
**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 September 30, 2018

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

(State or other jurisdiction of
incorporation or organization)

98-0505495

(I.R.S. Employer
Identification No.)

7707 Gateway Boulevard, Suite 140
Newark, California 94560-1160

(Address, including zip code, of registrant's principal executive offices)

(510) 474-0170

(Telephone number, including area code, of registrant's principal
executive offices)

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 and post 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	<input type="checkbox"/>	Accelerated filer	<input checked="" type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

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

Indicate the number of shares outstanding of each of the issuer's classes of common stock, as of the latest practicable date.

Class	Outstanding at October 31, 2018
Common Stock, \$0.00001 par value	24,186,019

PROTAGONIST THERAPEUTICS, INC.
FORM 10-Q
TABLE OF CONTENTS

	<u>Page</u>	
<u>PART I</u>	<u>FINANCIAL INFORMATION</u>	
<u>Item 1.</u>	<u>Condensed Consolidated Financial Statements (unaudited)</u>	
	<u>Condensed Consolidated Balance Sheets</u>	1
	<u>Condensed Consolidated Statements of Operations</u>	2
	<u>Condensed Consolidated Statements of Comprehensive Loss</u>	3
	<u>Condensed Consolidated Statements of Cash Flows</u>	4
	<u>Notes to Unaudited Condensed Consolidated Financial Statements</u>	5
<u>Item 2.</u>	<u>Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	26
<u>Item 3.</u>	<u>Quantitative and Qualitative Disclosures About Market Risk</u>	37
<u>Item 4.</u>	<u>Controls and Procedures</u>	37
<u>PART II</u>	<u>OTHER INFORMATION</u>	
<u>Item 1.</u>	<u>Legal Proceedings</u>	38
<u>Item 1A.</u>	<u>Risk Factors</u>	38
<u>Item 2.</u>	<u>Unregistered Sales of Equity Securities and Use of Proceeds</u>	91
<u>Item 3.</u>	<u>Defaults Upon Senior Securities</u>	91
<u>Item 4.</u>	<u>Mine Safety Disclosure</u>	91
<u>Item 5.</u>	<u>Other Information</u>	91
<u>Item 6.</u>	<u>Exhibits</u>	91
	<u>SIGNATURES</u>	94

PART I. – FINANCIAL INFORMATION**ITEM 1. FINANCIAL STATEMENTS**

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

	September 30, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	\$ 87,427	\$ 106,029
Restricted cash	10	10
Available-for-sale securities	51,090	37,972
Receivable from collaboration partner - related party	4,586	1,816
Research and development tax incentive receivable	1,155	1,347
Prepaid expenses and other current assets	3,234	3,773
Total current assets	147,502	150,947
Property and equipment, net	904	879
Restricted cash - noncurrent	450	450
Available-for-sale securities - noncurrent	—	11,458
Total assets	<u>\$ 148,856</u>	<u>\$ 163,734</u>
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$ 4,871	\$ 1,257
Payable to collaboration partner - related party	764	—
Accrued expenses and other payables	10,496	9,546
Deferred revenue - related party	7,970	31,752
Total current liabilities	24,101	42,555
Deferred rent - noncurrent	797	547
Total liabilities	24,898	43,102
Commitments and contingencies (Note 8)		
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; 24,138,102 and 21,088,306 shares issued and outstanding as of September 30, 2018 and December 31, 2017, respectively	—	—
Additional paid-in capital	250,670	222,188
Accumulated other comprehensive loss	(103)	(6)
Accumulated deficit	(126,609)	(101,550)
Total stockholders' equity	123,958	120,632
Total liabilities and stockholders' equity	<u>\$ 148,856</u>	<u>\$ 163,734</u>

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 September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
License and collaboration revenue - related party	\$ 6,117	\$ 8,781	\$ 28,572	\$ 8,781
Operating expenses:				
Research and development	12,145	11,168	45,249	34,457
General and administrative	3,361	2,593	10,180	8,708
Total operating expenses	<u>15,506</u>	<u>13,761</u>	<u>55,429</u>	<u>43,165</u>
Loss from operations	(9,389)	(4,980)	(26,857)	(34,384)
Interest income	654	155	1,798	479
Net loss	<u>\$ (8,735)</u>	<u>\$ (4,825)</u>	<u>\$ (25,059)</u>	<u>\$ (33,905)</u>
Net loss per share, basic and diluted	<u>\$ (0.38)</u>	<u>\$ (0.29)</u>	<u>\$ (1.15)</u>	<u>\$ (2.01)</u>
Weighted-average shares used to compute net loss per share, basic and diluted	<u>22,912,279</u>	<u>16,911,575</u>	<u>21,750,562</u>	<u>16,851,672</u>

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 September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Net loss	\$ (8,735)	\$ (4,825)	\$ (25,059)	\$ (33,905)
Other comprehensive loss:				
Loss (gain) on translation of foreign operations	(63)	73	(149)	324
Unrealized gain on available-for-sale securities	46	24	52	21
Comprehensive loss	<u>\$ (8,752)</u>	<u>\$ (4,728)</u>	<u>\$ (25,156)</u>	<u>\$ (33,560)</u>

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)

	Nine Months Ended	
	September 30,	
	2018	2017
CASH FLOWS FROM OPERATING ACTIVITIES		
Net loss	\$ (25,059)	\$ (33,905)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:		
Stock-based compensation	4,847	3,052
Net amortization of premium on available-for-sale securities	304	497
Depreciation and amortization	399	289
Loss on disposal of property and equipment	—	(62)
Changes in operating assets and liabilities:		
Research and development tax incentive receivable	96	1,530
Receivable from collaboration partner - related party	(2,770)	(520)
Prepaid expenses and other assets	526	1,034
Accounts payable	3,617	1,096
Payable to collaboration partner - related party	764	—
Accrued expenses and other payables	1,246	3,271
Deferred revenue - related party	(23,782)	41,739
Net cash provided by (used in) operating activities	(39,812)	18,021
CASH FLOWS FROM INVESTING ACTIVITIES		
Purchase of available-for-sale securities	(51,947)	(28,154)
Proceeds from maturities of available-for-sale securities	50,035	39,835
Purchases of property and equipment, net	(424)	(610)
Net cash provided by (used in) by investing activities	(2,336)	11,071
CASH FLOWS FROM FINANCING ACTIVITIES		
Proceeds from issuance of common stock and warrants in private placement, net of issuance costs	21,679	—
Proceeds from issuance of common stock in at-the-market offerings, net of issuance costs	1,025	—
Proceeds from issuance of common stock upon exercise of stock options and purchases under employee stock purchase plan	932	789
Payment of deferred offering costs	—	(297)
Net cash provided by financing activities	23,636	492
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(90)	177
Net increase (decrease) in cash, cash equivalents and restricted cash	(18,602)	29,761
Cash, cash equivalents and restricted cash, beginning of year	106,489	21,094
Cash, cash equivalents and restricted cash, end of period	\$ 87,887	\$ 50,855
SUPPLEMENTAL DISCLOSURES OF NON-CASH FINANCING AND INVESTING INFORMATION:		
Acquisition of new equipment upon trade-in for existing equipment	\$ —	\$ 185
Purchases of property and equipment in accounts payable	\$ —	\$ 6

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”) was incorporated in the state of Delaware on August 22, 2006 and is headquartered in Newark, California. The Company is a clinical-stage biopharmaceutical company with a proprietary technology platform that enables the discovery and development of novel constrained peptide-based drug candidates that address significant unmet medical needs. Protagonist Pty Limited (“Protagonist Australia”) is a wholly-owned subsidiary of the Company and is located in Brisbane, Queensland, Australia. Protagonist Australia was incorporated in Australia in September 2001. The Company became the parent of Protagonist Australia pursuant to a transaction in which all of the issued and outstanding capital stock of Protagonist Australia was exchanged for shares of the Company’s common stock and Series A preferred stock. The Company manages its operations as a single operating segment.

Liquidity

The Company has incurred net losses from operations since inception and has an accumulated deficit of \$126.6 million as of September 30, 2018. The Company’s ultimate success depends on the outcome of its research and development activities. The Company expects to incur additional losses in the future and it anticipates the need to raise additional capital to fully implement its business plan. Through September 30, 2018, the Company has financed its operations primarily through private placements of redeemable convertible preferred stock, offerings of common stock and payments received under a license and collaboration agreement.

In September 2017, the Company filed a registration statement on Form S-3 with the Securities and Exchange Commission (“SEC”) (File No. 333-220314), effective as of October 5, 2017, as amended, which permits the offering, issuance, and sale by the Company of up to a maximum aggregate offering price of \$200.0 million of its common stock. Up to a maximum of \$50.0 million of the maximum aggregate offering price of \$200.0 million may be issued and sold pursuant to an at-the-market (“ATM”) financing facility under a sales agreement with Cantor Fitzgerald & Co. (the “Sales Agreement”). The Company pays Cantor Fitzgerald & Co. up to 3% of gross proceeds for any common stock sold through the Sales Agreement. The Company sold 103,500 shares of its common stock pursuant to the Sales Agreement during the three and nine months ended September 30, 2018 for net proceeds of \$1.1 million. As of September 30, 2018, \$48.8 million of common stock remained available for sale under the ATM financing facility.

In October 2017, the Company completed an underwritten public offering of 3,530,000 shares of common stock at a public offering price of \$17.00 per share. In November 2017, the Company issued an additional 529,500 shares of its common stock at a price of \$17.00 per share following the underwriters’ exercise of their option to purchase additional shares. Net proceeds, after deducting underwriting commissions and offering costs paid by the Company, were \$64.5 million.

On August 6, 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 gross proceeds of approximately \$22.0 million, before 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

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

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*, and the net proceeds from the transaction were recorded as a credit to additional paid-in capital. As of September 30, 2018, none of the warrants have been exercised.

The Company will continue to seek funds through equity or debt financings, collaborative or other arrangements with corporate sources, or through other sources of financing, but there is no assurance that such financing will be available at terms acceptable to the Company, if at all.

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 of America (“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 consolidated balance sheet as of December 31, 2017 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 only of normal recurring adjustments) that are necessary for a fair statement of the Company’s consolidated financial information. The results of operations for the three and nine months ended September 30, 2018 are not necessarily indicative of the results to be expected for the year ending December 31, 2018 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, 2017 included in the Company’s Annual Report on Form 10-K, filed with the SEC on March 7, 2018.

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 assets and 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 related to revenue recognition, accruals for research and development activities, stock-based compensation, and income taxes. Estimates related to revenue recognition include actual costs incurred versus total estimated budgeted

PROTAGONIST THERAPEUTICS, INC.**Notes to Unaudited Condensed Consolidated Financial Statements (Continued)**

cost of the Company's deliverables, actual costs versus total estimated budget to determine percentage of completion, and application of constraint in the determination of transaction price under its license and collaboration agreement with Janssen Biotech, Inc. (the "Janssen License and Collaboration Agreement"). 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. Actual results may differ significantly from those estimates.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents and available-for-sale securities. Substantially all of the Company's cash is held by three financial institutions that management believes are of high credit quality. Such deposits may, at times, exceed federally insured limits. The primary focus of the Company's investment strategy is to preserve capital and to meet liquidity requirements. The Company's cash equivalents and available-for-sale securities are managed by external managers within the guidelines of the Company's investment policy. The Company's investment policy addresses the level of credit exposure by limiting concentration in any one corporate issuer and establishing a minimum allowable credit rating. To manage its credit risk exposure, the Company maintains its portfolio of cash equivalents and available-for-sale securities in fixed income securities denominated and payable in U.S. dollars. Permissible investments of fixed income securities include obligations of the U.S. government and its agencies, money market instruments including commercial paper and negotiable certificates of deposit, and highly rated corporate debt obligations and money market funds. The Company has not experienced any material credit losses on its investments.

Cash Equivalents

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

Restricted Cash

Restricted cash consists of cash balances primarily held as security in connection with a letter of credit related to the Company's facility lease entered into in March 2017 and the Company's corporate credit card.

Cash as Reported in 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 consolidated balance sheets.

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

	September 30,	
	2018	2017
Cash and cash equivalents	\$ 87,427	\$ 50,395
Restricted cash - current	10	10
Restricted cash - noncurrent	450	450
Cash balance in consolidated statements of cash flows	<u>\$ 87,887</u>	<u>\$ 50,855</u>

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

Available-for-Sale Securities

All marketable securities have been classified as “available-for-sale” and are carried at estimated fair value as determined based upon quoted market prices or pricing models for similar securities. Management determines the appropriate classification of its marketable securities at the time of purchase and reevaluates such designation as of each balance sheet date. Short-term marketable securities have maturities greater than three months but no longer than 365 days as of the balance sheet date. Long-term marketable securities have maturities of 365 days or longer as of the balance sheet date. Unrealized gains and losses are excluded from earnings and are reported as a component of comprehensive loss. Realized gains and losses and declines in fair value judged to be other than temporary, if any, on available-for-sale securities are included in interest income. The cost of securities sold is based on the specific-identification method. Interest on marketable securities is included in interest income.

Revenue Recognition

Effective July 1, 2017, the Company adopted Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers* (“ASC 606”) using the full retrospective transition method. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaborative arrangements under Accounting Standards Codification Topic 808, and financial instruments. Under ASC 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company entered into a license and collaboration agreement that became effective upon the resolution of regulatory requirements during the third quarter of 2017 which is within the scope of ASC 606, under which it has licensed certain rights to its PTG-200 product candidate to a third party and may enter into other such arrangements in the future. The terms of the arrangement include payment to the Company of one or more of the following: non-refundable, up-front license fees, development and regulatory and commercial milestone payments, and royalties on net sales of licensed products.

Licenses of intellectual property: If the license to the Company’s intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgement to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring proportional performance for purposes of recognizing revenue from non-refundable, up-front fees. The Company evaluates the

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

measure of proportional performance each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone payments: At the inception of each arrangement that includes development, regulatory or commercial milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price. ASC 606 suggests two alternatives to use when estimating the amount of variable consideration: the expected value method and the most likely amount method. Under the expected value method, an entity considers the sum of probability-weighted amounts in a range of possible consideration amounts. Under the most likely amount method, an entity considers the single most likely amount in a range of possible consideration amounts. Whichever method is used, it should be consistently applied throughout the life of the contract; however, it is not necessary for the Company to use the same approach for all contracts. The Company expects to use the most likely amount method for development and regulatory milestone payments. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis. The Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability or achievement of each such milestone and any related constraint, and if necessary, adjusts its estimates of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. To date, the Company has not recognized any milestone payments resulting from its collaboration arrangement.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from its collaboration arrangement.

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

Research and Development Costs

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

The Company accrues for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of pre-clinical studies and clinical trials, and contract manufacturing activities. The Company records the estimated costs of research and development activities based upon the estimated services provided but not yet invoiced and includes these costs in accrued expenses and other payables in the condensed

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

consolidated balance sheets and within research and development expense in the condensed consolidated statements of operations. These costs are a significant component of the Company's research and development expenses. The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with agreements established with its third-party service providers. The Company makes significant judgments and estimates in determining the accrued liabilities at each balance sheet date. As actual costs become known, the Company adjusts its accrued liabilities. The Company has not experienced any material differences between accrued liabilities and actual costs incurred. However, the status and timing of actual services performed, number of patients enrolled, and the rate of patient enrollment may vary from the Company's estimates, resulting in adjustments to expense in future periods. Changes in these estimates that result in material changes to the Company's accruals could materially affect the Company's results of operations.

Research and Development Tax Incentive

The Company is eligible under the AusIndustry research and development tax incentive program to obtain a cash amount from the Australian Taxation Office. The tax incentive is available to the Company on the basis of specific criteria with which the Company must comply. Specifically, the Company must have annual turnover of less than AUD 20.0 million and cannot be controlled by income tax exempt entities. The research and development tax incentive is recognized as a reduction to research and development expense when the right to receive has been attained and funds are considered to be collectible. The tax incentive is denominated in Australian dollars and, therefore, the related receivable is remeasured into U.S. dollars as of each reporting date.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding during the period, without consideration of potentially dilutive securities. Diluted net loss per share is the same as basic net loss per share for all periods presented since the effect of potentially dilutive securities is anti-dilutive given the net loss of the Company.

Recently Adopted Accounting Pronouncements

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments*, which clarifies the classification of certain cash receipts and cash payments in the statements of cash flow to eliminate the diversity in practice related to eight specific cash flow issues. This guidance is effective for fiscal years and interim periods within those years beginning after December 15, 2017, with early adoption permitted. The Company adopted this guidance effective January 1, 2018. The adoption of this guidance had no effect on the Company's consolidated financial statements and disclosures.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation - Stock Compensation (Topic 718): Scope of Modification Accounting*, which provides guidance on the types of changes to the terms and conditions of share-based payment awards to which an entity would be required to apply modification accounting. Specifically, an entity would not apply modification accounting if the fair value, vesting conditions and classification of the awards are the same immediately before and after the modification. This guidance is effective for fiscal years and interim periods within those years beginning after December 15, 2017, with early adoption permitted. The Company adopted this guidance effective January 1, 2018. The adoption of this guidance had no effect on the Company's consolidated financial statements and disclosures.

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

Recently Issued Accounting Pronouncements Not Adopted as of September 30, 2018

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*. In July 2018, the FASB issued ASU No. 2018-10, Codification Improvements to Topic 842, Leases, which provides clarification to ASU 2016-02. These ASUs (collectively, the new lease standard) require an entity to recognize a lease liability and a right-of-use asset on the balance sheet for leases with lease terms of more than twelve months. Lessor accounting is largely unchanged, while lessees will no longer be provided with a source of off-balance sheet financing. This guidance is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. Early adoption is permitted. Initial guidance required the adoption of the new lease standard using the modified retrospective transition method. In July 2018, the FASB issued ASU No. 2018-11, *Leases (Topic 842) - Targeted Improvements*, which allows entities to elect an optional transition method where entities may continue to apply the existing lease guidance during the comparative periods and apply the new lease requirements through a cumulative effect adjustment in the period of adoptions rather than in the earliest period presented. The Company plans to adopt the new standard on January 1, 2019 using the optional transition method. The Company established a cross-functional implementation team to develop a project plan and is currently reviewing its lease portfolio. While the Company continues to review its current accounting policies and practices to identify potential differences that would result from applying the new guidance, the Company expects that its non-cancellable operating lease commitments with a term of more than twelve months will be subject to the new guidance and recognized as right-of-use assets and operating lease liabilities on the Company's consolidated balance sheets upon adoption. The Company expects to elect transitional practical expedients such that the Company will not need to reassess whether contracts are leases and will retain lease classification and initial direct costs for leases existing prior to the adoption of the new lease standard.

