed by the laws of the state of California without reference to conflicts of law principles.

At Protagonist, we're creating a great environment for employees to work in synergy with each other, and are excited at the prospects of you joining us in this adventure. We look forward to your significant contributions towards accomplishing our common goals. I would like to emphasize that Protagonist offers exceptional opportunities for achieving valuable industrial experience, personal career growth, and individual recognition. Please do not hesitate to contact me if you have any questions.

To indicate your acceptance of our offer, please sign and date one copy of this letter in the space provided below and return it to us. If you accept our offer, we would like you to start working at the US site no later than April 18, 2022**.** This offer will remain open until March 25, 2022 at which time it will expire if not previously accepted.

Sincerely yours,

/s/ Dinesh V. Patel

Dinesh V. Patel, Ph.D.
President & CEO
Protagonist Therapeutics

I accept your offer of employment as described above:

/s/ Asif Ali	3/25/22
Asif Ali	Date

Enclosures: Proprietary Information Agreement

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 Quarterly Report on Form 10-Q 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 Rules13a-15(f) and 15d-15(f)) for the registrant and we 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: May 5, 2022

/s/ Dinesh V. Patel, Ph.D.
Dinesh V. Patel, Ph.D.
President, Chief Executive Officer
(Principal 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 Quarterly Report on Form 10-Q 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 we 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.

/s/ Asif Ali

Date: May 5, 2022

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 the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Dinesh V. Patel, Chief Executive Officer of Protagonist Therapeutics, Inc. (the "Company"), and Asif Ali, Chief Financial Officer of the Company, each hereby certify that, to the best of his knowledge:

1. The Company's Quarterly Report on Form 10-Q for the period ended March 31, 2022, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: May 5, 2022

/s/ Dinesh V. Patel, Ph.D.
Dinesh V. Patel, Ph.D.
President, Chief Executive Officer

Date: May 5, 2022

/s/ Asif Ali
Asif Ali
Executive Vice President, Chief Financial Officer

"This certification accompanies the Form 10-Q to which it relates, 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-Q), irrespective of any general incorporation language contained in such filing."