

**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 June 30, 2020

OR

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

For the transition period from \_\_\_\_ to \_\_\_\_

Commission file number: 001-37695

**Proteostasis Therapeutics, Inc.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or Other jurisdiction of  
Incorporation or organization)  
**80 Guest Street, Suite 500**  
**Boston, Massachusetts**  
(Address of Principal Executive Offices)

**20-8436652**  
(I.R.S. Employer  
Identification No.)

**02135**  
(Zip Code)

(617) 225-0096  
(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol	Name of exchange on which registered
Common stock, par value \$0.001 per share	PTI	The Nasdaq Stock Market LLC

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

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

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

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

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" 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). Yes  No

As of August 3, 2020, there were 52,175,861 shares of the registrant's common stock, \$0.001 par value per share, outstanding.

## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q, or this report, including the sections entitled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” contains forward-looking statements that involve risks and uncertainties, as well as assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Statements that are not purely historical are 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. These forward-looking statements are often identified by the words, “aim,” “anticipate,” “believes,” “can,” “continue,” “could,” “estimates,” “expects,” “intends,” “may,” “plans,” “potential,” “predicts,” “project,” “seek,” “should,” “target,” “will,” “would” or the negative of these terms or other comparable terminology intended to identify forward-looking statements. These forward-looking statements include, but are not limited to, statements about:

- our planned Phase 3 clinical trials with our combination therapy candidates, nesolicaftor (PTI-428), posenacftor (PTI-801), and dirocaftor (PTI-808), including timing of the progress and the potential filing of a Marketing Authorization Application, or MAA;
- the development of our product candidates, including statements regarding the timing of initiation, completion and the outcome of clinical studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- our ability to advance our product candidates into, and successfully complete, clinical trials;
- our ability to establish additional collaborations for our product candidates;
- our estimates regarding anticipated filing of investigational new drugs, or INDs and/or amended protocols for our product candidates;
- our ability to obtain and maintain regulatory approval of our combination solutions, for any indication, and any related restrictions, limitations or warnings of an approved drug or therapy;
- our ability to obtain and maintain sanctioning or favorable scoring of our clinical trials or protocols from other third parties, such as the Therapeutics Development Network, or TDN, of the Cystic Fibrosis Foundation, or CFF, or the Clinical Trial Network, or CTN, of the European Cystic Fibrosis Society;
- intense competition in the cystic fibrosis market and the ability of our competitors, many of whom have greater resources than we do, to run clinical trials that may limit the patients available for our trials, and to offer different, better or lower cost therapeutic alternatives than our product candidates;
- anticipated regulatory developments in the United States and foreign countries;
- our plans to research, develop, manufacture and commercialize our combination solutions, including expected preclinical and clinical results and timing;
- our ability to obtain and maintain intellectual property protection for our proprietary assets;
- the size and growth of the potential markets for our combination solutions, and our ability to serve those markets;
- the rate and degree of commercial scope and potential, as well as market acceptance of our combination solutions for any indication;
- the benefits of U.S. Food and Drug Administration, or FDA, and European Commission designations such as, including, without limitation, Fast Track, Orphan Drug and Breakthrough Therapy;
- our commercialization, marketing, and manufacturing capabilities and strategy;
- our ability to obtain additional financing;
- our estimates regarding expenses, future revenues and anticipated capital requirements;
- our ability to attract and retain qualified key scientific or management personnel;
- our expectations regarding the impact of the ongoing coronavirus disease 2019, or COVID-19, pandemic, including the expected duration of disruption and immediate and long-term impact and effect on our business and operations; and
- other forward-looking statements discussed elsewhere in this report.

You should refer to “Risk Factors” for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this report will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this report.