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 is effective for fiscal years and interim periods within those years beginning after December 15, 2019 and early adoption is permitted for fiscal years and interim periods within those years beginning after December 15, 2018. The Company is currently evaluating the impact of this new guidance on its consolidated financial statements and disclosures.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation - Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting*, which is intended to simplify the accounting for nonemployee share-based payment transactions by expanding the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. The guidance is effective for fiscal years and interim periods within those years beginning after December 15, 2018. Early adoption is permitted, but no earlier than an entity's adoption date of ASC 606. The Company is currently evaluating the impact of this new guidance on its consolidated financial statements and disclosures.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820) - Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement*, which modifies the disclosure requirements on fair value measurements and is intended to improve the effectiveness of disclosures, including the consideration of costs and benefits. The guidance is effective for the fiscal years and interim periods within those years beginning after January 1, 2020. Early adoption is permitted, and an entity is permitted to early adopt any removed or modified disclosures and delay adoption of additional disclosures until their effective date. The Company does not expect this new guidance to impact its consolidated financial statements and is currently evaluating the impact on its disclosures.

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

In August 2018, the FASB issued ASU No. 2018-15, *Intangibles -- Goodwill and Other -- Internal-Use Software (Subtopic 350-40), Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement that is a Service Contract*, which is intended to align the accounting for implementation costs for hosting arrangements, regardless of whether they convey a license to the hosted software. The amended guidance requires an entity (customer) in a hosting arrangement that is a service contract to follow the guidance in Subtopic 350-40 to determine which implementation costs to capitalize as an asset related to the service contract and which costs to expense. This guidance is effective for fiscal years and interim periods within those years beginning after January 1, 2020. Early adoption is permitted. The Company is currently evaluating the impact of this new guidance on its consolidated financial statements and disclosures.

Note 3. Janssen Collaboration Agreement

Agreement Terms

On May 26, 2017, the Company and Janssen Biotech, Inc., ("Janssen"), one of the Janssen Pharmaceutical Companies of Johnson & Johnson, entered into an exclusive license and collaboration agreement for the clinical development, manufacture and potential commercialization of PTG-200 worldwide for the treatment of Crohn's disease ("CD") and ulcerative colitis ("UC"). 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. PTG-200 is the Company's oral Interleukin 23 receptor ("IL-23R") antagonist drug candidate currently in development. The Janssen License and Collaboration Agreement became effective on July 13, 2017. Upon the effectiveness of the agreement, the Company received a non-refundable, upfront cash payment of \$50.0 million from Janssen.

Under the Janssen License and Collaboration Agreement, the Company granted to Janssen an exclusive worldwide license to develop, manufacture and commercialize PTG-200 and related IL-23R compounds for all indications, including CD and UC. The Company is responsible, at its own expense, for the conduct of the Phase 1 clinical trial for PTG-200, and Janssen will be responsible for the conduct of a potential Phase 2 clinical trial for PTG-200 in CD, including filing the Investigational New Drug application ("IND"). All such clinical trials will be conducted in accordance with a mutually agreed upon clinical development plan and budget. Development costs for the Phase 2 clinical trial will be shared between the parties on an 80%/20% basis, with Janssen assuming the larger share. Should Janssen elect to retain its license following completion of the Phase 2 clinical trial, it will be responsible, at its own expense, for the manufacture, continued development of, seeking regulatory approval for, and commercialization of PTG-200 worldwide. The parties' development activities under the Janssen License and Collaboration Agreement through the Phase 2 clinical trial will be overseen by a joint governance structure which will have equal representation by both parties unless both parties mutually agree to disband such structure or the Company has provided written notice to Janssen of its intention to disband and no longer participate in such structure.

The Company is eligible to receive a \$25.0 million payment upon filing of the IND. Following the conclusion of the planned Phase 2a portion of the Phase 2 clinical trial, if Janssen elects to maintain its license rights and continue the development of PTG-200 in the Phase 2b portion of such clinical trial (the "First Opt-in Election"), the Company would be eligible to receive a \$125.0 million payment. Following the conclusion of the planned Phase 2b portion of the Phase 2 clinical trial, if Janssen elects again to maintain its license rights (the "Second Opt-in Election"), the Company would be eligible to receive a \$200.0 million payment. In addition to the opt-in fees, the Company would be eligible to receive potential development, regulatory and sales milestone payments of up to an aggregate of \$590.0 million, and tiered royalties paid as a percentage of Janssen's worldwide net sales at rates ranging from ten to the mid-teens, with certain customary reductions under certain circumstances. If Janssen does not make either the First Opt-in Election or the Second Opt-in Election, the Janssen License and Collaboration Agreement will terminate. If Janssen does not make

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

the Second Opt-in Election, or if at any time after the Second Opt-in Election, Janssen terminates the Janssen License and Collaboration Agreement, the Company would be obligated to pay Janssen a low single-digit royalty on worldwide net sales of PTG-200. The Company would also have an option to provide up to 30% of the required U.S. details for PTG-200 to prescribers, using its own sales force personnel, upon commercial launch in the United States. If such right is exercised by the Company, the Company's detailing costs would be reimbursed by Janssen at a mutually agreed cost per primary detailing equivalent.

The Janssen License and Collaboration Agreement contains customary representations, warranties and covenants by the Company and Janssen and includes an obligation by the Company not to develop or commercialize other compounds which also target IL-23R outside of the Janssen License and Collaboration Agreement until completion of the Phase 2b portion of the Phase 2 clinical trial. Each of the Company and Janssen is required to indemnify the other party against all losses and expenses related to breaches of its representations, warranties and covenants under the Janssen License and Collaboration Agreement.

The Janssen License and Collaboration Agreement remains in effect until the royalty obligations cease following patent and regulatory expiry, unless terminated earlier. Either the Company or Janssen may terminate the Janssen License and Collaboration Agreement for uncured material breach. Janssen retains the right to terminate the Janssen License and Collaboration Agreement for convenience and without cause on written notice of a certain period to the Company. Upon a termination of the Janssen License and Collaboration 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 Company identified the following material promises under the Janssen License and Collaboration Agreement: (1) the license related to PTG-200, (2) the performance of development services, including regulatory support, during Phase 1 clinical trial for PTG-200 through the filing of the IND by Janssen, and (3) compound supply services for Phase 1 and Phase 2 activities. The Company considered that the license has standalone functionality and is capable of being distinct. However, the Company determined that the license is not distinct from the development and compound supply services within the context of the agreement because the development and compound supply services significantly increase the utility of the intellectual property.

Specifically, the Company's development, manufacturing and commercialization license can only provide benefit to Janssen in combination with the Company's development services in the Phase 1 study. The intellectual property ("IP") related to the peptide technology platform, which is proprietary to the Company, is the foundation for the development activities related to the treatment for CD. The compound supply services are a necessary and integral part of the development services as they could only be conducted utilizing the outcomes of these services. Given the development services under the Janssen Collaboration Agreement are expected to involve significant further development of the initial IP, the Company has concluded that the development and compound supply services are not distinct from the license, and thus the license, development services and compound supply services are combined into a single performance obligation. The nature of the combined performance obligation is to provide development and compound supply services to Janssen under the arrangement.

The Company also evaluated whether the fees related to the First Opt-in Election and Second Opt-in Election are options with material rights. These two options include additional sublicense rights and patent rights transferred to Janssen upon exercising both of these options. The Company concluded that Janssen's opt in rights are not options with material rights because the \$50.0 million upfront payment to the Company was not negotiated to provide incremental

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

discount for the future opt in payments at the end of Phase 2a and Phase 2b. The option to “opt in” provides Janssen with a license for IP that has been improved from the license initially granted for a term in the case of the opt in after completion Phase 2a and then a perpetual license in the case of “opt in” after completion of Phase 2b. Therefore, the First Opt-in Election and Second Opt-in Election options are not considered to be material rights. The option fees will be recognized as revenue when, and if, Janssen exercises its options because the Company has no further performance obligations at that point.

For revenue recognition purposes, the Company determined that the duration of the contract began on the effective date of July 13, 2017 and ends upon completion of Phase 2a activities. The contract duration is defined as the period in which parties to the contract have present enforceable rights and obligations. The Company analyzed the impact of Janssen terminating the agreement prior to the completion of Phase 2a and determined that there were significant economic penalties to Janssen for doing so. The Company believes that if Janssen terminates the agreement upon completion of Phase 2a, the forfeiture of the remaining license rights and payment of 50% of the remaining Phase 2 costs is not a significant economic penalty when compared to paying \$125.0 million as an opt in license fee to continue the use of the License. Thus, the duration of the contract is limited to the end of Phase 2a.

The Company determined that the transaction price of the Janssen License and Collaboration Agreement was \$56.4 million as of September 30, 2018, an increase of \$2.5 million from the transaction price of \$53.9 million at December 31, 2017. In order to determine the transaction price, the Company evaluated all the payments to be received during the duration of the contract. The Company determined that the \$50.0 million upfront payment, the \$25.0 million payment payable upon filing of the IND, which is fully constrained as of September 30, 2018 and December 31, 2017, and \$6.4 million of estimated variable consideration for cost-sharing payments from Janssen for agreed upon services related to Phase 2 activities as of September 30, 2018 constituted consideration to be included in the transaction price, which is to be allocated to the combined performance obligation. The increase in the transaction price was due to an increase in variable consideration related to compound supply services and was recognized as a cumulative catch-up adjustment. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

As part of the evaluation for determining that the \$25.0 million payment upon filing of the IND is fully constrained as of September 30, 2018, the Company considered several factors, including the stage of development of PTG-200 and that achievement of the milestone is outside of the Company’s control, and concluded that the filing of the IND is not probable at this time. If and when the filing of the IND becomes probable, the \$25.0 million payment will be constrained by contra revenue amounts for payments that the Company expects to make for 20% of the cost of Phase 2 activities to be performed by Janssen. The additional potential development, regulatory and sales milestone payments of up to an aggregate of \$590.0 million after the completion of Phase 2a activities that the Company is eligible to receive are outside the contract term and as such have been excluded from the transaction price. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Janssen and therefore have also been excluded from the transaction price. At the end of each reporting period, the Company will update its assessment of whether an estimate of variable consideration is constrained and update the estimated transaction price accordingly.

The Company uses the most likely amount method to estimate variable consideration. Variable consideration for cost-sharing payments related to agreed upon services for Phase 2 activities that the Company performs within the duration of the contract are included in the transaction price at an amount equal to 80% of the estimated budgeted costs for these activities, including primarily internal full-time equivalent effort and third party contract costs. The Company is responsible for 20% of the development costs for the Phase 2 clinical trial. Accordingly, a significant portion of this work is expected to be performed by Janssen. Because the Phase 2 clinical trial activity is related to the license, it is not

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

capable of being distinct. This is because both the Company and Janssen cannot benefit from these activities absent the Phase 1 activities. As the Phase 2 activities for which the Company will share 20% of the cost activities are not capable of being distinct and are not separately identifiable within the context of the contract, they 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 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 accounts for cost-sharing payments from Janssen as increases in license and collaboration revenue in its consolidated statements of operations, while cost-sharing payments to Janssen are accounted for as reductions in license and collaboration revenue, or contra-revenue. Costs incurred by the Company related to agreed upon services for Phase 2 activities under the Janssen License and Collaboration Agreement are recorded as research and development expenses in its consolidated statements of operations.

In summary, the license, the development activities for Phase 1 activities and the agreed upon services for Phase 2 activities are combined as one performance obligation that will be performed over the duration of the contract, which is from the effective date of the Janssen License and Collaboration Agreement through to the completion of Phase 2a activities. Since the Company has determined that the combined performance obligation is satisfied over time, ASC 606 requires the Company to select a single revenue recognition method for the performance obligation that faithfully depicts the Company's performance in transferring control of the services. The guidance allows entities to use two methods to measure its progress toward complete satisfaction of a performance obligation:

1. Output methods — recognize revenue on the basis of direct measurements of the value to the customer of the goods or services transferred to date relative to the remaining goods or services promised under the contract (e.g. surveys of performance completed to date, appraisals of results achieved, milestones reached, time elapsed and units of produced or units delivered); and
2. Input methods — recognize revenue on the basis of the entity's efforts or inputs to the satisfaction of a performance obligation (e.g., resources consumed, labor hours expended, costs incurred, or time elapsed) relative to the total expected inputs to the satisfaction of that performance obligation.

The Company concluded that it will utilize a cost-based input method to measure proportional performance and to calculate the corresponding amount of revenue to recognize. 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 applying the cost-based input methods of revenue recognition, the Company uses actual costs incurred relative to budgeted 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 budgeted costs as the Company completes its performance obligations, which the Company believes will be fulfilled within the next 12 months. A cost-based input method of revenue recognition requires management to make estimates of costs to complete the Company's performance obligations. 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 September 30, 2018, the Company recognized \$6.1 million of license and collaboration revenue, which included \$5.9 million of the transaction price for the Janssen License and Collaboration Agreement recognized based on proportional performance and \$0.2 million, net for other services related to Phase 2 activities performed by the Company on behalf of Janssen that are not included in the performance obligations identified under the Janssen License and Collaboration Agreement. For the nine months ended September 30, 2018, the Company

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

recognized \$28.6 million of license and collaboration revenue, which included \$27.9 million of the transaction price for the Janssen License and Collaboration Agreement recognized based on proportional performance and \$0.7 million, net for other services related to Phase 2 activities performed by the Company on behalf of Janssen that are not included in the performance obligations identified under the Janssen License and Collaboration Agreement.

For the three and nine months ended September 30, 2017, the Company recognized \$8.8 million of license and collaboration revenue, which included \$8.4 million of the transaction price for the Janssen License and Collaboration Agreement recognized based on proportional performance and \$0.4 million for other services related to Phase 2 activities performed by the Company on behalf of Janssen that are not included in the performance obligations identified under the Janssen License and Collaboration Agreement.

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

Three months ended September 30, 2018	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Contract assets:				
Receivable from collaboration partner - related party	\$ 5,785	\$ 1,385	\$ (2,584)	\$ 4,586
Contract liabilities:				
Deferred revenue - related party	\$ 13,202	\$ 696	\$ (5,928)	\$ 7,970
Payable to collaboration partner - related party	\$ 276	\$ 488	\$ —	\$ 764

Nine months ended September 30, 2018	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Contract assets:				
Receivable from collaboration partner - related party	\$ 1,816	\$ 6,012	\$ (3,242)	\$ 4,586
Contract liabilities:				
Deferred revenue - related party	\$ 31,752	\$ 4,147	\$ (27,929)	\$ 7,970
Payable to collaboration partner - related party	\$ —	\$ 1,068	\$ (304)	\$ 764

Three and nine months ended September 30, 2017	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Contract assets:				
Receivable from collaboration partner - related party	\$ —	\$ 520	\$ —	\$ 520
Contract liabilities:				
Deferred revenue - related party	\$ —	\$ 50,132	\$ (8,393)	\$ 41,739

Deferred revenue related to the Janssen License and Collaboration Agreement was \$8.0 million and \$31.8 million as of September 30, 2018 and December 31, 2017, respectively, and is recognized as the combined performance obligation is satisfied. Receivable from collaboration partner for cost sharing amounts payable from Janssen was \$4.6 million and \$1.8 million as of September 30, 2018 and December 31, 2017, respectively. As of September 30, 2018, the Company also recorded a \$0.8 million payable to collaboration partner for cost sharing amounts payable to Janssen.

PROTAGONIST THERAPEUTICS, INC.**Notes to Unaudited Condensed Consolidated Financial Statements (Continued)**

During the three months and nine months ended September 30, 2018, the Company recognized revenue of \$5.9 million and \$27.9 million, respectively, from amounts included in the contract liability balance at the beginning of the period. During the three and nine months ended September 30, 2017, the Company did not recognize any revenue from amounts included in the contract liability balance at the beginning of the period. During the three and nine months ended September 30, 2018 and 2017, no revenue was recognized from the contract asset balance at the beginning of the period or from performance obligations satisfied in previous periods. None of the costs to obtain or fulfill the contract were capitalized.

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).

	September 30, 2018			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	\$ 27,582	\$ —	\$ —	\$ 27,582
Corporate bonds	—	6,020	—	6,020
Commercial paper	—	62,386	—	62,386
Government bonds	—	39,192	—	39,192
Total financial assets	<u>\$ 27,582</u>	<u>\$ 107,598</u>	<u>\$ —</u>	<u>\$ 135,180</u>

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

	December 31, 2017			Total
	Level 1	Level 2	Level 3	
Assets:				
Money market funds	\$ 48,704	\$ —	\$ —	\$ 48,704
Corporate bonds	—	6,247	—	6,247
Commercial paper	—	58,524	—	58,524
Government bonds	—	40,303	—	40,303
Total financial assets	<u>\$ 48,704</u>	<u>\$ 105,074</u>	<u>\$ —</u>	<u>\$ 153,778</u>

The Company's corporate bonds, commercial paper and government bonds 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.

Note 5. Balance Sheet Components

Cash Equivalents and Available-for-sale Securities

Cash equivalents and available-for-sale securities consisted of the following (in thousands):

	September 30, 2018			
	Amortized Cost	Gross Unrealized		Fair Value
		Gains	Losses	
Money market funds	\$ 27,582	\$ —	\$ —	\$ 27,582
Corporate bonds	6,031	—	(11)	6,020
Commercial paper	62,386	—	—	62,386
Government bonds	39,261	—	(69)	39,192
Total cash equivalents and available-for-sale securities	<u>\$ 135,260</u>	<u>\$ —</u>	<u>\$ (80)</u>	<u>\$ 135,180</u>
Classified as:				
Cash equivalents				\$ 84,090
Available-for-sale securities - current				51,090
Total cash equivalents and available-for-sale securities				<u>\$ 135,180</u>

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

	December 31, 2017			
	Amortized Cost	Gross Unrealized		Fair Value
		Gains	Losses	
Money market funds	\$ 48,704	\$ —	\$ —	\$ 48,704
Corporate bonds	6,254	—	(7)	6,247
Commercial paper	58,524	—	—	58,524
Government bonds	40,428	—	(125)	40,303
Total cash equivalents and available-for-sale securities	<u>\$ 153,910</u>	<u>\$ —</u>	<u>\$ (132)</u>	<u>\$ 153,778</u>
Classified as:				
Cash equivalents				\$ 104,348
Available-for-sale securities - current				37,972
Available-for-sale securities - noncurrent				11,458
Total cash equivalents and available-for-sale securities				<u>\$ 153,778</u>

All available-for-sale securities - current held as of September 30, 2018 and December 31, 2017 had contractual maturities of less than one year. All available-for-sale securities - noncurrent held as of December 31, 2017 had contractual maturities of at least one year but less than two years. There were no material realized gains or realized losses on available-for-sale securities for the periods presented.

Accrued Expenses and Other Payables

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

	September 30, 2018	December 31, 2017
Accrued clinical and research related expenses	\$ 7,649	\$ 6,437
Accrued employee related expenses	2,410	2,718
Accrued professional service fees	332	267
Other	105	124
Total accrued expenses and other payables	<u>\$ 10,496</u>	<u>\$ 9,546</u>

Note 6. Research Collaboration and License Agreement

In October 2013, the Company's former collaboration partner decided to abandon a collaboration program with the Company and, pursuant to the terms of the agreement between the Company and the former collaboration partner, the Company elected to assume the responsibility for the development and commercialization of the product. Upon the former collaboration partner's abandonment, it assigned to the Company certain intellectual property arising from the collaboration and also granted the Company an exclusive license to certain background intellectual property rights of the former collaboration partner that relate to the products acquired by the Company. The nomination of PTG-300 as a development candidate triggered a \$250,000 payment from the Company to the former collaboration partner, which the Company recorded as research and development expense during the three months ended March 31, 2016. The initiation of a Phase 1 clinical study for PTG-300 triggered an additional \$250,000 payment obligation from the Company to the former collaboration partner, which the Company recorded as research and development expense during the three months ended June 30, 2017. The initiation of a Phase 2 clinical study for PTG-300, expected in the fourth quarter of 2018, would trigger an additional \$500,000 payment obligation from the Company to the former collaboration partner.

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

The Company has the right, but not the obligation, to further develop and commercialize the product and, if the Company successfully develops and commercializes PTG-300 without a partner, the Company will pay the former collaboration partner up to an additional aggregate of \$128.5 million for the achievement of certain development, regulatory and sales milestone events. In addition, the Company will pay the former collaboration partner a low single digit royalty on worldwide net sales of the product until the later of 10 years from the first commercial sale of the product or the expiration of the last patent covering the product.

Note 7. Government Programs

Research and Development Tax Incentive

The Company recognized AUD 409,000 (\$297,000) and AUD 1.6 million (\$1.3 million) as a reduction of research and development expenses for the three and nine months ended September 30, 2018, respectively, in connection with the research and development tax incentive from Australia. The Company recognized AUD 493,000 (\$389,000) and AUD 1.1 million (\$0.9 million) for the three and nine months ended September 30, 2017, respectively, in connection with the research and development tax incentive from Australia. As of September 30, 2018, and December 31, 2017, the research and development tax incentive receivable was AUD 1.6 million (\$1.2 million) and AUD 1.7 million (\$1.3 million), respectively.

Based on the nature of the amounts received under the Janssen License and Collaboration Agreement, the Company concluded that these amounts should be classified as statutory income for Australian taxation purposes. Accordingly, these amounts are not included in the calculation of annual turnover for the purposes of determining eligibility for the refundable research and development tax offset.

SBIR Grant

In September 2018, the Company was awarded a Phase 2 Small Business Innovation Research ("SBIR") Grant from the National Heart, Lung and Blood Institute of the National Institutes of Health ("NIH") in support of research aimed at developing the Company's novel hepcidin mimetic PTG-300 for the potential treatment of chronic anemia and iron overload in rare blood disorders, including beta-thalassemia. The total grant award was \$1.5 million and is for the period from September 2018 to August 2020.

In May 2017, the Company was awarded a Phase 2 SBIR Grant from the National Institute of Diabetes and Digestive and Kidney Diseases of the NIH in support of research aimed at developing biomarkers that define IL-23R target engagement by oral peptide antagonists and the effects of that engagement of downstream signaling. The total grant award was \$1.3 million and is for the period from May 2017 to April 2019.

In July 2016, the Company was awarded a Phase 1 SBIR Grant from the National Institute of Heart and Lung Diseases of the NIH in support of pre-clinical research aimed at discovering and optimizing lead molecules as novel peptide mimetics of the natural hepcidin hormone. The total grant award was \$219,000 and was for the period from August 2016 to January 2017.

The Company recognizes a reduction to research and development expenses when expenses related to the grants have been incurred and the grant funds become contractually due from NIH. The Company recorded \$229,000 and \$354,000 as a reduction of research and development expenses for the three and nine months ended September 30, 2018, respectively. The Company recorded \$103,000 and \$123,000 as a reduction of research and development expenses for the three and nine months ended September 30, 2017, respectively. The Company recorded a receivable for \$229,000

PROTAGONIST THERAPEUTICS, INC.**Notes to Unaudited Condensed Consolidated Financial Statements (Continued)**

and \$58,000 as of September 30, 2018 and December 31, 2017, respectively, to reflect the eligible costs incurred under the grants that are contractually due to the Company, and such amounts are included in prepaid expenses and other current assets on the condensed consolidated balance sheets.

Note 8. Commitments and Contingencies

In March 2017, the Company entered into a lease agreement for office and laboratory space located in Newark, California. The Company relocated its operations to the new facility in May 2017. The Company provided the landlord with a \$450,000 letter of credit collateralized by restricted cash as security deposit for the lease, which expires in May 2024. The Company is entitled to tenant improvement allowances of approximately \$469,000, any unused portion of which expires in December 2018. The Company records tenant improvement allowances as deferred rent when funds are received and associated capital expenditures as leasehold improvements that will be amortized over the shorter of their useful life or the remaining term of the lease.

The following table summarizes the Company's minimum lease payments related to the Newark facility as of September 30, 2018 (in thousands):

Year Ending December 31:	Amount
2018 (remaining three months)	\$ 477
2019	1,941
2020	2,000
2021	2,060
2022	2,121
Thereafter	3,106
Total	\$ 11,705

Note 9. Equity Plans***Equity Incentive Plans***

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 September 30, 2018, approximately 201,579 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, a non-stockholder approved stock plan, under which it reserved and authorized up to 750,000 shares of the Company's common stock in order to award 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

PROTAGONIST THERAPEUTICS, INC.**Notes to Unaudited Condensed Consolidated Financial Statements (Continued)**

grant. As of September 30, 2018, approximately 645,000 shares were available for issuance under the 2018 Inducement Plan.

Stock Options

Stock options generally have an exercise price equal to the fair market value of the Company's common stock on the grant date. Employee stock options generally vest over a period of four years. Non-employee director initial stock options generally vest over a period of three years, and non-employee director annual refresher stock options generally vest over a period of approximately one year. Non-employee consultant options generally vest over a period of one to four years.

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

	<u>Options Outstanding</u>	<u>Weighted- Average Exercise Price Per Share</u>	<u>Weighted- Average Remaining Contractual Life (years)</u>	<u>Aggregate Intrinsic Value (in millions)</u>
Balances at December 31, 2017	2,438,151	\$ 11.51	8.26	
Options granted	1,005,400	13.51		
Options exercised	(142,014)	2.79		
Options forfeited	(148,058)	14.99		
Balances at September 30, 2018	<u>3,153,479</u>	\$ 12.37	8.21	\$ 7.8
Options exercisable – September 30, 2018	<u>1,311,184</u>	\$ 11.05	7.48	\$ 4.6
Options vested and expected to vest – September 30, 2018	<u>3,153,479</u>	\$ 12.37	8.21	\$ 7.8

- (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 September 30, 2018. The calculation excludes options with an exercise price higher than the closing price of the Company's common stock on September 30, 2018.

During the nine months ended September 30, 2018, the estimated weighted-average grant-date fair value of common stock underlying options granted to employees was \$8.35 per share.

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

Employee Stock Options Valuation

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 September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Expected term (in years)	5.49 - 6.08	6.08	5.49 - 6.08	5.50 - 6.08
Expected volatility	61.2% - 65.1%	62.1%	62.0% - 66.5%	62.1% - 65.4%
Risk-free interest rate	2.75% - 2.98%	2.00%	2.42% - 2.98%	1.88 - 2.07%
Dividend yield	—	—	—	—

Restricted Stock Units

A restricted stock unit is an agreement to issue shares of the Company's common stock at the time of vesting. Restricted stock units vest in four equal installments on approximately the first, second, third and fourth anniversaries of the grant date.

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 at December 31, 2017	—	—
Restricted stock units granted	426,025	\$ 10.53
Restricted stock units forfeited	(5,375)	16.95
Unvested at September 30, 2018	420,650	\$ 10.45

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

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. As of September 30, 2018, a total of 102,950 shares of common stock have been issued under the 2016 ESPP, and 425,155 shares were available for issuance.

PROTAGONIST THERAPEUTICS, INC.**Notes to Unaudited Condensed Consolidated Financial Statements (Continued)****Stock-Based Compensation**

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Research and development	\$ 1,046	\$ 600	\$ 2,424	\$ 1,399
General and administrative	971	607	2,423	1,653
Total stock-based compensation expense	\$ 2,017	\$ 1,207	\$ 4,847	\$ 3,052

As of September 30, 2018, total unrecognized stock-based compensation expense related to stock options was approximately \$17.6 million, which the Company expects to recognize over a weighted-average period of approximately 2.25 years.

Note 10. Income Taxes

On December 22, 2017, the Tax Cuts and Jobs Act of 2017 (“Tax Act”) was signed into law making significant changes to the Internal Revenue Code. Changes include, but are not limited to, a corporate tax rate decrease from 35% to 21% effective for tax years beginning after December 31, 2017, the transition of U.S. international taxation from a worldwide tax system to a territorial system, and a one-time transition tax on the mandatory deemed repatriation of cumulative foreign earnings as of December 31, 2017. On December 22, 2017, Staff Accounting Bulletin No. 118 was issued to address the application of U.S. GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Tax Act. For the three and nine months ended September 30, 2018, the Company noted no additional guidance or information that affects the provisional amounts initially recorded at zero for the transition tax and the remeasurement of the deferred tax assets for the year ended December 31, 2017. As a result, the Company recorded no adjustment to the transition tax and the remeasurement of the deferred tax assets. The Company will continue to monitor and analyze any additional guidance and information that may be issued by the federal and state tax authorities. Any subsequent adjustment to these amounts will be recorded to current tax expense in the quarter of 2018 when the analysis is complete.

In January 2018, the FASB released guidance on the accounting for tax on the global intangible low-taxed income (“GILTI”) provisions of the Tax Act. The GILTI provisions impose a tax on foreign income in excess of a deemed return on tangible assets of foreign corporations. The Company has elected to treat any potential GILTI inclusions as a period cost as it is not projecting any material impact from GILTI inclusions and any deferred taxes related to any inclusion would be immaterial. During the three and nine months ended September 30, 2018, the Company has not made any measurement-period adjustments related to GILTI.

PROTAGONIST THERAPEUTICS, INC.

Notes to Unaudited Condensed Consolidated Financial Statements (Continued)

Note 11. Net Loss per Share

As the Company had net losses for the three and nine months ended September 30, 2018 and 2017, all potential 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 September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Numerator:				
Net loss	\$ (8,735)	\$ (4,825)	\$ (25,059)	\$ (33,905)
Denominator:				
Weighted-average shares used to compute net loss per common share, basic and diluted	22,912,279	16,911,575	21,750,562	16,851,672
Net loss per shares, basic and diluted	\$ (0.38)	\$ (0.29)	\$ (1.15)	\$ (2.01)

The following outstanding shares of potentially dilutive securities have been excluded from diluted net loss per share computations for the three and nine months ended September 30, 2018 and 2017 because their inclusion would be anti-dilutive:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Options to purchase common stock	3,153,479	2,537,744	3,153,479	2,537,744
Common stock warrants	2,750,000	—	2,750,000	—
Restricted stock units	420,650	—	420,650	—
ESPP shares	52,682	26,610	52,682	26,610
Total	6,376,811	2,564,354	6,376,811	2,564,354

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, 2017, included in our Annual Report on Form 10-K filed with the Securities and Exchange Commission (“SEC”) on March 7, 2018.

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,” “intends,” “may,” “plans,” “potential,” “predicts,” “projects,” “should,” “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 agreement with Janssen, future operating results or the ability to generate sales, income or cash flow 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 clinical stage biopharmaceutical company with a proprietary technology platform that enables the discovery and development of novel peptide-based drug candidates that address significant unmet medical needs. Our product candidates are designed to affect critical steps in the biological pathways of particular diseases, for example, by blocking protein-protein interactions. We believe our peptide-based approach has advantages over alternative approaches such as small molecules and antibodies. Our clinical stage product candidates PTG-100 and PTG-200 are oral drugs that block biological pathways currently targeted by marketed injectable antibody drugs and offer targeted delivery to the gastrointestinal (“GI”) tissue compartment. We believe that, as 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 therapy.

PTG-100, an oral, alpha-4-beta-7 (“ $\alpha 4\beta 7$ ”) integrin antagonist, is being developed for potential treatment of inflammatory bowel disease (“IBD”), GI diseases consisting primarily of ulcerative colitis (“UC”), and Crohn’s disease

("CD"). In March 2018, we announced the discontinuation of a global Phase 2 clinical trial for the treatment of moderate-to-severe UC. This decision followed a planned interim futility analysis by an independent Data Monitoring Committee ("DMC"). The interim data revealed an unusually high placebo rate of clinical remission that led to a futility decision and discontinuation of the trial. In August 2018, we announced that an independent, blinded re-read of endoscopies from the study had demonstrated signals of clinical efficacy. A human error in the initial endoscopy reads by the original vendor which was characterized by an unusually high placebo effect led to the original futile outcome reported in March 2018. If the re-read of endoscopy results had been utilized for the interim futility analysis, the trial would have continued. In addition, a pre-specified blinded histopathology analysis of colon biopsies from the trial indicated high rates of histologic remission which supported the observations of clinical remission and endoscopy responses for PTG-100. These clinical data were presented at the recent United European Gastroenterology Week and demonstrated that PTG-100 was well tolerated and associated with higher rates of clinical remission relative to placebo. The totality of the data from the Phase 2 study provides first evidence of safety and clinical efficacy and supports further development of PTG-100.

PTG-200 is a potential first-in-class oral, Interleukin-23 receptor ("IL-23R") antagonist for the treatment of IBD. The IL-12/23 pathway blockade is an approach that has been validated through an FDA approved injectable antibody drug. We have entered into a worldwide license and collaboration agreement with Janssen Biotech, Inc. ("Janssen"), a Johnson & Johnson company, to co-develop and co-detail PTG-200 for all indications, including IBD. See Note 3 to the condensed consolidated financial statements included elsewhere in this report for additional information. Top-line results from the successfully completed Phase 1 study of PTG-200 in 80 normal healthy volunteers demonstrated that PTG-200 treatment was well tolerated, with no serious adverse events or dose-limiting toxicities observed. We and Janssen are working towards filing an Investigational New Drug application ("IND") in the United States in the coming months to support the initiation of a global Phase 2 study of PTG-200 in CD. This IND filing would trigger a milestone payment from Janssen of \$25.0 million under the Janssen License and Collaboration Agreement.

Our novel peptides have potential applicability in a wide range of therapeutic areas in addition to GI diseases. We have applied our versatile platform outside of the GI disease areas and are developing PTG-300, an injectable hepcidin mimetic, for the potential treatment of anemia and iron overload in certain rare blood disorders, with an initial focus on beta-thalassemia. In the fourth quarter of 2017, we completed a successful Phase 1 study of PTG-300 in healthy volunteers which established safety and pharmacodynamic-based clinical proof of concept. PTG-300 received an orphan drug designation from the FDA for the treatment of beta-thalassemia in March 2018 and a Fast Track designation for the treatment of beta-thalassemia in September 2018. The European Medicines Agency granted orphan drug designation for PTG-300 for the treatment of beta-thalassemia in August 2018. We successfully filed an IND in the United States in the second quarter of 2018 and plan to initiate a global Phase 2 study of PTG-300 in patients with beta-thalassemia in the fourth quarter of 2018. Treatment of patients with polycythemia vera, myelodysplastic syndromes and hereditary hemochromatosis may represent additional opportunities for future development of PTG-300.

In addition, we continue to use our peptide technology platform to discover product candidates against targets in disease areas with significant unmet medical needs.

We have not generated any revenue from product sales and we do not currently have any products approved for commercialization. We have never been profitable and have incurred net losses in each year since inception and we do not anticipate that we will achieve sustained profitability in the near term. Our net losses were \$8.7 million and \$25.1 million for the three and nine months ended September 30, 2018, respectively, and \$4.8 million and \$33.9 million for the three and nine months ended September 30, 2017, respectively. As of September 30, 2018, we had an accumulated deficit of \$126.6 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 and product development, including clinical development activities under the Janssen License and Collaboration Agreement,

[Table of Contents](#)

and 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.

In October 2017, we completed an underwritten public offering of our common stock pursuant to which we issued 3,530,000 shares of our common stock at a public offering price of \$17.00 per share. In November 2017, we issued an additional 529,500 shares of our common stock at a price of \$17.00 per share following the underwriters' exercise of their option to purchase additional shares. Net proceeds, after deducting underwriting commissions and offering costs, were \$64.5 million.

On August 6, 2018, we entered into a Securities Purchase Agreement with certain accredited investors (each, an "Investor" and, collectively, the "Investors"), pursuant to which we sold an aggregate of 2,750,000 shares of our common stock at a price of \$8.00 per share, aggregate net proceeds, before deducting underwriting commissions and offering costs, were \$22.0 million. In a concurrent private placement, we issued and sold the Investors warrants to purchase an aggregate of 2,750,000 shares of our common stock (each, a "Warrant," and collectively, the "Warrants"). Each Warrant is exercisable from August 8, 2018 through August 8, 2023. Warrants to purchase 1,375,000 shares of our common stock have an exercise price of \$10.00 per share and Warrants to purchase 1,375,000 shares of our 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 will be exercisable on a "cashless" basis. In connection with the issuance and sale of the common stock and Warrants, we granted the Investors certain registration rights with respect to the Warrants and the Warrant Shares. As of September 30, 2018, none of the warrants have been exercised.

During the three and nine months ended September 30, 2018, we sold 103,500 shares of our common stock pursuant to an at-the market ("ATM") financing facility under a Sales Agreement with Cantor Fitzgerald & Co. for net proceeds of \$1.1 million. As of September 30, 2018, \$48.8 million of our common stock remained available for sale under the ATM financing facility.

Janssen License and Collaboration Agreement

On May 26, 2017, we and Janssen, one of the Janssen Pharmaceutical Companies of Johnson & Johnson, entered into an exclusive license and collaboration agreement (the "Janssen License and Collaboration Agreement") for the clinical development, manufacture and potential commercialization of PTG-200 worldwide for the treatment of CD and UC. 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. During the third quarter of 2017, we received a non-refundable, upfront cash payment of \$50.0 million from Janssen. We can also receive up to an additional \$940.0 million in payments, including potential license option payments of \$125.0 million at the Phase 2 interim analysis and \$200.0 million at Phase 2 completion, and \$615.0 million in other potential clinical development, regulatory approval and sales milestones. We and Janssen will co-develop and co fund PTG-200 through Phase 2 clinical development. Janssen will be responsible for funding Phase 3 studies in CD and UC. We will receive double-digit tiered royalties on future net sales and retain the option to co-detail PTG-200 in the United States. See Note 3 to the condensed consolidated financial statements included elsewhere in this report for additional information.