Any forward-looking statements in this report reflect our current views with respect to future events and with respect to our future financial performance and 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, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those described under Part II, Item 1A. Risk Factors and elsewhere in this report. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This report contains estimates, projections and other information concerning our industry, the general business environment, and the markets for certain diseases, including estimates regarding the potential size of those markets and the estimated incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events, circumstances or numbers, including actual disease prevalence rates and market size, may differ materially from the information reflected in this report. Unless otherwise expressly stated, we obtained this industry, business information, market data, prevalence information and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources, in some cases applying our own assumptions and analysis that may, in the future, not prove to have been accurate.

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## Item 1. CONDENSED FINANCIAL STATEMENTS (Unaudited)

## PROTEOSTASIS THERAPEUTICS, INC.

**CONDENSED BALANCE SHEETS**  
(In thousands, except share and per share amounts)  
(Unaudited)

	June 30, 2020	December 31, 2019
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 42,868	\$ 25,008
Short-term investments	5,998	44,459
Prepays and other current assets	1,964	1,404
Total current assets	50,830	70,871
Operating lease, right-of-use asset	12,002	12,631
Property and equipment, net	308	394
Restricted cash	828	828
Total assets	<u>\$ 63,968</u>	<u>\$ 84,724</u>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 1,504	\$ 2,283
Accrued expenses	4,157	6,864
Operating lease liabilities	1,204	1,153
Short-term borrowings	735	—
Total current liabilities	7,600	10,300
Derivative liability	3	3
Operating lease liabilities, net of current portion	11,429	12,043
Total liabilities	19,032	22,346
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, \$0.001 par value; 5,000,000 shares authorized; no shares issued and outstanding as of June 30, 2020 and December 31, 2019	—	—
Common stock, \$0.001 par value; 125,000,000 shares authorized; 52,147,656 and 52,116,629 shares issued and outstanding as of June 30, 2020 and December 31, 2019, respectively	52	52
Additional paid-in capital	400,315	398,979
Accumulated other comprehensive income	—	7
Accumulated deficit	(355,431)	(336,660)
Total stockholders' equity	44,936	62,378
Total liabilities and stockholders' equity	<u>\$ 63,968</u>	<u>\$ 84,724</u>

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

PROTEOSTASIS THERAPEUTICS, INC.

CONDENSED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS  
(In thousands, except share and per share amounts)  
(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Revenue	\$ —	\$ —	\$ —	\$ 5,000
Operating expenses:				
Research and development	4,584	16,925	11,102	33,072
General and administrative	4,366	3,682	7,953	7,626
Total operating expenses	8,950	20,607	19,055	40,698
Loss from operations	(8,950)	(20,607)	(19,055)	(35,698)
Interest income	54	297	261	654
Interest expense	(6)	—	(9)	—
Other income, net	9	292	32	608
Net loss	\$ (8,893)	\$ (20,018)	\$ (18,771)	\$ (34,436)
Net loss per share—basic and diluted	\$ (0.17)	\$ (0.39)	\$ (0.36)	\$ (0.67)
Weighted average common shares outstanding—basic and diluted	52,147,656	51,097,456	52,147,145	51,037,514
Other comprehensive income:				
Unrealized gain (loss) on investments	(43)	15	(7)	32
Comprehensive loss	\$ (8,936)	\$ (20,003)	\$ (18,778)	\$ (34,404)

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

CONDENSED STATEMENTS OF STOCKHOLDERS' EQUITY  
(In thousands, except share amounts)  
(Unaudited)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
<b>Balances at March 31, 2020</b>	52,147,656	\$ 52	\$ 399,583	\$ 43	\$ (346,538)	\$ 53,140
Stock-based compensation expense	—	—	732	—	—	732
Other comprehensive income (loss)	—	—	—	(43)	—	(43)
Net loss	—	—	—	—	(8,893)	(8,893)
<b>Balances at June 30, 2020</b>	<u>52,147,656</u>	<u>\$ 52</u>	<u>\$ 400,315</u>	<u>\$ —</u>	<u>\$ (355,431)</u>	<u>\$ 44,936</u>