Critical Accounting Policies 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 assets and 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. Actual results may differ from these estimates under different assumptions or conditions. In making estimates and judgements, management employs critical accounting policies.

There have been no material changes in our critical accounting policies during the nine months ended September 30, 2018, 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 on Form 10-K for the year ended December 31, 2017 filed with the SEC on March 7, 2018.

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 study 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.

[Table of Contents](#)

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 tax incentive that are not subject to refund provisions as a reduction of research and development expenses. The amounts are determined on a cost reimbursement basis and, as the incentive is related to our research and development expenditures and is generally non-refundable, the amounts have been recorded as a reduction of research and development expenses. The Australian research and development tax incentive is recognized when there is reasonable assurance that the incentive will be received, the relevant expenditure has been incurred and the amount of the consideration can be reliably measured.

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. We initiated a Phase 1 clinical study of PTG-300 during the second quarter of 2017. We have presented separately in the table below costs associated with the PTG-300 program beginning in June 2017. We initiated a Phase 1 clinical study of PTG-200 during the fourth quarter of 2017. We have presented separately in the table below costs associated with the PTG-200 program beginning in December 2017. Our development and compound supply expenses incurred under the Janssen License and Collaboration Agreement prior to December 2017 are included in pre-clinical and drug discovery research expense.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
	(In thousands)			
Clinical and development expense — PTG-100	\$ 2,434	\$ 6,177	\$ 16,871	\$ 20,261
Clinical and development expense — PTG-200	2,776	—	12,505	—
Clinical and development expense — PTG-300	4,147	1,505	9,804	2,035
Milestone payment obligation to former collaboration partner	—	—	—	250
Pre-clinical and drug discovery research expense	3,314	3,977	7,683	12,902
Less: Reimbursement of expenses under grants and incentives	(526)	(491)	(1,614)	(991)
Total research and development expenses	<u>\$ 12,145</u>	<u>\$ 11,168</u>	<u>\$ 45,249</u>	<u>\$ 34,457</u>

We expect our research and development expenses will increase as we progress our product candidates, including development activities under the Janssen License and Collaboration Agreement, advance our discovery research projects into the pre-clinical stage and continue our early stage research. The process of conducting research, identifying potential product candidates and conducting pre-clinical and clinical trials necessary to obtain regulatory approval is costly and time consuming. We may never succeed in achieving marketing approval for our product candidates. The probability of success of our product candidates may be affected by numerous factors, including pre-clinical data, clinical data, competition, manufacturing capability and commercial viability. 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 may be 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. 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 incur additional expenses to support the growth of our operations and as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the SEC and those of the national securities exchange on which our securities are traded, additional insurance expenses, investor relations activities and other administrative and professional services.

Interest Income

Interest income consists of interest earned on our cash, cash equivalents and available-for-sale securities.

Results of Operations**Comparison of the Three Months Ended September 30, 2018 and 2017**

	Three Months Ended September 30,		Dollar Change	%
	2018	2017		
	(Dollars in thousands)			
License and collaboration revenue - related party	\$ 6,117	8,781	\$ (2,664)	30
Operating expenses:				
Research and development ⁽¹⁾	12,145	11,168	977	9
General and administrative ⁽²⁾	3,361	2,593	768	30
Total operating expenses	<u>15,506</u>	<u>13,761</u>	<u>1,745</u>	<u>13</u>
Loss from operations	(9,389)	(4,980)	(4,409)	89
Interest income	654	155	499	322
Net loss	<u>\$ (8,735)</u>	<u>\$ (4,825)</u>	<u>\$ (3,910)</u>	<u>81</u>

(1) Includes \$1.0 million and \$0.6 million of non-cash stock-based compensation expense for the three months ended September 30, 2018 and 2017, respectively.

(2) Includes \$1.0 million and \$0.6 million of non-cash stock-based compensation expense for the three months ended September 30, 2018 and 2017, respectively.

License and Collaboration Revenue

License and collaboration revenue decreased \$2.7 million, or 30%, from \$8.8 million for the three months ended September 30, 2017 to \$6.1 million for the three months ended September 30, 2018. The decrease was primarily due to a \$2.5 million decrease in the amount of deferred revenue recognized for the Janssen License and Collaboration Agreement, based on proportional performance as measured by actual costs incurred as a percentage of budgeted costs, and a decrease of \$0.2 million for other services, net, related to Phase 2 activities performed by us on behalf of Janssen that are not included in the performance obligations identified under the Janssen License and Collaboration Agreement.

We determined that the transaction price of the Janssen License and Collaboration Agreement was \$56.4 million as of September 30, 2018, an increase of \$2.5 million from the transaction price of \$53.9 million at December 31, 2017. In order to determine the transaction price, we evaluated all the payments to be received during the duration of the contract. We determined that the \$50.0 million upfront payment, the \$25.0 million payment payable upon filing of

[Table of Contents](#)

the IND, which is fully constrained as of September 30, 2018, and \$6.4 million of estimated variable consideration for cost-sharing payments from Janssen for agreed upon services related to Phase 2 activities as of September 30, 2018 constituted consideration to be included in the transaction price, which is to be allocated to the combined performance obligation. The increase in transaction price was due to an increase in variable consideration related to compound supply services. We will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Research and Development Expenses

Research and development expenses increased \$1.0 million, or 9%, from \$11.2 million for the three months ended September 30, 2017, to \$12.1 million for the three months ended September 30, 2018. The increase was primarily due to \$2.8 million for PTG-200 clinical trial and development expenses and \$2.6 million for PTG-300 clinical trial and development expenses, partially offset by a decrease of \$3.7 million in PTG-100 clinical trial and development expenses and a decrease of \$0.7 million in pre-clinical and discovery research expenses. Research and development expenses for the three months ended September 30, 2018 included an increase in personnel costs due to increased research and development headcount from 39 employees at September 30, 2017 to 47 employees at September 30, 2018.

General and Administrative Expenses

General and administrative expenses increased \$0.8 million, or 30%, from \$2.6 million for the three months ended September 30, 2017 to \$3.4 million for the three months ended September 30, 2018. The increase was primarily due to an increase of \$0.7 million in personnel costs due to an increase in headcount to support the growth of our operations, an increase of \$0.2 million in consultant and contract labor expenses and an increase of \$0.2 million in legal fees, partially offset by a decrease of \$0.2 million in accounting fees.

Interest Income

Interest income increased \$0.5 million, or 322%, from \$0.2 million for the three months ended September 30, 2017 to \$0.7 million for the three months ended September 30, 2018. The increase was due primarily to the investment of funds from sales of our common stock during the fourth quarter of 2017 and third quarter of 2018.

Comparison of the Nine Months Ended September 30, 2018 and 2017

	Nine Months Ended September 30,		Dollar Change	% Change
	2018	2017		
	(Dollars in thousands)			
License and collaboration revenue - related party	\$ 28,572	8,781	\$ 19,791	225
Operating expenses:				
Research and development ⁽¹⁾	\$ 45,249	34,457	10,792	31
General and administrative ⁽²⁾	10,180	8,708	1,472	17
Total operating expenses	55,429	43,165	12,264	28
	(26,857)			
Loss from operations		(34,384)	7,527	22
Interest income	1,798	479	1,319	275
Net loss	\$ (25,059)	\$ (33,905)	\$ 8,846	26

(1) Includes \$2.4 million and \$1.4 million of non-cash stock-based compensation expense for the nine months ended September 30, 2018 and 2017, respectively.

(2) Includes \$2.4 million and \$1.7 million of non-cash stock-based compensation expense for the nine months ended September 30, 2018 and 2017, respectively.

License and Collaboration Revenue

License and collaboration revenue increased \$19.8 million, or 225%, from \$8.8 million for the nine months ended September 30, 2017 to \$28.6 million for the nine months ended September 30, 2018. The increase was primarily due to a \$19.5 million increase in the amount of deferred revenue recognized for the Janssen License and Collaboration Agreement, based on proportional performance as measured by actual costs incurred as a percentage of budgeted costs, and an increase of \$0.3 million for other services, net, related to Phase 2 activities performed by us on behalf of Janssen that are not included in the performance obligations identified under the Janssen License and Collaboration Agreement. The Janssen License and Collaboration Agreement became effective in July 2017.

Research and Development Expenses

Research and development expenses increased \$10.8 million, or 31%, from \$34.5 million for the nine months ended September 30, 2017 to \$45.2 million for the nine months ended September 30, 2018. The increase was primarily due to \$12.5 million for PTG-200 clinical trial and development expenses and \$7.8 million for PTG-300 clinical trial and development expenses. These increases were partially offset by a decrease of \$5.2 million in pre-clinical and discovery research expenses as PTG-200 and PTG-300 advanced to the clinical stage, a decrease of \$3.4 million in PTG-100 clinical trial and development expenses, a decrease of \$0.6 million related to higher expense reimbursement under grant and incentive programs and a decrease of \$0.3 million related to a milestone payment to a former collaboration partner during the second quarter of 2017. Research and development expenses for the nine months ended September 30, 2018 included an increase in personnel costs due to increased research and development headcount from 39 employees at September 30, 2017 to 47 employees at September 30, 2018.

General and Administrative Expenses

General and administrative expenses increased \$1.5 million, or 17%, from \$8.7 million for the nine months ended September 30, 2017 to \$10.2 million for the nine months ended September 30, 2018. The increase was primarily due to an increase of \$1.7 million in personnel costs due to an increase in headcount to support the growth of our operations, an increase of \$0.3 million in consulting and contract labor expenses and an increase of \$0.2 million in franchise and other business taxes, partially offset by a \$0.6 million decrease in legal expenses and a \$0.2 million decrease in accounting fees.

Interest Income

Interest income increased \$1.3 million, or 275%, from \$0.5 million for the nine months ended September 30, 2017 to \$1.8 million for the nine months ended September 30, 2018. The increase was due primarily to the investment of the \$50.0 million upfront payment from Janssen during the third quarter of 2017 and funds from sales of our common stock during the fourth quarter of 2017 and third quarter of 2018.

Liquidity and Capital Resources

As of September 30, 2018, we had \$138.5 million of cash, cash equivalents and available-for-sale securities and an accumulated deficit of \$126.6 million. Our operations have been financed by net proceeds from the sale of shares of our capital stock and revenue from the Janssen License and Collaboration Agreement. During the third quarter of 2017 we became eligible for and received a non-refundable, upfront cash payment of \$50.0 million from Janssen.

In September 2017, we filed a registration statement on Form S-3 with the Securities and Exchange Commission (File No. 333-220314), effective as of October 5, 2017, as amended, which permits the offering, issuance,

and sale by us of up to a maximum aggregate offering price of \$200.0 million of our common stock. Up to a maximum of \$50.0 million of the maximum aggregate offering price of \$200.0 million may be issued and sold pursuant to an at-the-market financing facility under a Sales Agreement. We pay up to 3% of gross proceeds for any common stock sold through the Sales Agreement. We sold 103,500 shares of our common stock pursuant to the Sales Agreement during the three and six months ended September 30, 2018 for net proceeds of \$1.1 million. As of September 30, 2018, \$48.8 million of common stock remained available for sale under the ATM financing facility.

In October 2017, we completed an underwritten public offering of 3,530,000 shares of our common stock at a public offering price of \$17.00 per share. In November 2017, we issued an additional 529,500 shares of our common stock at a price of \$17.00 per share following the underwriters' exercise of their option to purchase additional shares. Net proceeds, after deducting underwriting commissions and offering costs, were \$64.5 million.

On August 6, 2018, we entered into a Securities Purchase Agreement with the Investors, pursuant to which we sold an aggregate of 2,750,000 shares of our common stock at a price of \$8.00 per share, for aggregate gross proceeds of approximately \$22.0 million, before deducting offering expenses payable by us. In a concurrent private placement, we agreed to issue the Investors Warrants to purchase an aggregate of 2,750,000 shares of our common stock. Each Warrant is exercisable from August 8, 2018 through August 8, 2023. Warrants to purchase 1,375,000 shares of our common stock have an exercise price of \$10.00 per share and Warrants to purchase 1,375,000 shares of our common stock have an exercise price of \$15.00 per share. The exercise price and number of 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 will be exercisable on a "cashless" basis. In connection with the issuance and sale of the common stock and Warrants, we granted the Investors certain registration rights with respect to the Warrants and the Warrant Shares. As of September 30, 2018, none of the warrants have been exercised.

Our primary uses of cash are to fund operating expenses, primarily research and development expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

We believe, based on our current operating plan and expected expenditures, that our existing cash, cash equivalents and available-for-sale 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, and we could utilize our available capital resources sooner than we currently expect. If our planned pre-clinical and clinical trials are successful, or our other product candidates enter clinical trials or advance beyond the discovery stage, we will need to raise additional capital in order to further advance our product candidates towards potential regulatory approval. We will continue to require additional financing to advance our current product candidates through clinical development, to develop, acquire or in-license other potential product candidates and to fund operations for the foreseeable future. We will continue to seek funds through equity or debt financings, collaborative or other arrangements with corporate sources, or through other sources of financing, but such financing may not be available at terms acceptable to us, if at all. We anticipate that we will need to raise substantial additional capital, the requirements of which will depend on many factors, including:

- the progress, timing, scope, results and costs of our pre-clinical studies and 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;

[Table of Contents](#)

- 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, 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 PTG-200, 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; and
- the costs of maintaining, expanding and protecting our intellectual property portfolio.

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 and other research and development activities. 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. We currently have no credit facility and, with the exception of payments we may receive under the Janssen License and Collaboration Agreement, we do not currently have any commitments for future external financing. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated product development programs.

[Table of Contents](#)

The following table summarizes our cash flows for the periods indicated (in thousands):

	Nine Months Ended September 30,	
	2018	2017
	(In thousands)	
Cash provided by (used in) operating activities	\$ (39,812)	\$ 18,021
Cash provided by (used in) investing activities	(2,336)	10,621
Cash provided by financing activities	23,636	492

Cash Flows from Operating Activities

Cash used in operating activities for the nine months ended September 30, 2018 was \$39.8 million, consisting of our net loss of \$25.1 million and a net change of \$20.3 million in net operating assets, partially offset by non-cash charges of \$5.6 million. The change in net operating assets and liabilities was due primarily to a net decrease of \$23.8 million in deferred revenue related to the Janssen License and Collaboration Agreement and an increase of \$2.8 million in receivable from collaboration partner, partially offset by an increase of \$3.6 million in accounts payable, an increase of \$1.2 million in accrued expenses and other payables, an increase of \$0.8 million in payable to collaboration partner and a decrease of \$0.5 million in prepaid expenses and other current assets. Non-cash charges were primarily comprised of \$4.9 million of stock-based compensation, \$0.4 million of depreciation and amortization and \$0.3 million of net amortization of premium on available-for-sale securities.

Cash provided by operating activities for the nine months ended September 30, 2017 was \$18.0 million, consisting of a net change of \$48.1 million in net operating assets and liabilities and non-cash charges of \$3.8 million, partially offset by our net loss of \$33.9 million. The change in net operating assets and liabilities was due primarily to an increase of \$41.7 million in deferred revenue related to the Janssen License and Collaboration Agreement, an increase of \$4.4 million in accounts payable and accrued expenses related primarily to an increase in research and development activities and other general and administrative professional services, a decrease of \$1.5 million in the receivable related to the Australian research and development tax incentive receivable and a decrease of \$1.0 million in prepaid expenses and other assets, partially offset by a decrease of \$0.5 million in receivable from collaboration partner. Non-cash charges were primarily comprised of \$3.1 million of stock-based compensation, \$0.5 million of net amortization of premium on available-for-sale securities and \$0.3 million of depreciation and amortization.

Cash Flows from Investing Activities

Cash used in investing activities for the nine months ended September 30, 2018 was \$2.3 million, consisting of purchases of available-for-sale securities of \$51.9 million and purchases of property and equipment of \$0.4 million, partially offset by proceeds from maturities of available-for-sale securities of \$50.0 million.

Cash provided by investing activities for the nine months ended September 30, 2017 was \$11.1 million, consisting of proceeds from maturities of available-for-sale securities of \$39.8 million, partially offset by purchases of available-for-sale securities of \$28.2 million and purchases of property and equipment of \$0.6 million. Purchases of property and equipment related primarily to purchases of scientific equipment.

Cash Flows from Financing Activities

Cash provided by financing activities for the nine months ended September 30, 2018 was \$23.6 million, consisting of \$21.7 million of net proceeds from issuance of our common stock and warrants in a private placement, \$1.0 million of net proceeds from sales through our ATM financing facility and \$0.9 million from the issuance of common stock upon exercise of stock options and purchases of common stock under our employee stock purchase plan.

Cash provided by financing activities for the nine months ended September 30, 2017 was \$0.5 million, consisting of proceeds of \$0.8 million from the issuance of common stock upon exercise of stock options and purchases of common stock under our employee stock purchase plan, partially offset by payments of \$0.3 million for deferred offering costs related to our S-3 filing during the third quarter of 2017.

Contractual Obligations and Other Commitments

During the nine months ended September 30, 2018, 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, 2017 filed with the SEC on March 7, 2018.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements, as defined under SEC rules, including the use of structured finance, special purpose entities or variable interest entities.

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.

We had \$138.5 million and \$155.5 million in cash, cash equivalents and available-for-sale securities at September 30, 2018 and December 31, 2017, respectively. Cash and cash equivalents consist of cash, money market funds, commercial paper and government bonds. Available-for-sale securities consist of corporate bonds, commercial paper and government bonds. Short-term available-for-sale securities have maturities of greater than three months but no longer than 365 days as of the balance sheet date. Long-term available-for-sale securities have maturities of 365 days or longer as of the balance sheet date. Such interest earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been material. We had no outstanding debt as of September 30, 2018.

Approximately \$1.5 million and \$1.2 million of our cash balance was located in Australia at September 30, 2018 and December 31, 2017, 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 the 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 consolidated financial results of operations.

ITEM 4. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

As required by Rule 13a-15(b) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of the design and operation 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 Quarterly Report. Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

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

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting that occurred during the quarter ended September 30, 2018 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

We may become subject to litigation and claims arising in the ordinary course of business, including the matter described below.

On September 26, 2017, Medical Diagnostic Laboratories, LLC (“MDL”) filed a lawsuit for alleged infringement of U.S. Patent No. 8,946,150 (“the ‘150 patent”) by our polypeptide PTG-200 (the “Complaint”). We have licensed PTG-200 to Janssen Biotech, Inc. for clinical development. On December 1, 2017, we filed a motion to dismiss the case, urging that all of our activities, as described in the Complaint, fall within the safe harbor of 35 U.S.C. 271(e)(1) – precluding infringement for FDA-research related activities. On February 7, 2018, our motion to dismiss the case was granted by the U.S. District Court for the Northern District of California. The Court dismissed the case without prejudice to MDL attempting to amend its Complaint within thirty days to attempt to allege new facts that would support a case or suing in the future when commercial activity is imminent or concrete. No amended Complaint was filed by MDL and no appeal was taken by MDL, and the deadlines for such actions have now passed. Accordingly, the case is now concluded.