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
<b>Balances at December 31, 2019</b>	52,116,629	\$ 52	\$ 398,979	\$ 7	\$ (336,660)	\$ 62,378
Stock-based compensation expense	—	—	1,310	—	—	1,310
Issuance of common stock pursuant to employee stock purchase plan	31,027	—	26	—	—	26
Other comprehensive income (loss)	—	—	—	(7)	—	(7)
Net loss	—	—	—	—	(18,771)	(18,771)
<b>Balances at June 30, 2020</b>	<u>52,147,656</u>	<u>\$ 52</u>	<u>\$ 400,315</u>	<u>\$ —</u>	<u>\$ (355,431)</u>	<u>\$ 44,936</u>

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
<b>Balances at March 31, 2019</b>	51,043,158	\$ 51	\$ 392,851	\$ 18	\$ (291,953)	\$ 100,967
Stock-based compensation expense	—	—	949	—	—	949
Issuance of common stock for payment of consulting services	56,149	—	72	—	—	72
Other comprehensive income (loss)	—	—	—	15	—	15
Net loss	—	—	—	—	(20,018)	(20,018)
<b>Balances at June 30, 2019</b>	<u>51,099,307</u>	<u>\$ 51</u>	<u>\$ 393,872</u>	<u>\$ 33</u>	<u>\$ (311,971)</u>	<u>\$ 81,985</u>

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
<b>Balances at December 31, 2018</b>	50,808,422	\$ 51	\$ 391,825	\$ 1	\$ (277,535)	\$ 114,342
Exercise of stock options	2,543	—	3	—	—	3
Stock-based compensation expense	—	—	1,749	—	—	1,749
Issuance of common stock for payment of consulting services	102,302	—	242	—	—	242
Issuance of common stock pursuant to employee stock purchase plan	22,615	—	53	—	—	53
Vesting of restricted stock units	163,425	—	—	—	—	—
Other comprehensive income (loss)	—	—	—	32	—	32
Net loss	—	—	—	—	(34,436)	(34,436)
<b>Balances at June 30, 2019</b>	<u>51,099,307</u>	<u>\$ 51</u>	<u>\$ 393,872</u>	<u>\$ 33</u>	<u>\$ (311,971)</u>	<u>\$ 81,985</u>

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

**PROTEOSTASIS THERAPEUTICS, INC.**  
**CONDENSED STATEMENTS OF CASH FLOWS**  
(In thousands)  
(Unaudited)

	<u>Six Months Ended June 30,</u>	
	<u>2020</u>	<u>2019</u>
<b>Cash flows from operating activities:</b>		
Net loss	\$ (18,771)	\$ (34,436)
Adjustments to reconcile net loss to cash used in operating activities:		
Depreciation and amortization	86	101
Non-cash lease expense	629	603
Accretion of short-term investments	(34)	(614)
Stock-based compensation expense	1,310	1,749
Stock issued for consulting services	—	242
Changes in operating assets and liabilities:		
Prepays and other current assets	(560)	(585)
Other assets	—	(75)
Accounts payable	(779)	1,276
Accrued expenses	(2,707)	1,202
Operating lease liabilities	(563)	(514)
Net cash used in operating activities	<u>(21,389)</u>	<u>(31,051)</u>
<b>Cash flows from investing activities:</b>		
Purchases of short-term investments	(11,229)	(43,170)
Proceeds received from maturities of short-term investments	49,717	74,000
Purchases of property and equipment	—	(9)
Net cash provided by investing activities	<u>38,488</u>	<u>30,821</u>
<b>Cash flows from financing activities:</b>		
Proceeds from exercise of stock options	—	3
Proceeds from issuance of common stock pursuant to employee stock purchase plan	26	53
Proceeds from issuance of short-term borrowings	1,220	—
Repayment of short-term borrowings	(485)	—
Net cash provided by financing activities	<u>761</u>	<u>56</u>
<b>Net increase in cash, cash equivalents and restricted cash</b>	<b>17,860</b>	<b>(174)</b>
Cash, cash equivalents and restricted cash at beginning of period	25,836	29,638
Cash, cash equivalents and restricted cash at end of period	<u>\$ 43,696</u>	<u>\$ 29,464</u>

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

NOTES TO CONDENSED FINANCIAL STATEMENTS  
(Unaudited)**1. Nature of the Business**

Proteostasis Therapeutics, Inc. (the “Company”) was incorporated in Delaware on December 13, 2006. The Company is a clinical stage biopharmaceutical company committed to the discovery and development of novel therapeutics to treat cystic fibrosis (“CF”) through theratyping, or the process of matching modulators to individual response to treatment regardless of cystic fibrosis transmembrane conductance regulator (“CFTR”) mutations. CF is a disease caused by defects in the function or abundance of CFTR protein. Although, CF is defined as a monogenic recessive genetic disorder caused by mutations in the CFTR gene, there is a broad range of disease activity for different organ systems in CF, including lung disease, meconium ileus, diabetes, and liver disease, even for CF patients who are homozygous for the most common mutation, F508del mutation. In summary, CF genotype does not always match CF phenotype.

Since its inception, the Company has devoted substantially all of its efforts to organizing and staffing the Company, business planning, raising capital, acquiring and developing product and technology rights, and conducting research and development activities. It has funded its operations to date with proceeds from the sale of preferred stock, the issuance of convertible promissory notes, proceeds from its initial public offering in February 2016, proceeds from its follow-on public offerings, and payments received in connection with collaboration agreements and a research grant, as well as funds from the sale of stock under the at-the-market offering program described below. The Company does not have any products approved for sale and has not generated any revenue from product sales.

The Company has not generated any commercial revenue since inception. As a result, the Company has incurred recurring losses and requires significant cash resources to execute its business plans. In accordance with ASC 205-40, *Going Concern* (“ASC 205-40”), the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company’s ability to continue as a going concern within one year after the date the financial statements are issued. As of June 30, 2020, the Company had an accumulated deficit of \$355.4 million. The Company has incurred losses and negative cash flows from operations since its inception. During the six months ended June 30, 2020, the Company incurred losses of \$18.8 million and used \$21.4 million of cash in operations. The Company expects that its operating losses and negative cash flows will continue for the foreseeable future. The Company currently expects that its cash, cash equivalents and short-term investments of \$48.9 million will be sufficient to fund its operating expenses and capital requirements, based upon its current operating plan, for at least 12 months from the date that these financial statements are issued. The Company will require additional funding to fund its proposed Phase 3 Modulator Options to RestorE CFTR (“MORE”) trial, its CHOICES program, and to advance its proprietary combination therapy candidates through regulatory approval and into commercialization, if approved. Accordingly, the Company is in the process of considering various financing alternatives to support its operating and capital needs, including public or private equity or debt financings, third-party funding, marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these approaches. The Company is also considering strategic alternatives for its CF portfolio, including its proprietary combination therapy candidates posenacftor, dirocaftor, and nesolicaftor, with the goal of maximizing stockholder value of these assets. However, the Company does not currently have any commitments for future external funding and additional financing may not be available on a timely basis, on acceptable terms, or at all.

The novel coronavirus (“COVID-19”) pandemic continues to rapidly evolve and has already resulted in a significant disruption of global financial markets. If the disruption persists and deepens, the Company could experience an inability to access additional capital, when and if needed. If the Company is unable to implement any strategic or financing alternative and adequate funds are not available in the future, the Company may be required to delay, limit, reduce or terminate its clinical development or future commercialization efforts or obtain funds through arrangements with collaborators or others that may require it to relinquish rights to develop and market product candidates that it would otherwise prefer to develop and market themselves.