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. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. If any of these risks occur, our business, results of operations or financial condition could suffer, the market price of our common stock could decline and you could lose all or part of your investment in our common stock.

We have marked with an asterisk (*) those risks described below that reflect substantive changes from the risks described under Part I, Item 1A “Risk Factors” included in our Annual Report on Form 10-K for the year ended December 31, 2017 filed with the Securities and Exchange Commission on March 7, 2018.

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 since our inception. As of September 30, 2018, we have incurred cumulative losses of \$126.6 million, and our net loss for the three month and nine months ended September 30, 2018 was \$8.7 million and \$25.1 million, respectively. Our prior losses, combined with expected future losses, have had and

will continue to have an adverse effect on our stockholders' equity and working capital. We expect to continue to incur significant research, development and other expenses related to our ongoing operations and product development, including clinical development activities under our exclusive license and collaboration agreement (the "Janssen License and Collaboration Agreement") with Janssen Biotech, Inc., a Pennsylvania corporation ("Janssen"), and 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 peptide-based product candidates.

We do not anticipate generating revenue from sales of products for the foreseeable future, if ever, and we do not currently have any product candidates in registration or pivotal clinical trials. If any of our peptide-based product candidates fail in clinical trials or do not gain regulatory approval, or even if approved, fail to achieve market acceptance, we may never become profitable. Furthermore, any revenues generated from the Janssen License and Collaboration Agreement may not be sufficient alone to sustain our operations as there can be no assurance that we will receive any opt-in election fees, development, regulatory, or sales milestone payments, or royalties from Janssen in the future pursuant to the Janssen License and Collaboration Agreement. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. 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.

If one or more of our peptide-based product candidates is approved for commercial sale and we retain commercial rights, we anticipate incurring significant costs associated with manufacturing and commercializing such approved peptide-based product candidate. Therefore, even if we are able to generate revenue from the sale of any approved product, we may never become profitable.

We are an early clinical-stage biopharmaceutical company with no approved products and no historical product revenue, which makes it difficult to assess our future prospects and financial results.*

We are an early clinical-stage biopharmaceutical company with a limited operating history. 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 early stage clinical trials of our pipeline candidates, PTG-100, PTG-200 and PTG-300, and conducting research to identify additional product candidates. We successfully filed Clinical Trial Notifications in Australia to support our completed Phase 1 clinical trials of PTG-100, PTG-200 and PTG-300. We successfully filed a U.S. Investigational New Drug ("IND") application, and regulatory submissions in other countries as well, to support our global Phase 2 study of PTG-100 in ulcerative colitis ("UC"), however in March 2018 we announced that we were discontinuing this Phase 2 study following a planned interim futility analysis by an independent Data Monitoring Committee ("DMC"). The interim data revealed an unusually high placebo rate of clinical remission that led to a futility decision and discontinuation of the trial. In August 2018, we announced that an independent, blinded re-read of endoscopies from the study had demonstrated signs of clinical efficacy. A human error in the initial endoscopy reads by the original vendor which was characterized by an unusually high placebo effect led to the original futile outcome reported in March 2018. If the re-read of endoscopy results had been utilized for the interim futility analysis, the trial would have continued. In addition, a pre-specified blinded histopathology analysis of colon biopsies from the trial indicated high rates of histologic remission which supported the observations of clinical remission and endoscopy responses for PTG-100. The totality of the data from the Phase 2 study provides first evidence of safety and clinical efficacy and supports further development of PTG-100. We also successfully filed a U.S. IND application to support the initiation of a Phase 2 clinical trial of PTG-300 in beta-thalassemia.

As an early clinical-stage company, we have not yet demonstrated an ability to generate revenue or successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields such as biopharmaceutical drug discovery and development. 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.

[Table of Contents](#)

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, but not limited to:

- the clinical outcomes from the continued development of our product candidates;
- potential side effects of our product candidates that could delay or prevent approval or cause an approved drug to be taken off the market;
- our ability to obtain, as well as the timeliness of obtaining, additional funding to develop and potentially manufacture and commercialize our product candidates, including payments, if any, under the Janssen License and Collaboration Agreement;
- competition from existing products directed against the same biological target or therapeutic indications of our product candidates as well as new products that may receive marketing approval;
- the entry of generic versions of products that compete with our product candidates;
- the timing of regulatory review and approval of our product candidates;
- market acceptance of our product candidates that receive regulatory approval, if any;
- our ability to establish an effective sales and marketing infrastructure directly or through collaborations with third parties;
- the ability of patients or healthcare providers to obtain coverage or sufficient reimbursement for our products;
- the ability of third party manufacturers to manufacture in accordance with current good manufacturing practices (“cGMP”) our product candidates for the conduct of clinical trials and, if approved, for successful commercialization;
- our ability as well as the ability of any third-party collaborators, to obtain, maintain and protect intellectual property rights covering our product candidates and technologies, and our ability to develop, manufacture and commercialize our product candidates without infringing on the intellectual property rights of others;
- our ability to add infrastructure and manage adequately our future growth; and
- our ability to attract and retain key personnel with appropriate expertise and experience to manage our business effectively.

Accordingly, the likelihood of our success must be evaluated in light of many potential challenges and variables associated with an early 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 will 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. We conducted Phase 1 clinical trial of PTG-100, PTG-200 and PTG-300 in healthy volunteers and we initiated a global Phase 2 clinical trial of PTG-100 in patients with moderate-to-severe UC. In March 2018, we announced that we were discontinuing the global Phase 2 clinical trial of PTG-100 for the treatment of moderate-to-severe UC. In August 2018, we announced that an

[Table of Contents](#)

independent, blinded re-read of endoscopies from the study had demonstrated signs of clinical efficacy. A human error in the initial endoscopy reads by the original vendor which was characterized by an unusually high placebo effect led to the original futile outcome reported in March 2018. If the re-read of endoscopy results had been utilized for the interim futility analysis, the trial would have continued. In addition, a pre-specified blinded histopathology analysis of colon biopsies from the trial indicated high rates of histologic remission which supported the observations of clinical remission and endoscopy responses for PTG-100. The totality of the data from the Phase 2 study provides first evidence of safety and clinical efficacy and supports further development of PTG-100.

Developing pharmaceutical product candidates, including conducting pre-clinical studies and clinical trials, is expensive. We will require substantial additional future capital in order to complete clinical development and, if we are successful, to commercialize any of our current product candidates. If the FDA or any foreign regulatory agency, such as the European Medicines Agency (“EMA”), requires that we perform studies or trials in addition to those that we currently anticipate with respect to the development of PTG-100, PTG-200, PTG-300 or any of our other product candidates, or repeat studies or trials, our expenses would further increase beyond what we currently expect, and any delay resulting from such further or repeat studies or trials could also result in the need for additional financing.

Further, in the event our Janssen License and Collaboration Agreement is terminated, we may not receive any development fees, milestone payments, or royalties under the Janssen License and Collaboration Agreement, and we would be required to fund all clinical development, manufacturing, and commercial activities for PTG-200, which would require us to raise additional capital or establish alternative collaborations with third-party collaboration partners, which may not be possible.

As of September 30, 2018, we had cash, cash equivalents and available-for-sale securities of \$138.5 million. Based upon our current operating plan and expected expenditures, we believe that our existing cash, cash equivalents, and available-for-sale securities will be sufficient to fund our operations for at least the next 12 months. Our existing capital resources will not be sufficient to enable us to initiate any pivotal clinical trials. Accordingly, we expect that we will need to raise substantial additional funds in the future in order to complete clinical development or commercialize any of our product candidates. Our funding requirements and the timing of our need for additional capital are subject to change based on a number of factors, including:

- the rate of progress and the cost of our studies of PTG-100, PTG-200, and PTG-300 and any other product candidates;
- the number of product candidates that we intend to develop using our technology platform;
- the costs of research and pre-clinical studies to support the advancement of other product candidates into clinical development;
- the timing of, and costs involved in, seeking and obtaining approvals from the FDA and comparable foreign regulatory authorities, including the potential by the FDA or comparable regulatory authorities to require that we perform more studies than those that we currently expect;
- the achievement of development, regulatory, and sales milestones resulting in the payment to us from Janssen under the Janssen License and Collaboration Agreement and the timing of receipt of such payments, if any;
- changes or delays in our and/or Janssen’s development plans for PTG-200;
- the costs of preparing to manufacture PTG-100, PTG-200 or PTG-300 on a scale sufficient to enable large-scale clinical trials and commercial supply;

[Table of Contents](#)

- the timing and cost of transitioning our product formulations into the formulations we intend to use in registration trials and commercialize;
- the costs of commercialization activities if PTG-100, PTG-300 or any future product candidate is approved, including the formation of a sales force;
- Janssen's ability to successfully market and sell PTG-200, upon regulatory approval and clearance, in the United States and other countries;
- the timing, receipt and amount of royalties under the Janssen License and Collaboration Agreement on worldwide net sales of PTG-200, upon regulatory approval and clearance, if any;
- the sales price and availability of coverage and adequate third-party reimbursement for our product candidates that may receive regulatory approval, if any;
- the degree and rate of market acceptance of any products launched by us or our partners;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- our need and ability to hire and retain additional personnel;
- our ability to enter into additional collaboration, licensing, commercialization or other arrangements and the terms and timing of such arrangements; and
- the emergence of competing technologies or other adverse market developments.

If our existing capital resources, future interest income, upfront payment and potential opt-in election fees, milestone payments, and royalties under the Janssen License and Collaboration Agreement are insufficient to meet future capital requirements, and if we are unable to obtain additional funding from equity offerings or debt financings, including on a timely basis, we may be required to:

- seek collaborators for one or more of our peptide-based product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available;
- relinquish or license on unfavorable terms our rights to technologies or peptide-based product candidates that we otherwise would seek to develop or commercialize ourselves; or
- significantly curtail one or more of our research or development programs or cease operations altogether.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our peptide-based 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. For example, on August 6, 2018 we entered into a stock purchase agreement with investors including BVF Partners L.P. and their affiliates pursuant to which we agreed to sell an aggregate of 2,750,000 shares of our common stock at a price of \$8.00 per share for gross proceeds of \$22.0 million. In a concurrent private placement, we issued warrants to purchase an aggregate of 2,750,000 shares of our common stock. The exercise of some or all of the warrants will dilute the

ownership interests of existing stockholders and any sales in the public market of the common stock issuable upon such exercise could adversely affect prevailing market prices of our common stock. To the extent that we raise additional capital through the sale of equity securities, including sales of up to \$50.0 million worth of shares of our common stock pursuant to our Sales Agreement with Cantor Fitzgerald & Co. (the “Sales Agreement”), or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. 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 peptide-based product candidates that we otherwise would seek to develop or commercialize ourselves or potentially reserve for future potential arrangements when we might be able to achieve more favorable terms.

Risks Related to Our Business and Industry

We are heavily dependent on the success of our lead product candidates, PTG-100, PTG-200 and PTG-300, which are in early-stage 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 be able to 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 lead product candidates, PTG-100 and PTG-200 targeting inflammatory bowel disease (“IBD”) and PTG-300 which targets anemia associated with certain rare blood disorders, and the development of other product candidates. We cannot be certain that PTG-100, PTG-200, PTG-300 or any other product candidates will receive regulatory approval or, if approved, be successfully commercialized. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of PTG-100, PTG-200, and PTG-300 will remain subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, each of which has differing regulations. 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 after approval of a marketing application by corresponding regulatory authorities. We completed a Phase 1 clinical trial for PTG-100 in June 2016 and initiated a global Phase 2 clinical trial of PTG-100 in patients with moderate to severe UC. In March 2018, we announced that we were discontinuing the global Phase 2 clinical trial for the treatment of moderate-to-severe UC. The interim data revealed an unusually high placebo rate of clinical remission that led to a futility decision and discontinuation of the trial. In August 2018, we announced that an independent, blinded re-read of endoscopies from the study had demonstrated signs of clinical efficacy. A human error in the initial endoscopy reads by the original vendor which was characterized by an unusually high placebo effect led to the original futile outcome reported in March 2018. If the re-read of endoscopy results had been utilized for the interim futility analysis, the trial would have continued. In addition, a pre-specified blinded histopathology analysis of colon biopsies from the trial indicated high rates of histologic remission which supported the observations of clinical remission and endoscopy responses for PTG-100. The totality of the data from the Phase 2 study provides first evidence of safety and clinical efficacy and supports further development of PTG-100. We also completed Phase 1 clinical trials for PTG-300 in December 2017 and PTG-200 in the third quarter of 2018. 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, and we do not expect to be in a position to do so for the near term. We may not receive any preferential or expedited review of any application for regulatory approval by virtue of the fact that our product candidates target biological pathways that are also targeted by currently marketed injectable antibody drugs, and our product candidates will be subject to the regulatory review processes applicable to completely new drugs.

[Table of Contents](#)

We have not previously submitted an NDA to the FDA, or similar drug approval filings to comparable foreign authorities, for any product candidate, and we cannot be certain that any of our product candidates will be successful in clinical trial or receive regulatory approval. Filing an application and obtaining regulatory approval for a pharmaceutical product candidate is an extensive, lengthy, expensive and inherently uncertain process, and the regulatory authorities may delay, limit or deny approval of our product candidates for many reasons, including:

- we may not be able to demonstrate that any of our product candidates are safe and effective to the satisfaction of the FDA or comparable foreign regulatory authorities;
- the FDA or comparable foreign regulatory authorities may require additional pre-clinical studies or clinical trials prior to granting approval, which would increase our costs and extend the pre-approval development process;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory authorities for approval;
- the FDA may disagree with the number, design, size, conduct or statistical analysis of one or more of our clinical trials;
- contract research organizations (“CROs”) that we retain to conduct clinical trials may take actions outside of our control that materially and adversely impact our clinical trials;
- the FDA or comparable foreign regulatory authorities may disagree with, or not accept, our interpretation of data from our pre-clinical studies and clinical trials;
- the FDA may require development of a costly and extensive risk evaluation and mitigation strategy (“REMS”), as a condition of approval;
- the FDA or other regulatory authorities may require post-marketing studies as a condition of approval;
- the FDA may identify deficiencies in our manufacturing processes or facilities or those of our third-party manufacturers which would be required to be corrected prior to regulatory approval;
- the success or further approval of competitor products approved in indications in which we undertake development of our product candidates may change the standard of care or change the standard for approval of our product candidate in our proposed indications; and
- the FDA or comparable foreign regulatory authorities may change their approval policies or adopt new regulations.

Our peptide-based product candidates will require additional research, clinical development, manufacturing activities, regulatory approval in multiple jurisdictions (if regulatory approval can be obtained at all), securing sources of commercial manufacturing supply and building of or partnering with a commercial organization. We cannot assure you that our clinical trials for PTG-100, PTG-200 or PTG-300 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 peptide-based product candidates into clinical trials. Moreover, any delay or setback in the development of any product candidate, in particular PTG-100, PTG-200, or PTG-300, would be expected to adversely affect our business and cause our stock price to fall. For example, the announcement of the discontinuation of the global Phase 2 clinical trial of PTG-100 for the treatment of

moderate-to-severe UC due to the interim analysis meeting the futility criterion on the primary endpoint of clinical remission significantly depressed our stock price.

If Janssen does not elect to continue the development of PTG-200 through an Opt-In Election, our business and business prospects would be significantly harmed.

Under the terms of the Janssen License and Collaboration Agreement, Janssen is not obligated to make any additional payments to us as we have already received the upfront payment that was due in the third quarter of 2017 pursuant to the terms of the Janssen License and Collaboration Agreement, until such time as it affirmatively elects to continue to advance the development of PTG-200 (the “First Opt-In Election”) within a period of time following completion date of the Phase 1 studies and the Phase 2a portion of the CD Phase 2 clinical trial and any related activities set forth in a clinical development plan (“Phase 2a Activities”). The timing of Janssen’s First Opt-In Election and whether Janssen elects to continue further clinical development of PTG-200 also affects the timing and availability of potential future milestone and royalty payments, if any. If the Phase 2a Activities are terminated early, suspended for an extended period of time, or are otherwise unsuccessful, Janssen may determine not to elect to continue further clinical development of PTG-200, in which case, the Janssen License and Collaboration Agreement would terminate and our business and business prospects would be materially adversely affected.

There may be disagreements between Janssen and Protagonist 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, including those regarding the development, manufacture, and commercialization of PTG-200, interpretation of the Janssen License and Collaboration Agreement, and ownership of proprietary rights. In addition, in certain circumstances, we may believe that a particular milestone has been achieved and Janssen may disagree with our belief. In that case, receipt of that milestone payment may be delayed or may never be received, which would adversely affect our financial condition and may require us to adjust our operating plans.

The joint governance structure contemplated by the Janssen License and Collaboration Agreement will cease to have decision-making authority once the development term ends, which will preclude our ability to participate in any further decision-making for PTG-200. Reliance on a joint governance structure also subjects us to the risk that changes in key management personnel who are members of the various joint committees may materially and adversely affect the functioning of these committees, which could significantly delay or preclude PTG-200 development and/or commercialization. As a result of possible disagreements with Janssen, we also may become involved in litigation or arbitration, which would be time-consuming for our management and employees and expensive.

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

Our business and future profitability is substantially dependent on our ability to successfully develop, obtain regulatory approval for and then successfully commercialize our most advanced peptide-based product candidates, PTG-100, which was in a global Phase 2 trial that was halted in March 2018, PTG-300, which completed a Phase 1 clinical trial in December 2017, and PTG-200, which is in a Phase 1 clinical trial. In August 2018, we announced that an independent, blinded re-read of endoscopies from the study had demonstrated signs of clinical efficacy. A human error in the initial endoscopy reads by the original vendor which was characterized by an unusually high placebo effect led to the original futile outcome reported in March 2018. If the re-read of endoscopy results had been utilized for the interim futility analysis, the trial would have continued. In addition, a pre-specified blinded histopathology analysis of colon biopsies from the trial indicated high rates of histologic remission which supported the observations of clinical remission

and endoscopy responses for PTG-100. The totality of the data from the Phase 2 study provides first evidence of safety and clinical efficacy and supports further development of PTG-100.

We are not permitted to market or promote any of our peptide-based 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 peptide-based product candidates. The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of regulatory authorities. 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;
- 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;
- 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;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data submitted in support of regulatory approval;
- the data collected from pre-clinical studies and clinical trials of our peptide-based product candidates may not be sufficient to support the submission of an NDA, supplemental NDA, or other regulatory submissions necessary to obtain regulatory approval in the United States or elsewhere;
- 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.

The lengthy regulatory approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market PTG-100, PTG-200 and PTG-300, our lead product candidates, or any other product candidate, which would harm our business, results of operations and prospects significantly.

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 REMS, 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 have not previously submitted an NDA, a Marketing Authorization Application (“MAA”), or any corresponding drug approval filing to the FDA, the EMA or any comparable foreign authority for any peptide-based product candidate. Further, our product candidates may not receive regulatory approval even if we complete such filings. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

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. In addition to our planned pre-clinical studies and clinical trials, we expect to have to complete at least two 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 initiated a Phase 2 clinical trial, which we halted in March 2018, and have never conducted a Phase 3 clinical trial or submitted an NDA, and as a result, we have no history or track record to rely on when entering these phases of the development cycle. In August 2018, we announced that an independent, blinded re-read of endoscopies from the study had demonstrated signs of clinical efficacy. A human error in the initial endoscopy reads by the original vendor which was characterized by an unusually high placebo effect led to the original futile outcome reported in March 2018. If the re-read of endoscopy results had been utilized for the interim futility analysis, the trial would have continued. In addition, a pre-specified blinded histopathology analysis of colon biopsies from the trial indicated high rates of histologic remission which supported the observations of clinical remission and endoscopy responses for PTG-100. The totality of the data from the Phase 2 study provides first evidence of safety and clinical efficacy and supports further development of PTG-100. 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. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. 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 delays related to:

- obtaining regulatory approvals to commence a clinical trial;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- fraud or negligence on the part of CROs, contract manufacturing organizations (“CMOs”), consultants or contractors;
- obtaining institutional review board (“IRB”) or ethics committee (“EC”), approval at each site;

[Table of Contents](#)

- recruiting suitable patients to participate in a clinical trial;
- having patients complete a clinical trial or return for post-treatment follow-up;
- clinical sites deviating from the clinical trial protocol or dropping out of a clinical trial;
- adding new clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

We could encounter delays if a clinical trial is modified, suspended or terminated by us, by the IRBs or ECs 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, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical trial protocols, inspection of the clinical trial operations or clinical trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed and our ability to generate product revenue from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

In addition, data obtained from trials and studies are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit or prevent regulatory approval.

Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control.*

We may encounter delays in enrolling, be unable to enroll or maintain, a sufficient number of patients to complete any of our clinical trials. Patient enrollment and retention in clinical trials is a significant factor in the timing of clinical trials and depends on many factors, including the size and nature of the patient population, the nature of the trial protocol, the existing body of safety and efficacy data with respect to the study drug, the number and nature of competing treatments and ongoing clinical trials of competing drugs for the same indication, the proximity of patients to clinical trial sites and the eligibility criteria for the clinical trial. There are a significant number of global clinical trials in UC that are currently ongoing, especially in Phases 2 and 3, making it highly competitive and challenging to recruit subjects. More broadly, we are aware of a number of therapies that are commercialized or are being developed for IBD and we expect to face competition from these investigational drugs or approved drugs for potential subjects in our clinical trials, which may delay the pace of enrollment in our planned clinical trials. Furthermore, any negative results we may report in clinical trials of our product candidates, such as the halting of our Phase 2 clinical trial of PTG-100 for the treatment of moderate-to-severe UC due to futility that was subsequently confirmed to be due to human error in endoscopy reads by the original vendor, 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, which could have a harmful effect on our ability to develop our product candidates or could render further development impossible.

All of our peptide-based product candidates other than PTG-100, PTG-200 and PTG-300 are in research or pre-clinical development and have not entered into clinical trials. If we are unable to develop, test and commercialize our peptide-based product candidates, our business will be adversely affected.

As part of our strategy, we also seek to discover, develop and commercialize a portfolio of new peptide-based product candidates in addition to PTG-100, PTG-200, and PTG-300. 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, including:

- our financial and internal resources are insufficient;
- our research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates uncompetitive;
- our other product candidates may be shown to have harmful side effects or other characteristics that indicate such product candidate is unlikely to be effective or otherwise unlikely to achieve applicable regulatory approval;
- our product candidates may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- a product candidate may not be accepted by patients, the medical community, healthcare providers or third-party payors.

Our research and development strategy for our lead product candidates relies in large part on clinical data and results obtained from antibody and small molecule products that are approved or in late-stage development that could ultimately prove to be inaccurate or unreliable for use with our peptide-based product candidate approach.

As part of our strategy to mitigate clinical development risk for PTG-100 and PTG 200, we seek to develop peptide-based product candidates against validated biological targets and pathways that have been targeted by approved or later stage products in development. While we utilize pre-clinical in vivo and in vitro models as well as clinical biomarkers to assess potential safety and efficacy early in the candidate selection and development process, this strategy necessarily relies upon clinical data and other results obtained by third parties that may ultimately prove to be inaccurate or unreliable or otherwise not applicable to the indications in which we develop our peptide-based product candidates. We will have to conduct clinical trials to show the safety and efficacy of our peptide-based product candidates against the identified biological targets and pathways to show that our peptide-based product candidates can address the identified mechanism of action shown by these third party results. For example, PTG-100 is an $\alpha 4\beta 7$ integrin antagonist that targets the same target as the currently marketed injectable antibody drug, Entyvio®, approved for treatment in UC and CD, and PTG-200 targets the IL-23 biological pathway, which is a pathway targeted by the currently marketed injectable antibody drug, Stelara®, approved for treatment of psoriasis, psoriatic arthritis, and CD. If our interpretation of the third party clinical data and results from molecules directed against the same biological target or pathway or our pre-clinical in vivo and in vitro models prove inaccurate or our assumptions and conclusions about the applicability of our peptide-based product candidates against the same biological targets or pathways are incorrect or inaccurate, then our development efforts may prove unsuccessful or longer and more extensive and our research and development strategy and business and operations could be significantly harmed.

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. We cannot assure you that our peptide platform will work, nor that any of these potential targets or other aspects of our proprietary drug discovery and design platform will yield product candidates that could enter clinical development and, ultimately, be commercially valuable. Although we expect to continue to enhance the capabilities of our proprietary platform by developing and integrating existing and new research technologies, we may not be successful in any of our enhancement and development efforts. For example, we may not be able to enter into agreements on suitable terms to obtain technologies required to develop certain capabilities of our peptide platform. In addition, we may not be successful in developing the conditions necessary to simulate specific tissue function from multiple species, or otherwise develop assays or cell cultures necessary to expand these capabilities. If our enhancement or development efforts are unsuccessful, 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 impacting safety that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in limiting the commercial opportunity for our product candidates if approved.

Undesirable side effects that may be caused by our product candidates or caused by similar approved drugs or product candidates in development by other companies, could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or adverse events related to our product candidates. In such an event, our clinical trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of our product candidates for any or all targeted indications. In addition, drug-related side effects could negatively affect patient recruitment or the ability of enrolled patients to complete the trial and even if our clinical trials are completed and our product candidate is approved, drug-related side effects could restrict the label or result in potential product liability claims. Any of these occurrences could significantly harm our business, financial condition and prospects significantly.

Moreover, since our product candidates PTG-100 and PTG-200 have been developed for indications for which injectable antibody drugs have been approved, we expect that our clinical trials would need to show a risk/benefit profile that is competitive with those existing products and product candidates in order to obtain regulatory approval or, if approved, a product label that is favorable for commercialization.

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

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

Any of these events could prevent us from achieving or maintaining market acceptance of the particular peptide-based product candidate which could significantly harm our business and prospects.

If there are any safety or efficacy results that cause the benefit-risk profile of PTG-200 to become unacceptable, the clinical development of PTG-200 would be delayed or halted, and as a result, Janssen may terminate the Janssen License and Collaboration Agreement, which would severely and adversely affect our business prospects, and may cause us to cease operations.

PTG-200 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 for PTG-200. If regulatory submissions requesting approval to market PTG-200 are submitted, after reviewing the data in such submissions, the FDA and regulatory agencies in other countries may conclude that the overall benefit-risk profile of PTG-200 treatment is unacceptable, and the clinical development of PTG-200 would be delayed or halted. Any of these events would severely harm our business and prospects.

Clinical trials by their nature examine the effects of a potential therapy in a sample of the potential future patient population. As such, clinical trials conducted with PTG-200 may not uncover all possible adverse events that patients treated with PTG-200 may experience. In collaboration with Janssen, we may in the future observe or report dose-limiting or other safety issues in potential future clinical trials of PTG-200. If such toxicities or other safety issues in any clinical trial of PTG-200 result in an unacceptable benefit-risk profile, then:

- the commencement and/or completion of any future clinical trials would likely be delayed or prevented; or
- additional, unforeseen trials, or preclinical studies may be required to be conducted.

The occurrence of any of these events may cause Janssen to abandon their development of PTG-200 entirely and terminate the Janssen License and Collaboration Agreement. Any termination of the Janssen License and Collaboration Agreement by Janssen would have a material adverse effect on our results of operations, financial condition, business prospects and the future of PTG-200.

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 duties 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 CROs to monitor and manage clinical trials and collect data for our pre-clinical studies and clinical programs. We rely on these parties for execution of our pre-clinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that their conduct meets regulatory requirements and that each of our studies and trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. Thus, we and our CROs are required to comply with good clinical practices (“GCPs”), which are regulations and guidelines promulgated by the FDA, the EMA and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. 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. We cannot assure you that upon inspection by a regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCPs. While we have agreements governing activities of our CROs, we may have limited influence over

their actual performance and the qualifications of their personnel conducting work on our behalf. In addition, significant portions of the clinical studies for our peptide-based product candidates are expected to be conducted outside of the United States, which will make it more difficult for us to monitor CROs and perform visits of our clinical trial sites and will force us to rely heavily on CROs to ensure the proper and timely conduct of our clinical trials and compliance with applicable regulations, including GCPs. Failure to comply with applicable regulations in the conduct of the clinical studies for our peptide-based product candidates may require us to repeat clinical trials, which would delay the regulatory approval process.

Some of our CROs have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated.

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. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our pre-clinical and clinical programs. 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 peptide-based product candidates. As a result, our results of operations and the commercial prospects for our peptide-based product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

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 peptide-based product candidate.*

Our clinical trials must be conducted with product manufactured under current good manufacturing practices and for Europe and other major countries, International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (“ICH”) guidelines, and we rely on contract manufactures to manufacture and provide product for us that meet these requirements. We do not currently have nor do we plan to acquire the infrastructure or capability internally to manufacture our pre-clinical and clinical drug supplies and we lack the resources and the capability to manufacture any of our peptide-based product candidates on a clinical or commercial scale. 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 GMP manufacturing processes required for cost-effective and large scale production. If these efforts are not successful in developing cost-effective processes and if the contract manufacturers are not successful in converting it to commercial scale manufacturing, then our development and/or commercialization of PTG-100, PTG-200 or PTG-300 could be materially adversely affected. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. Moreover, our contract manufacturers are the sole source of supply for our clinical product candidates, including PTG-100 PTG-200 and PTG-300. If we were to

experience an unexpected loss of supply for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or termination of our clinical study 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 peptide-based product candidates for our clinical trials. There are a limited number of suppliers for raw materials that we 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 peptide-based product candidates for our clinical trials, and if approved, for commercial sale. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. 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 peptide-based product candidate to complete the clinical trial, any significant delay in the supply of a peptide-based 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 peptide-based product candidates. If our contract manufacturers or we are unable to purchase these raw materials after regulatory approval has been obtained for our peptide-based product candidates, the commercial launch of our peptide-based product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenue from the sale of our peptide-based product candidates.

If we submit an application for regulatory approval of any of our product candidates, the facilities used by our contract manufacturers to manufacture our product candidates will be subject to inspection and approval by the FDA or other regulatory authorities. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our peptide-based product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our peptide-based product candidates, if approved.

We may fail to obtain orphan drug designations from the FDA 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. Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biologic intended to treat a rare disease or condition, which is defined as one occurring in a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug or biologic will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full NDA or BLA, to market the same drug or biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity.

In March 2018, we were granted orphan drug designation in the United States by the FDA for PTG-300 for the treatment of patients with beta-thalassemia. Despite this designation, we may be unable to maintain the benefits associated with orphan drug designation status, including market exclusivity. We may not be the first to obtain regulatory approval of a product candidate for the beta-thalassemia or any other orphan-designated indication that we

may pursue due to the uncertainties associated with developing pharmaceutical products. 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 the needs of patients with the orphan-designated disease or condition. 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 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. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process. In addition, while we may seek orphan drug designation for our product candidates, we may never receive such designations.

We may not be successful in obtaining or maintaining development and commercialization collaborations, and any potential partner may not devote sufficient resources to the development or commercialization of our product candidates or may otherwise fail in development or commercialization efforts, which could adversely affect our ability to develop certain of our product candidates and our financial condition and operating results.

Other than our Janssen License and Collaboration Agreement, we have no active collaborations for any of our product candidates. Even if we are able to establish other collaboration arrangements, any such collaboration, including the Janssen License and Collaboration Agreement, may not ultimately be successful, which could have a negative impact on our business, results of operations, financial condition and growth prospects. While we currently plan to enter into collaborations that are limited to certain identified territories, there can be no assurance that we would maintain significant rights or control of future development and commercialization of such product candidate. Accordingly, if we collaborate with a third party for development and commercialization of a product candidate, we may relinquish some or all of the control over the future success of that product candidate to the third party, and that partner may not devote sufficient resources to the development or commercialization of our product candidate or may otherwise fail in development or commercialization efforts, in which event the development and commercialization of the product candidate in the collaboration could be delayed or terminated and our business could be substantially harmed. In addition, the terms of any potential collaboration or other arrangement that we may establish may not be favorable to us or may not be perceived as favorable, which may negatively impact the price of our common stock. In some cases, we may be responsible for continuing development of a product candidate or research program under a collaboration, and the payments we receive from our partner may be insufficient to cover the cost of this development or may result in a dispute between the parties. Moreover, collaborations and sales and marketing arrangements are complex and time consuming to negotiate, document and implement, and they may require substantial resources to maintain, which may be detrimental to the development of our other product candidates.

We are subject to a number of additional risks associated with our dependence on collaborations with third parties, the occurrence of which could cause our collaboration arrangements to fail. Conflicts may arise between us and partners, such as conflicts concerning the implementation of development plans, efforts and resources dedicated to the product candidate, interpretation of clinical data, the achievement of milestones, the interpretation of financial provisions or the ownership of intellectual property developed during the collaboration. If any such conflicts arise, a collaborator could act in its own self-interest, which may be adverse to our interests. Any such disagreement between us and a partner could result in one or more of the following, each of which could delay or prevent the development or commercialization of our product candidates, and in turn prevent us from generating sufficient revenue to achieve or maintain profitability:

- reductions in the payment of royalties or other payments we believe are due pursuant to the applicable collaboration arrangement;

[Table of Contents](#)

- actions taken by a partner inside or outside our collaboration which could negatively impact our rights or benefits under our collaboration; or
- unwillingness on the part of a partner to keep us informed regarding the progress of its development and commercialization activities or to permit public disclosure of the results of those activities.

In addition, the termination of a collaboration may limit our ability to obtain rights to the product or intellectual property developed by our collaborator under terms that would be sufficiently favorable for us to consider further development or investment in the terminated collaboration product candidate, even if it were returned to us.

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. Mergers and acquisitions in our industry may result in even more resources being concentrated in our competitors. 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.

We believe our principal competition in the treatment of IBD is from companies with approved agents in the following therapeutic classes, among others:

- Infused α 4B7 antibody: Takeda Pharmaceutical Company
- Infused IL-23 and IL-12 antibody: Johnson & Johnson
- Injectable or infused anti-TNF α therapy: AbbVie, Johnson & Johnson, Amgen, Pfizer, UCB S.A., Boehringer Ingelheim, Merck

We are also aware of several companies developing therapeutic product candidates for the treatment of IBD, including, but not limited to AbbVie (rizankizumab and upadacitinib in Phase 3), Allergan, Atlantic Healthcare Plc, Aprogen (biosimilar TNF- α antibody in Phase 3) Arena Pharmaceuticals, Inc., AstraZeneca, Biogen, Boehringer

[Table of Contents](#)

Ingelheim (adalimumab biosimilar in Pre-Registration), Bristol-Myers Squibb, Celgene (ozanimod hydrochloride in Phase 3 clinical trials), Eli Lilly and Company, Galapagos/Gilead (filgotinib in Phase 3), Janssen (ustekinumab in Phase 3), Lycera Corp., Mitsubishi Tanabe Pharma Corporation, Pfizer (tofacitinib citrate), Roche/Genentech (etrolizumab in Phase 3), Samsung Bioepis (adalimumab biosimilar in Pre-Registration), Sandoz (adalimumab biosimilar in Phase 3), Shire/Pfizer (PF-00547659), Shire/Takeda (SHP647 in Phase 3) and UCB S.A.

We believe our principal competition in the treatment of disorders characterized by chronic anemia and iron overload, such as beta-thalassemia, myelodysplastic syndromes will come from other pipeline products being developed by companies such as Acceleron (luspatercept in Phase 3), bluebird bio (LentiGlobin in Phase 3), Bristol-Myers Squibb, Emmaus Medical (glutamine in pre-registration), Gilead, GlaxoSmithKline, Global Blood Therapeutics, Inc., La Jolla Pharmaceutical and Novartis AG, among others. We believe competition will also include approved iron chelation therapies that have been developed by Novartis AG and Apotex Inc., among others.

We believe that our ability to successfully compete will depend on, among other things:

- the efficacy and safety of our product candidates, in particular compared to marketed products and products in late-stage development;
- the time it takes for our product candidates to complete clinical development and receive regulatory approval, if at all;
- the ability to commercialize and market any of our product candidates that receive regulatory approval;
- the price of our products, including in comparison to branded or generic competitors;
- whether coverage and adequate levels of reimbursement are available under private and governmental health insurance plans, including Medicare;
- the ability to protect intellectual property rights related to our product candidates;
- the ability to manufacture and sell commercial quantities of any of our product candidates that receive regulatory approval; and
- acceptance of any of our approved product candidates by physicians, payors and other healthcare providers.

Because our research approach depends on our proprietary technology platform, it may be difficult for us to continue to successfully compete in the face of rapid changes in technology. If we fail to continue to advance our technology platform, technological change may impair our ability to compete effectively and technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical.

We have not yet negotiated our agreement with Janssen specifying all of the terms of our Co-Detailing Option and would need to develop our own internal sales force.