**2. Summary of Significant Accounting Policies*****Unaudited Interim Financial Information***

The condensed balance sheet as of December 31, 2019 was derived from audited financial statements but does not include all disclosures required by accounting principles generally accepted in the United States of America (“GAAP”). The accompanying condensed financial statements, as of June 30, 2020 and for the three and six months ended June 30, 2020, are unaudited and have been prepared by the Company pursuant to the rules and regulations of the Securities and Exchange Commission (the “SEC”) for interim financial statements. Certain information and footnote disclosures normally included in financial statements prepared in accordance with GAAP have been condensed or omitted pursuant to such rules and regulations. The Company believes that the disclosures are adequate to make the information presented not misleading. These unaudited condensed financial statements should be read in conjunction with the Company’s audited financial statements and the notes thereto for the year ended December 31, 2019 included in the Company’s Annual Report on Form 10-K for the year ended December 31, 2019 filed with the SEC on March 10, 2020. In the opinion of management, all adjustments, consisting only of normal recurring adjustments, as necessary for the fair statement of the Company’s financial position as of June 30, 2020, results of its operations for the three and six months ended June 30, 2020, stockholders’ equity for the three and six months ended June 30, 2020, and cash flows for the six months ended June 30, 2020,

have been made. The results of operations for the three and six months ended June 30, 2020 are not necessarily indicative of the results of operations to be expected for the year ending December 31, 2020.

### ***Summary of Significant Accounting Policies***

The Company's significant accounting policies, which are disclosed in the audited financial statements for the year ended December 31, 2019 and the notes thereto, are included in the Company's Annual Report on Form 10-K that was filed with the SEC on March 10, 2020. There were no changes to significant accounting policies during the three and six months ended June 30, 2020.

### ***Risks and Uncertainties***

The Company is monitoring the potential impact of COVID-19, if any, on the carrying value of certain assets. To date, the Company has not experienced material business disruption, nor has it incurred impairment of any assets as a result of COVID-19. The extent to which these events may impact the Company's business, clinical development and regulatory efforts, and the value of its common stock, will depend on future developments, which are highly uncertain and cannot be predicted at this time. The duration and intensity of these impacts and resulting disruption to the Company's operations is uncertain and the Company will continue to assess the financial impact.

In addition, the Company is subject to other challenges and risks specific to its business and its ability to execute on its business plan and strategy, as well as risks and uncertainties common to companies in the biopharmaceutical industry with development and commercial operations, including, without limitation, risks and uncertainties associated with: obtaining regulatory approval of its late-stage product candidates; delays or problems in obtaining clinical supply, loss of single source suppliers or failure to comply with manufacturing regulations; identifying, acquiring or in-licensing additional products or product candidates; biopharmaceutical product development and the inherent uncertainty of clinical success; and the challenges of complying with applicable regulatory requirements. In addition, to the extent the ongoing COVID-19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties discussed above.

### ***Use of Estimates***

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenue and expenses during the reporting periods. Significant estimates and assumptions reflected in these condensed financial statements include, but are not limited to, revenue recognition, the accrual for research and development expenses, and the valuation the derivative liability. Estimates are periodically reviewed in light of changes in circumstances, facts, and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ from those estimates.

### ***Reclassifications***

Certain prior year amounts have been reclassified for consistency with the current year presentation. An adjustment has also been made to the condensed statement of cash flows for the period ended June 30, 2019, to reclassify non-cash lease expense out of depreciation and amortization.

### ***Recently Issued and Adopted Accounting Pronouncements***

ASU No. 2018-13, *Fair Value Measurement (Topic 820): Changes to the Disclosure Requirements for Fair Value Measurement*

In August 2018, the FASB issued ASU No. 2018-13, *Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"). The new standard modifies the disclosure requirements on fair value measure in Topic 820, including removals of existing disclosures, modifications of existing disclosures, and additions of new disclosures. Certain amendments on changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair values measurements, and the narrative description of measurement uncertainty should be applied prospectively for only the most recent interim of annual period presented in the initial fiscal year of adoption. All other amendments should be applied retrospectively to all periods presented upon their effective date. Early adoption is permitted for any removed or modified disclosure. The new standard is effective for the Company on January 1, 2020. The adoption of this standard did not have a material impact on the Company's condensed financial statements.

### ***Recently Issued Accounting Pronouncements***

ASU No. 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"). The FASB subsequently issued amendments to ASU 2016-13, which have the same effective date and transition date of January 1, 2022, as the Company is a smaller reporting company. These standards require that credit losses be reported using an expected losses model rather than the incurred losses model that is currently used, and establishes additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, these standards

now require allowances to be recorded instead of reducing the amortized cost of the investment. These standards limit the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value and requires the reversal of previously recognized credit losses if fair value increases. Based on the composition of the Company's investment portfolio and other financial assets, current market conditions and historical credit loss activity, the adoption of these standards is not expected to have a material impact on the Company's condensed financial statements.

### 3. Short-Term Investments

The following table summarizes the Company's short-term investments as of June 30, 2020 and December 31, 2019 (in thousands):

	June 30, 2020			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities	\$ 5,998	\$ —	\$ —	\$ 5,998
	<u>\$ 5,998</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 5,998</u>
	December 31, 2019			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S government-sponsored enterprise securities	\$ 20,456	\$ 2	\$ (1)	\$ 20,457
U.S. treasury securities	23,996	7	(1)	24,002
	<u>\$ 44,452</u>	<u>\$ 9</u>	<u>\$ (2)</u>	<u>\$ 44,459</u>

Short-term investments represent holdings of available-for-sale debt securities and are reported at fair value with unrealized gains and losses reported net of taxes, if material, in other comprehensive income. The Company did not have any realized gains or losses on its short-term investments for the three and six months ended June 30, 2020 and 2019. There were no other-than-temporary impairments recognized for the three and six months ended June 30, 2020 and 2019.

#### 4. Fair Value of Financial Assets and Liabilities

The following tables present information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values (in thousands):

	Fair Value Measurements as of June 30, 2020 using:			
	Level 1	Level 2	Level 3	Total
<b>Assets:</b>				
Cash equivalents:				
Money market funds	\$ 27,873	\$ —	\$ —	\$ 27,873
U.S. treasury securities	—	13,998	—	13,998
Short-term investments:				
U.S. treasury securities	—	5,998	—	5,998
	<u>\$ 27,873</u>	<u>\$ 19,996</u>	<u>\$ —</u>	<u>\$ 47,869</u>
<b>Liabilities:</b>				
Derivative liability	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 3</u>	<u>\$ 3</u>
	Fair Value Measurements as of December 31, 2019 using:			
	Level 1	Level 2	Level 3	Total
<b>Assets:</b>				
Cash equivalents:				
Money market funds	\$ 23,906	\$ —	\$ —	\$ 23,906
Short-term investments:				
U.S. government-sponsored enterprise securities	—	20,457	—	20,457
U.S. treasury securities	—	24,002	—	24,002
	<u>\$ 23,906</u>	<u>\$ 44,459</u>	<u>\$ —</u>	<u>\$ 68,365</u>
<b>Liabilities:</b>				
Derivative liability	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 3</u>	<u>\$ 3</u>

During the periods ended June 30, 2020 and December 31, 2019, there were no transfers between Level 1, Level 2 and Level 3.

The derivative liability relates to a cash settlement option associated with the change of control provision in the Company's Cystic Fibrosis Foundation, Inc. ("CFF") agreement, which meets the definition of a derivative. The fair value of the derivative liability is based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy. The fair value of the derivative instrument was originally determined using the Monte-Carlo simulation analysis. In determining the fair value of the derivative liability, the inputs impacting fair value include the fair value of the Company's common stock, expected term of the derivative instrument, expected volatility of the common stock price, risk-free interest rate, expected sales-based milestone payments, discount rate, probability of a change of control event, and the probability that the counterparty would elect to accept the alternative cash payment in lieu of its right to the future sales-based milestone payments.

The fair value of the derivative liability was not material at June 30, 2020 and December 31, 2019.