Pursuant to the Janssen License and Collaboration Agreement, we have a co-detailing option, which, if PTG-200 is approved for commercial sale, allows us to elect to provide up to 30% of the PTG-200 selling effort in the United States with sales force personnel (the “Co-Detailing Option”). While the Janssen License and Collaboration Agreement includes the material terms of our Co-Detailing Option, Janssen and we mutually agreed to negotiate a separate agreement specifying the detailed activities and responsibilities in respect of the marketing and co-promotion of PTG-200 following our election to exercise our Co-Detailing Option. We will need to negotiate this separate agreement with

Janssen and, as a result, Janssen may place restrictions or additional obligations on us, including financial obligations. Any restrictions or additional obligations may restrict our co-detailing activities or involve more significant financial or other obligations than we currently anticipate. In addition, we have no sales experience as a company. There are risks involved with establishing our own sales force capabilities. Developing an internal sales force and function will require substantial expenditures and will be time-consuming, may expose us to unforeseen costs and expenses, and we may not be able to effectively recruit, train or retain sales personnel. Accordingly, we may be unable to establish our own sales force which could effectively preclude our ability to take any advantage of participating in co-detailing PTG-200 in the United States. In addition, any sales force we establish may not be effective, or may be less effective than the any sales force that Janssen utilizes to promote PTG-200. In such event, the commercialization of PTG-200 may be adversely affected, which could materially and adversely affect any sales milestone payments or royalties we may receive under the Janssen License and Collaboration Agreement.

We currently have no marketing and sales organization. To the extent any of our peptide-based 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 peptide-based product candidates, we may not be able to effectively market and sell any peptide-based product candidates, 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 peptide-based product candidates that receive marketing approval, we would 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 peptide-based 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, which would require us to establish a U.S. sales team. If we are unable to enter into collaborations with third parties for the commercialization of approved products, if any, on acceptable terms or at all, or if any such partner does not devote sufficient resources to the commercialization of our product or otherwise fails in commercialization efforts, we may not be able to successfully commercialize any of our peptide-based product candidates that receive regulatory approval. If we are not successful in commercializing our peptide-based product candidates, either on our own or through collaborations with one or more third parties, our future revenue will be materially and adversely impacted.

Even if our peptide-based product candidates receive marketing approval, they may fail to achieve market acceptance by physicians, patients, government payors (including Medicare and Medicaid programs), private insurers, and other third-party payors, or others in the medical community necessary for commercial success.

If any of our peptide-based product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, government payors, other third-party payors and other healthcare providers. If any of our approved peptide-based products fail to achieve an adequate level of acceptance, we may not generate significant revenue to become profitable. The degree of market acceptance, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- the efficacy and potential advantages compared to alternative treatments;
- effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments;

[Table of Contents](#)

- our ability to offer our peptide-based product candidates for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the willingness of the medical community to offer customers our peptide-based product candidates in addition to or in the place of current injectable therapies;
- the strength of marketing and distribution support;
- the availability of government and third-party coverage and adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our product candidates together with other medications.

Because we expect sales of our peptide-based product candidates, if approved, to generate revenue for us to achieve profitability, the failure of our peptide-based product candidates to achieve market acceptance would harm our business and could require us to seek collaborations or undertake additional financings sooner than we would otherwise plan.

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 discovery and development of PTG-100 and PTG-200, GI-restricted drugs that target the same biological pathways as currently marketed injectable antibody drugs for the treatment of IBD and the development of PTG-300 for treatment of anemia associated with certain rare blood disorders. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration 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.

Even if we obtain and maintain approval for any of our product candidates from the FDA, we may never obtain approval for our product candidates outside of the United States, which would limit our market opportunities and adversely affect our business.

Sales of our product candidates outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval and, to the extent that we retain commercial rights following clinical development, we would plan to seek regulatory approval to commercialize our peptide-based product candidates in the United States, the EU and additional foreign countries. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries must also approve the manufacturing and marketing of the product candidates in those countries. Approval procedures vary among jurisdictions and can involve requirements

and administrative review periods different from, and greater than, those in the United States, including additional pre-clinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our products is also subject to approval. We may decide to submit an MAA to the EMA for approval in the EEA. As with the FDA, obtaining approval of an MAA from the EMA is a similarly lengthy and expensive process and the EMA has its own procedures for approval of peptide-based product candidates. Even if a product is approved, the FDA or the EMA, as the case may be, may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the United States and the EEA also have requirements for approval of drug candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. Also, regulatory approval for any of our peptide-based product candidates may be withdrawn. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our peptide-based product candidates will be harmed and our business will be adversely affected.

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, 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, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering, or paying remuneration, directly or indirectly, in cash or in kind, in exchange for or to induce either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation;
- the federal false claims laws, including the False Claims Act, which impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious, or fraudulent; knowingly making, using, or causing to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the government; or knowingly making, using, or causing to be made or used, a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government; in addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

[Table of Contents](#)

- the federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which imposes additional criminal and civil liability for, among other things, willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false or fraudulent statements relating to healthcare matters; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- 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 and their business associates with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal civil monetary penalties statute, which prohibits, among other things, the offering or giving of remuneration to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary’s selection of a particular supplier of items or services reimbursable by a federal or state governmental program;
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program (with certain exceptions) to report annually to the government information related to certain payments and other “transfers of value” made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and requires applicable manufacturers to report annually to the government ownership and investment interests held by the physicians described above and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state and local laws that require the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Further, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the “ACA”), among other things, amended the intent requirements of the federal Anti-Kickback Statute and certain criminal statutes governing healthcare fraud. A person or entity can now be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. In addition, ACA provided that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act. 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, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Responding to investigations can be time-and resource-consuming and can divert management's attention from the business. 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 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 PTG-200 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 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.

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 peptide-based product candidates for which we obtain marketing approval.

For example, in the United States in March 2010, 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. Among the provisions of the ACA of importance to our potential peptide-based product candidates are the following:

- an annual, non-tax deductible fee payable by any entity that manufactures or imports specified branded prescription drugs and biologic agents payable to the federal government based on each company's market share of prior year total sales of branded products to certain federal healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;

[Table of Contents](#)

- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs in certain states;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (70% commencing January 1, 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries under their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

The financial impact of the ACA over the next few years will depend on a number of factors including but not limited to the policies reflected in implementing regulations and guidance and changes in sales volumes for products affected by the new system of rebates, discounts and fees.

Some of the provisions of the ACA have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the current administration to repeal or replace certain aspects of the ACA. Since January 2017, the President has signed two 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 has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been enacted. The Tax Cuts and Jobs Act of 2017 (the "Tax Act") includes 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 that is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, the President signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain fees mandated fees under the ACA, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, 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". Congress may consider other legislation to repeal or replace other elements of the ACA

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 2027 unless additional action is taken by Congress. 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. In addition, recently there has been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their commercial products. 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.

Further, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Such scrutiny 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. At the federal level, the current administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the current administration have both stated that they will continue to seek new legislative and/or administrative measures to control drug costs. 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.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare therapies, which could result in reduced demand for our peptide-based product candidates or additional pricing pressures.

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.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidate. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution or arbitrage between low-priced and high-priced countries, can further reduce prices. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies, which is time-consuming and costly. If coverage and reimbursement of our product candidates are unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

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.*

Our industry has experienced a high rate of turnover of management personnel in recent years. Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific, medical and regulatory personnel. We are highly dependent on our existing senior management team, especially Dinesh V. Patel, Ph.D., our President and Chief Executive Officer, David Y. Liu,

Ph.D., our Chief Scientific Officer and Head of Research and Development, Richard S. Shames, M.D., our Chief Medical Officer, Tom O'Neil, our Chief Financial Officer and Samuel Saks, M.D., our Chief Development Officer. In order to induce valuable employees to continue their employment with us, we have provided stock options that vest over time. The value to employees of stock options that vest over time is significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to maintain retention incentives or counteract more lucrative offers from other companies. For example, since March 26, 2018, when we announced the discontinuation of our Phase 2b clinical trial of PTG-100 due to futility, our stock price has been lower than the exercise prices of a majority of our outstanding stock options, significantly reducing the retentive power of those options. All of our employees may terminate their employment with us at any time, with or without notice. 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 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. Our competitors may provide higher compensation or more diverse opportunities and better opportunities for career advancement. Any or all of these competing factors may limit our ability to continue to attract and retain high quality personnel, which could negatively affect our ability to successfully develop and commercialize peptide-based product candidates and to grow our business and operations as currently contemplated.

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

As of September 30, 2018, we had 62 full-time employees, including 47 employees engaged in research and development. As our development and commercialization plans and strategies develop and continue to operate as a public company, we expect to need additional managerial, operational, scientific, sales, marketing, development, regulatory, manufacturing, financial and other resources. Future growth would impose significant added responsibilities on members of management, including:

- designing and managing our clinical trials effectively;
- identifying, recruiting, maintaining, motivating and integrating additional employees;
- managing our manufacturing and development efforts effectively;
- improving our managerial, development, operational and financial systems and controls; and
- expanding our facilities.

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 peptide-based 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 and computer viruses that may result in the impairment of key business processes. In addition, our systems are potentially vulnerable to data security breaches-whether 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 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 because of lost or misappropriated information, including sensitive patient data. In addition, these breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. Moreover, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. While we have implemented security measures to protect our data security and information technology systems, such measures may not prevent such events. Any such disruptions and breaches of security could have a material adverse effect on the development of our product candidates as well as our business and financial condition.

Our insurance policies are expensive and only protect us from some business risks, which will leave us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, property, cyber, auto liability, workers' compensation, clinical trial, products liability and directors' and officers' insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage to insure risks which could arise from our operations. Any significant uninsured losses or liabilities may require us to pay substantial amounts from corporate cash intended to fund operations, which would adversely affect our financial position and results of operations.

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. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. 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.

If we, or our contractors or agents are unable to comply with federal, state and county environmental and safety laws and regulations, including those governing laboratory procedures and the handling of biohazardous materials, chemicals and various radioactive compounds, considerable additional costs or liabilities could be assessed that would have a material adverse effect on our financial condition. We, our collaborators, contractors or agents may be required to incur significant costs to comply with current or future environmental laws and regulations and may be adversely affected by the cost of compliance with these laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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 and 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, including those laws that require the reporting of true, complete and accurate information to the FDA, (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. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in our pre-clinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and third-parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. 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 any of our peptide-based product candidates, if approved.

We face an inherent risk of product liability as a result of the clinical testing of our peptide-based product candidates and will face an even greater risk if we commercialize any products. For example, 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. Claims could also be asserted under state consumer protection acts. 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 peptide-based product candidates.

Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

[Table of Contents](#)

- delay or termination of clinical studies;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management’s time and our resources;
- substantial monetary awards to trial participants or patients;
- decreased demand for our peptide-based product candidates;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue from product sales; and
- the inability to commercialize any our peptide-based product candidates, if approved.

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 peptide-based 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.

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 peptide-based product candidates outside of the United States. We are thus subject to risks associated with doing business outside of the United States. With respect to our peptide-based 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 outside of the United States or in lieu of our own sales force and distribution systems, which would indirectly expose us to these risks. 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 peptide-based product candidates, if approved, outside of the United States, including:

- Medical standard of care and diagnostic criteria may differ in foreign jurisdictions, which may impact our ability to enroll and successfully complete trials designed for U.S. marketing;

[Table of Contents](#)

- efforts to develop an international sales, marketing and distribution organization may increase our expenses, divert our management's attention from the acquisition or development of peptide-based product candidates or cause us to forgo profitable licensing opportunities in these geographies;
- changes in a specific country's or region's political and cultural climate or economic condition;
- unexpected changes in foreign laws and regulatory requirements;
- difficulty of effective enforcement of contractual provisions in local jurisdictions;
- inadequate intellectual property protection in foreign countries;
- trade-protection measures, import or export licensing requirements such as Export Administration Regulations promulgated by the US Department of Commerce and fines, penalties or suspension or revocation of export privileges;
- regulations under the U.S. Foreign Corrupt Practices Act and similar foreign anti-corruption laws;
- the effects of applicable foreign tax structures and potentially adverse tax consequences; and
- significant adverse changes in foreign currency exchange rates which could make the cost of our clinical trials, to the extent conducted outside of the US, more expensive.

Our headquarters and certain of our data storage facilities are 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, such as data storage, are vulnerable to damage from catastrophic events, such as power loss, natural disasters, terrorism and similar unforeseen events beyond our control. Our corporate headquarters and other 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.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, damaged critical infrastructure, such as our data storage facilities or financial systems, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. We do not have a disaster recovery and business continuity plan in place. We may incur substantial expenses as a result of the absence or limited nature of our internal or third party service provider disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business. Furthermore, integral parties in our supply chain are operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our development plans and business.

The insurance coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our peptide-based 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 peptide-based 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 peptide-based 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. In the United States, the principal decisions about reimbursement for new products are typically made by the Centers for Medicare & Medicaid Services (“CMS”), an agency within the United States Department of Health and Human Services. CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree, but also have their own methods and approval process. Therefore, 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. Reimbursement agencies in Europe may be more conservative than CMS.

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 tablet vaccine candidates on less favorable terms than we currently anticipate. In many countries, particularly the countries of the European Union, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In these countries, 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 peptide-based product candidates to other available therapies. In general, the prices of products under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our peptide-based 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.

Moreover, increasing efforts by governmental and third-party payors, in the United States and internationally, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our tablet vaccine candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products into the healthcare market.

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. The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner, or in all jurisdictions. 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. There is no assurance that all the potentially relevant prior art relating to our patent and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents have been issued, or do successfully issue, from our patent applications, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, 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 the patent and patent applications we hold, obtain or pursue with respect to our product candidates and technologies is challenged, or if they fail to provide meaningful exclusivity for our product candidates and technologies, it could threaten our ability to commercialize our product candidates and technologies. Several patent applications covering our product candidates and technologies have been filed. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such 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 these patents or any other patents owned by or, if applicable in the future, licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates and technologies that we may develop. Further, 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. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we or our licensors were the first to file any patent application related to our product candidates and technologies. In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available however the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications.

If, in the future, we obtain licenses from third parties, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications or to maintain any patents, covering technology that we license from third parties. We may also require the cooperation of our licensors to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Moreover, if we do obtain necessary licenses, we will likely have obligations under those licenses, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license could have a material adverse impact on our business.

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.

While we hold issued patents and have filed patent applications to protect certain aspects of our product candidates, 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.

We seek to protect our proprietary information, data and processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and partners. Although these agreements are designed to protect our proprietary information, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. 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 we be 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.

We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. We cannot guarantee that our trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets.

Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time-consuming, and the outcome is unpredictable. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. The enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. We cannot guarantee that our employees, former employees or consultants will not file patent applications claiming our inventions. Because of the “first-to-file” laws in the United States, such unauthorized patent application filings may defeat our attempts to obtain patents on our own inventions.

Trade secrets and know-how can be difficult to protect as trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles, and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. If we are unable to prevent material disclosure of the intellectual property related to our technologies to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

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. Competitors could purchase our products and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, in the absence of patent protection, we would have no

right to prevent them, or those to whom they communicate, from using that technology or information to compete with us. 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 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.

Interference or derivation proceedings provoked by third parties or brought by us, the PTO or any foreign patent authority may be necessary to determine the priority or ownership of inventions with respect to our patent or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms, if any license is offered at all. Our defense of litigation, interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees.

We may not be able to prevent misappropriation of our intellectual property, trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

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.

If we initiate legal proceedings against a third party to enforce a patent covering our product candidates or technologies, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the PTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, inter parties review, post grant review, and equivalent proceedings in foreign jurisdictions, such as opposition or derivation proceedings. Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover and protect our product candidates or technologies. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our patent counsel, and the patent examiner were unaware of during prosecution. If a defendant were to prevail on a legal

assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business.

As more groups become engaged in scientific research and product development in fields related to our product candidates, such as the IL-23 receptor, 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. Challenges to our patents through these procedures can be extremely expensive and time-consuming, even if the outcome is favorable to us. 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 us to litigation, or otherwise preventing Janssen or us from commercializing PTG-200 or other product candidates in the relevant jurisdiction(s);
- requiring Janssen or us to obtain licenses to the disputed patents;
- forcing Janssen or us to cease using the disputed technology; or
- requiring Janssen or us to 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. Additionally, if patent protection is not available on any patents we have licensed to Janssen in one or more countries, our potential royalties obtained in those countries from Janssen may be non-existent or lower than we currently expect and could be reduced in accordance to the terms of the Janssen License and Collaboration Agreement.

The lives of any patents issued as a result of our pending or future patent applications may not be sufficient to effectively protect our products and business.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its first effective filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications. For example, our granted U.S. patents covering PTG-100 and PTG-200 expire in 2035, and our granted U.S. patent covering PTG-300 expires in 2034. In addition, although upon issuance in the United States the life of a patent can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. If we do not have sufficient patent life to protect our products, our business and results of operations will be adversely affected.

Competitors could enter the market with generic versions of our product candidates, which may result in a material decline in sales of our product candidates.

Under the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application (“ANDA”), seeking approval of a generic copy of an approved innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit an NDA under section 505(b)(2) that references the FDA’s finding of safety and effectiveness of a previously approved drug. A 505(b)(2) NDA product may be for a new or improved version of the original innovator product. Innovative small molecule drugs may be eligible for certain periods of regulatory exclusivity (e.g., five years for new chemical entities, three years for changes to an approved drug requiring a new clinical study, seven years for orphan drugs), which preclude FDA approval (or in some circumstances, FDA filing and review of) an

[Table of Contents](#)

ANDA or 505(b)(2) NDA relying on the FDA's finding of safety and effectiveness for the innovative drug. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the FDA publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," known as the "Orange Book." If there are patents listed in the Orange Book, a generic applicant that seeks to market its product before expiration of the patents must include in the ANDA or 505(b)(2) what is known as a "Paragraph IV certification," challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must be given to the innovator, too, and if within 45 days of receiving notice the innovator sues to protect its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, if our product candidates are approved, competitors could file ANDAs for generic versions of our product candidates, or 505(b)(2) NDAs that reference our product candidates. If there are patents listed for our product candidates in the Orange Book, those ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict whether any patents issuing from our pending patent applications will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents, or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any patents that are granted and listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could more immediately face generic competition and its sales would likely decline materially. Should sales decline, we may have to write off a portion or all of the intangible assets associated with the affected product and our results of operations and cash flows could be materially and adversely affected.

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. There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, derivation proceedings, post grant reviews, inter partes reviews, and reexamination proceedings before the PTO or oppositions and other comparable proceedings in foreign jurisdictions. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, 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, including our competitors, 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, we cannot assure you that marketing of our product candidates or practice of our technologies will not infringe existing patents or patents that may be granted in the future. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, 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 a patent holder believes our product candidates or technologies infringe on its patent, the patent holder may sue us even if we have received patent protection for our product candidates and technologies. In addition, third parties may obtain patents in the future and claim that our product candidates or technologies infringe upon these patents. If any third-party patents were 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 the biotechnology and pharmaceutical industries expand 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 further practice our technologies or develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. 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, which could harm our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement (which may include situations in which we had knowledge of an issued patent but nonetheless proceeded with activity which infringed such patent), 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.