#### 5. Prepaids and Other Current Assets

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

	June 30, 2020	December 31, 2019
Prepaid clinical, manufacturing and scientific expenses	\$ 398	\$ 767
Prepaid insurance expenses	1,174	125
Other prepaid expenses and other current assets	392	512
	<u>\$ 1,964</u>	<u>\$ 1,404</u>

## 6. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	June 30, 2020	December 31, 2019
Accrued payroll and related expenses	2,095	3,203
Accrued research and development expenses	\$ 1,075	\$ 3,186
Accrued professional fees	964	397
Accrued other	23	78
	<u>\$ 4,157</u>	<u>\$ 6,864</u>

## 7. Short-Term Borrowings

As of June 30, 2020, the Company had short-term borrowings of \$0.7 million consisting of a Commercial Insurance Premium Finance and Security Agreement (the "Finance and Security Agreement") entered into on February 27, 2020. The Finance and Security Agreement has a ten-month repayment period with an annual interest rate of 2.59% and a maturity of December 11, 2020. Collateral under the Finance and Security Agreement includes the right, title, and interest in the underlying business insurance policies. As of June 30, 2020, the Company has paid less than \$0.1 million in interest on short-term borrowings.

## 8. Stock-Based Compensation

### 2016 Stock Option and Incentive Plan

On February 3, 2016, the Company's stockholders approved the 2016 Stock Option and Incentive Plan (the "2016 Plan"), which became effective on February 9, 2016. The 2016 Plan provides for the grant of incentive stock options, nonqualified stock options, stock appreciation rights, restricted stock units, restricted stock awards and other stock-based awards. The number of shares initially reserved for issuance under the 2016 Plan was 1,581,839 shares. The number of shares of common stock that may be issued under the 2016 Plan will automatically increase each January 1, beginning January 1, 2017, by the lesser of 3% of the shares of the Company's common stock outstanding on the immediately preceding December 31, or an amount determined by the Company's board of directors or the compensation committee of the board of directors. The shares of common stock underlying any awards that are forfeited, canceled, repurchased, or are otherwise terminated by the Company under the 2016 Plan and the 2008 Equity Incentive Plan, as amended (the "2008 Plan") will be added back to the shares of common stock available for issuance under the 2016 Plan. On January 1, 2020, an additional 1,563,498 shares were reserved for issuance under the 2016 Plan. As of June 30, 2020, the total number of shares of the Company's common stock reserved for issuance under the 2016 Plan was 6,914,838, of which 1,275,795 shares are available for future issuance under the 2016 Plan.

### 2016 Employee Stock Purchase Plan

On February 3, 2016, the Company's stockholders approved the 2016 Employee Stock Purchase Plan (the "2016 ESPP"), which became effective in connection with the completion of the Company's initial public offering. A total of 138,757 shares of common stock were initially reserved for issuance under the 2016 ESPP. In addition, the number of shares of common stock that may be issued under the 2016 ESPP will automatically increase each January 1, beginning January 1, 2017, by the lesser of (i) 138,757 shares of common stock, (ii) 1% of the Company's shares of common stock outstanding on the immediately preceding December 31, or (iii) an amount determined by the Company's board of directors or the compensation committee of the board of directors.

During the six months ended June 30, 2020, 31,027 shares of common stock were issued pursuant to the 2016 ESPP. As of June 30, 2020, the total number of shares reserved under the 2016 ESPP was 580,742 shares. The Company recognized less than \$0.1 million of stock-based compensation during the three and six months ended June 30, 2020 related to the 2016 ESPP.

### Restricted Stock Units (RSUs)

On February 4, 2020, the Company's board approved payment to be made to a nonemployee through a grant of RSUs based on the February 4, 2020 closing share price of the Company's common stock. The requisite service period for the awards is from February 4, 2020 to August 4, 2020 (the vesting period). The Company recognized employee stock-based compensation expense for the RSU grant on a straight-line basis over the vesting period of the awards. As of June 30, 2020, 4,519 RSUs were granted and the Company recognized less than \$0.1 million of stock-based compensation expense during the three and six months ended June 30, 2020.