For example, in September 2017, Medical Diagnostic Laboratories, LLC ("MDL") filed a lawsuit for alleged infringement of U.S. Patent No. 8,946,150 ("the '150 patent") by our polypeptide PTG-200, which we licensed to Janssen Biotech, Inc. for clinical development. Although our motion to dismiss the case, urging that all of our activities as described in the complaint fall within the safe harbor of 35 U.S.C. 271(e)(1), was granted and the case is now concluded, MDL could bring another lawsuit if PTG-200 is approved and marketed. If further actions occur and we fail in defending any such claims, in addition to paying monetary damages, we may be enjoined from marketing PTG-200 and other IL-23 inhibitor compounds. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may not identify relevant third party patents or may incorrectly interpret the relevance, scope or expiration of a third party patent which might adversely affect our ability to develop and market our products.

We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction.

The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. We may incorrectly determine that our products are not covered by a third party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.

Because of the expense and uncertainty of litigation, we may conclude that even if a third party is infringing our issued patents, any patents that may be issued on as a result of our pending or future patent applications or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our stockholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

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

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time-consuming and, even if resolved in our favor, is 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. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to 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.

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. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The requirements for patentability differ, in varying degrees, from country to country. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patent and other intellectual property rights, especially those relating to life sciences. 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. This could make it difficult for us to stop the infringement of any patents we obtain or the misappropriation of our other intellectual property rights. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.

Proceedings to enforce our patent rights in foreign jurisdictions, regardless of whether successful, would result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets.

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.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

Similarly, 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.

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

The PTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the PTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We employ reputable law firms and other professionals and rely on such third parties to help us comply with these requirements and effect payment of these fees with respect to the patent and patent applications that we own, and if we in-license intellectual property we may have to rely upon our licensors to comply with these requirements and effect payment of these fees with respect to any patents and patent applications that we license. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, the Leahy-Smith America Invents Act (“Leahy-Smith Act”) was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The PTO has developed regulations and procedures to govern administration of the Leahy-Smith Act, but many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, did not become effective until March 2013, 18 months after its enactment. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. Depending on decisions by the U.S.

Congress, the federal courts, and the PTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patent and patents that we might obtain in the future.

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

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 or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of our issued patents or any pending patent applications we may have;
- we might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own;
- we might not have been the first to file patent applications covering an invention;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- pending patent applications that we own or license may not lead to issued patents;
- the issued patents that we own or any issued patents that we license may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

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. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, 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. We are not aware of

any threatened or pending claims related to these matters or concerning the agreements with our senior management or scientific founders, but in the future litigation may be necessary to defend against such claims. 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 also 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. For example, we work with third-party contractors in formulating and manufacturing our product candidates. While we believe we have all rights to any intellectual property related to our product candidates, a third party-contractor may claim they have ownership rights. 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. For example, some of our consultants are employees of the University of Queensland. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership.

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.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

We have not yet registered trademarks for a commercial trade name for our product candidates and failure to secure such registrations could adversely affect our business.

We have not yet registered trademarks for a commercial trade name for our product candidates. During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the PTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Moreover, any name we propose to use with our product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it,

as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

We may find that our programs require the use of proprietary rights held by third parties or the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights. We may be unable to acquire or in-license compositions, methods of use, processes or other third party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, financial resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. Even if we are able to obtain a license to intellectual property of interest, we may not be able to secure exclusive rights, in which case others could use the same rights and compete with us.

If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business and financial condition could suffer.

Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our product candidates.

We may seek collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of our product candidates depending on the merits of retaining commercialization rights for ourselves as compared to entering into collaboration arrangements. We will face, to the extent that we decide to enter into collaboration agreements, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time-consuming to negotiate, document, implement and maintain. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements should we so chose to enter into such arrangements. The terms of any collaborations or other arrangements that we may establish may not be favorable to us.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include that:

- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;

[Table of Contents](#)

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that causes the delay or termination of the research, development or commercialization of our current or future products or that results in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated, and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable current or future products;
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

Risks Related to Ownership of our Common Stock

The price of our stock may be volatile, and you could lose all or part of your investment.*

The trading price of our common stock has been, and is likely to be, highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in these "Risk Factors" and elsewhere in this Quarterly Report on Form 10-Q, these factors include, but are not limited to:

- any delay in the commencement, enrollment and ultimate completion of clinical trials;
- actual or anticipated results in our clinical trials or those of our competitors, such as the initial announcement of the halting of our Phase 2 clinical trial of PTG-100 for the treatment of moderate-to-severe UC in March 2018;
- positive outcomes, or faster development results than expected, by parties developing peptide-based product candidates that are competitive with our peptide-based product candidates, as well as approval of any such competitive peptide-based product candidates;

[Table of Contents](#)

- failure to successfully develop commercial-scale manufacturing capabilities;
- unanticipated serious safety concerns related to the use of any of our peptide-based product candidates;
- failure to secure collaboration agreements for our peptide-based product candidates or actual or perceived unfavorable terms of such agreements;
- adverse regulatory decisions;
- changes in the structure of healthcare payment systems;
- changes in laws or regulations applicable to our product candidates, including but not limited to clinical trial requirements for approvals;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our peptide-based product candidates;
- our dependence on third parties, including CROs as well as manufacturers;
- our failure to successfully commercialize any of our peptide-based product candidates, if approved;
- additions or departures of key scientific or management personnel;
- failure to meet or exceed any financial guidance or development timelines that we may provide to the public;
- actual or anticipated variations in quarterly operating results;
- failure to meet or exceed the estimates and projections of the investment community;
- overall performance of the equity markets and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies;
- conditions or trends in the biotechnology and biopharmaceutical industries;
- announcements of significant acquisitions, strategic collaborations, joint ventures or capital commitments by us or our competitors;
- our ability to maintain an adequate rate of growth and manage such growth;
- issuances of debt or equity securities;
- significant lawsuits, including patent or stockholder litigation;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;

[Table of Contents](#)

- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- ineffectiveness of our internal controls;
- general political and economic conditions; and
- effects of natural or man-made catastrophic events.

In addition, the stock market in general, and The Nasdaq Global Market and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in these “Risk Factors,” could have a dramatic and material adverse impact on the market price of our common stock.

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, such as the decline we experienced in March 2018 upon the initial announcement of the halting of our Phase 2 clinical trial of PTG-100 for the treatment of moderate-to-severe UC due to futility, which was subsequently identified as resulting from human error by the CRO. This risk is especially relevant for us because pharmaceutical companies have experienced significant share price volatility in recent years. 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.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Our executive officers, directors, holders of 5% or more of our capital stock and their respective together beneficially own a significant percentage of our stock. Therefore, these stockholders will have substantial influence and may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This concentration of voting power could, among other things, delay or prevent an acquisition of our company on terms that other stockholders may desire, which in turn could depress our stock price and may prevent attempts by our stockholders to replace or remove the board of directors or management.

We have identified material weaknesses in our internal control over financial reporting and may identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, which may result in material misstatements of our financial statements or cause us to fail to meet our periodic reporting obligations.

Prior to the IPO, we were a private company and had limited accounting and financial reporting personnel and other resources with which to address our internal controls and procedures. In connection with the audit of our consolidated financial statements for the years ended December 31, 2015 and 2014, we and our independent registered public accounting firm identified two material weaknesses in our internal control over financial reporting. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis.

[Table of Contents](#)

The first material weakness related to a deficiency in the operation of our internal controls over the accounting for non-routine, complex equity transactions, which resulted in material post-closing adjustments to the convertible preferred stock, additional paid-in capital, interest expense, and gain from modification of the redeemable convertible preferred stock balances in the consolidated financial statements for the year ended December 31, 2013. Our lack of adequate accounting personnel has resulted in the identification of a second material weakness in our internal control over financial reporting for the years ended December 31, 2015 and 2014. Specifically, we did not, and have not historically, appropriately designed and implemented controls over the review and approval of manual journal entries and the related supporting journal entry calculations.

Neither we nor our independent registered public accounting firm has performed or was required to perform an evaluation of our internal control over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act. We have taken steps to remediate the material weaknesses, including increasing the depth and experience within our accounting and finance organization, and implemented an approval process related to manual journal entries and the related supporting journal entry calculations. In addition, we continued to work on designing and implementing additional improved processes and internal controls. We completed the implementation of this plan as of December 31, 2017, and management determined that we remediated the material weaknesses as of December 31, 2017. We can give no assurance that additional material weaknesses or significant deficiencies in our internal control over financial reporting will not be identified in the future. Our failure to implement and maintain effective internal controls over financial reporting could result in errors in our financial statements that could result in a restatement of our financial statements and cause us to fail to meet our reporting obligations.

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. Our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting until our first Annual Report required to be filed with the SEC following the date we are no longer an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012 (the “JOBS Act”). At such time as we are required to obtain auditor attestation, if we then have a material weakness, we would receive an adverse opinion regarding our internal control over financial reporting from our independent registered accounting firm.

Our compliance with Section 404 requires that we incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will 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 our current material weaknesses, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition or results of operations. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our ordinary shares could

decline, and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

We are an “emerging growth company” and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.

We are an “emerging growth company” as defined in the JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We will remain an emerging growth company, and thus may continue to rely on these exemptions, until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of the IPO, (b) in which we have total annual gross revenue of at least \$1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700.0 million as of the prior June 30th, and (2) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

Under Section 107(b) of the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption, and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not “emerging growth companies.”

Future sales of our common stock may depress our share price.*

Sales of a substantial number of shares of our common stock in the public market, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. At September 30, 2018, we had a total of 24,138,102 shares of common stock outstanding, notwithstanding any potential exercises of outstanding options and issuance of shares under the employee stock purchase plan.

If additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Any sales of securities by our stockholders could have an adverse effect on the trading price of our common stock. In addition, in the future we may issue common stock or other securities, including sales of up to \$50.0 million worth of shares of our common stock pursuant to our sales agreement with Cantor Fitzgerald & Co. (the “Sales Agreement”). The number of shares of our new common stock issued in connection with raising additional capital could constitute a material portion of our then outstanding common stock.

If we sell shares of our common stock in future financings, stockholders may experience immediate dilution and, as a result, our stock price may decline.

We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock. As a result, our stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. If we issue common stock or securities convertible into common stock, including sales of up to \$50.0 million worth of shares of our common stock pursuant to the Sales Agreement, our common stockholders would experience additional dilution and, as a result, our stock price may decline.

We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management has been required and will continue to be required to devote substantial time to maintain compliance with our public company responsibilities and corporate governance practices.

We have incurred and will continue to incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and regulations regarding corporate governance practices. The listing requirements of The Nasdaq Global Market require that we satisfy certain corporate governance requirements relating to director independence, distributing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel have devoted and will continue to need to devote a substantial amount of time to ensure that we comply with all of these requirements. Moreover, the reporting requirements, rules and regulations will increase our legal and financial compliance costs and will make some activities more time consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors’ and officers’ insurance, on acceptable terms.

As a public company, and particularly after we are no longer an “emerging growth company,” we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies. Our management and other personnel will need to devote a substantial amount of time to compliance with these requirements. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain directors’ and officers’ liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We cannot predict or estimate the amount of additional costs we will incur as a public company or the timing of such costs.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

During the course of our review and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we will be required to file accurate and timely quarterly and Annual Reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The Nasdaq Global Market or other adverse consequences that would materially harm our business.

Any changes to existing accounting pronouncements or taxation rules or practices may cause adverse fluctuations in our reported results of operations or affect how we conduct our business.

A change in accounting pronouncements or taxation rules or practices can have a significant effect on our reported results and may affect our reporting of transactions completed before the change is effective. New accounting pronouncements, taxation rules and varying interpretations of accounting pronouncements or taxation rules have occurred in the past and may occur in the future. The change to existing rules, future changes, if any, or the need for us to modify a current tax or accounting position may adversely affect our reported financial results or the way we conduct our business.

Nasdaq may delist our securities from its exchange, which could limit investors' ability to make transactions in our securities and subject us to additional trading restrictions.

Our common stock is listed on The Nasdaq Global Market. We cannot assure you that, in the future, our securities will meet the continued listing requirements to be listed on The Nasdaq Global Market. If The Nasdaq Global Market delists our common stock, we could face significant material adverse consequences, including:

- a limited availability of market quotations for our securities;
- a determination that our common stock is a "penny stock" which will require brokers trading in our common stock to adhere to more stringent rules and possibly resulting in a reduced level of trading activity in the secondary trading market for our common stock;
- a limited amount of news and analyst coverage for our company; and
- a decreased ability to issue additional securities or obtain additional financing in the future.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us or our business. In the event one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price could be adversely affected. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our common stock could decrease, and we could lose visibility in the financial markets, which might cause our stock price and trading volume to decline.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third party claims against us and may reduce the amount of money available to us generally.

Our amended and restated certificate of incorporation provides that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into and will enter into with our directors and officers provide that:

- we will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful;
- we may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law;
- we are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification;
- we will not be obligated pursuant to our bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification;
- the rights conferred in our bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons; and
- we may not retroactively amend our bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

As a result, if we are required to indemnify one or more of our directors or executive officers, it may reduce our available funds to satisfy successful third party claims against us, may reduce the amount of money available to us and may have a material adverse effect on our business and financial condition.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, would be your sole source of gain.

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our common stock would be your sole source of gain on an investment in our common stock for the foreseeable future.

Provisions in our corporate charter documents could make an acquisition of us more difficult and may prevent attempts by our stockholders to replace or remove our current management.

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

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

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. 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 with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

Our board of directors has certain characteristics which may delay or prevent a change of our management or a change in control.

Our board of directors has the following characteristics which may delay or prevent a change of management or a change in control:

- our board of directors has the right to elect directors to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- our stockholders may not act by written consent or call special stockholders' meetings; as a result, a holder, or holders, controlling a majority of our capital stock would not be able to take certain actions other than at annual stockholders' meetings or special stockholders' meetings called by the board of directors, the chairman of the board or the chief executive officer;

[Table of Contents](#)

- our certificate of incorporation does not provide for cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- stockholders must provide advance notice and additional disclosures in order to nominate individuals for election to the board of directors or to propose matters that can be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company; and
- our board of directors may issue, without stockholder approval, shares of undesignated preferred stock; the ability to issue undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to acquire us.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

In December 2017, the Tax Act was enacted which significantly changes the Internal Revenue Code, as amended (the "Code"). The Tax Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%; limitation of the tax deduction for interest expense to 30% of adjusted earnings; for net operating losses generated after 2017, limitation of the deduction to 80% of current year taxable income, indefinite carryforward of net operating losses and elimination of net operating loss carrybacks; changes in the treatment of offshore earnings regardless of whether they are repatriated; mandatory capitalization of research and development expenses beginning in 2022; immediate deductions for certain new investments instead of deductions for depreciation expense over time; further deduction limits on executive compensation; and modifying, repealing and creating many other business deductions and credits, including the reduction in the orphan drug credit from 50% to 25% of qualifying expenditures. We continue to examine the impact this tax reform legislation may have on our business. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the Tax Act is uncertain and our business and financial condition could be adversely affected. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. This annual report does not discuss any such tax legislation or the manner in which it might affect us or our stockholders in the future. We urge our stockholders to consult with their legal and tax advisors with respect to such legislation.

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

We have incurred substantial losses during our history. We do not anticipate generating revenue from sales of products for the foreseeable future, if ever, and we may never achieve profitability. 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 Section 382 of the Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percentage points change (by value) in its equity ownership over a rolling three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. Based on a review of our equity transactions since inception, we believe a portion of our net operating loss carryforwards and credit carryforwards may be limited due to an equity financing that occurred in 2015. We may experience ownership changes in the future or subsequent shifts in our stock ownership, some of which are outside our control. As of December 31, 2017, we had federal net operating loss carryforwards of approximately \$79.2 million that could be limited if we have experienced, or if in the future we experience, an ownership change, which could have an adverse effect on our future results of operations.

Provisions under Delaware law and California law could make an acquisition of our company more difficult, limit attempts by our stockholders to replace or remove our current management and limit the market price of our common stock.

Because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any holder of at least 15% of our capital stock for a period of three years following the date on which the stockholder acquired at least 15% of our common stock. Likewise, because our principal executive offices are located in California, the anti-takeover provisions of the California Corporations Code may apply to us under certain circumstances now or in the future.

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	001-3785237852	3.1	8/16/2016
3.2	Amended and Restated Bylaws	S-1/A	333-212476	3.2	8/1/2016
4.1	Specimen stock certificate evidencing the shares of common stock	S-1/A	333-212476	4.1	8/1/2016
4.2	Amended and Restated Investor Rights Agreement, by and among Protagonist Therapeutics, Inc. and the stockholders named therein, dated July 10, 2015.	S-1/A	333-212476	4.2	8/1/2016
4.3	Form of Class A Common Stock Purchase Warrant	8-K	001-37852	4.1	8/7/2018
4.4	Form of Class B Common Stock Purchase Warrant	8-K	001-37852	4.2	8/7/2018
10.1	Registration Rights Agreement, by and among Protagonist Therapeutics, Inc. and certain parties identified on the signature pages thereto, dated August 8, 2018.	8-K	001-37852	4.3	8/7/2018
10.2	Securities Purchase Agreement, by and among Protagonist Therapeutics, Inc. and certain purchasers identified on the signature pages thereto, dated August 6, 2018.	S-3	333-227216	10.1	9/7/2018
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				
101.SCH+	XBRL Taxonomy Extension Schema Document				
101.CAL+	XBRL Taxonomy Extension Calculation Linkbase Document				

[Table of Contents](#)

101.DEF+	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB+	XBRL Taxonomy Extension Labels Linkbase Document
101.PRE+	XBRL Taxonomy Extension Presentation Linkbase Document

* Indicates a management contract or compensatory plan or arrangement.

† Confidential treatment requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

+ Filed herewith

** 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: November 6, 2018

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

Date: November 6, 2018

By: /s/ Thomas P. O'Neil
Thomas P. O'Neil
Chief Financial Officer
(Principal Financial and Accounting Officer)

**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 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 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: November 6, 2018

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

CERTIFICATION OF CHIEF FINANCIAL OFFICER
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Thomas P. O'Neil, 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 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: November 6, 2018

/s/ Thomas P. O'Neil
Thomas P. O'Neil
Chief Financial Officer

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 Thomas P. O'Neil, 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 September 30, 2018, 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: November 6, 2018

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

Date: November 6, 2018

/s/ Thomas P. O'Neil
Thomas P. O'Neil
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."