On June 29, 2020, the Company's board approved the grant of RSU awards with an aggregate fair market value equal to the RSU value of \$1.2 million (each an "Award") to two consultants (each, a "Grantee") in consideration for services. Each Award shall vest in full immediately prior to, but subject to the occurrence of, a specific strategic event (the "Vesting Date"), so long as the

respective Grantee remains in service to the Company through the Vesting Date. If the Awards vest as provided for above, the Company shall issue a number of shares of stock equal to the RSU value, divided by the volume-weighted average price per share of the Company's stock for the 10-day period ending on the Vesting Date. The Company also has the option to issue each Grantee the respective cash equivalent of the Award in part or in full satisfaction of the delivery of the stock in connection with the vesting of each Award. As of June 30, 2020, the Company recognized no compensation costs associated with the Awards as the performance condition of the completion of certain strategic events is not considered probable.

The following table summarizes the Company's RSU activity for the six months ended June 30, 2020:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested balance at December 31, 2019	—	\$ —
Granted	4,519	1.77
Vested	—	—
Forfeited	—	—
Unvested balance at June 30, 2020	<u>4,519</u>	<u>\$ —</u>

### Stock-Based Compensation

Stock-based compensation expense, including shares issued to consultants for services, was classified in the statements of operations as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Research and development	\$ 266	\$ 399	\$ 496	\$ 769
General and administrative	465	622	814	1,222
	<u>\$ 731</u>	<u>\$ 1,021</u>	<u>\$ 1,310</u>	<u>\$ 1,991</u>

The following table summarizes the Company's stock option activity for the six months ended June 30, 2020 (in thousands except share and per share amounts):

	Number of Shares	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding at December 31, 2019	4,364,839	\$ 5.30	7.32	\$ 132
Granted	1,663,000	1.56		
Forfeited	(388,796)	6.11		
Outstanding at June 30, 2020	<u>5,639,043</u>	\$ 4.14	7.65	\$ 33
Exercisable at June 30, 2020	<u>2,675,930</u>	\$ 5.72	6.34	\$ 16
Vested and expected to vest at June 30, 2020	<u>5,555,793</u>	\$ 4.17	7.76	\$ 33

The grant date fair value of options granted during the period was \$1.8 million, or \$1.09 per share on a weighted-average basis, and will be recognized as compensation expense over the requisite service period of four years.

As of June 30, 2020, there was \$4.9 million of unrecognized compensation cost related to employee and nonemployee unvested stock options granted under the 2016 Plan, which is expected to be recognized over a weighted-average remaining service period of 2.4 years. Stock compensation costs have not been capitalized by the Company.

Prior to 2013, the Company issued options to purchase 203,964 shares of common stock to nonemployees, primarily members of the Company's scientific advisory board, that vest upon the achievement of specified development and clinical milestones. As of June 30, 2020, options for the purchase of 83,250 shares held by nonemployees remained unvested, pending achievement of the specified milestones.

## 9. Significant Agreements

### **Genentech**

In December 2018, the Company entered into a Technology Transfer and License Agreement (the "Genentech Agreement") with Genentech, Inc. ("Genentech") under which the Company granted Genentech an exclusive worldwide license for technology and materials relating to potential therapeutic small molecule modulators of an undisclosed target within the proteostasis network. The rights do not include CFTR modulators and are unrelated to the Company's investigational medicines or other ongoing research programs in cystic fibrosis. In connection with the terms of the Genentech Agreement, the Company was entitled to a nonrefundable cash payment of \$5.0 million following the successful completion of the technology and materials transfer to Genentech and future milestone payments in the aggregate of approximately \$96.0 million upon the achievement of specified development, regulatory, and commercial milestones. In addition, Genentech is obligated to pay the Company tiered royalties in the low single-digits based on net sales of products covered by the licenses granted under the Genentech Agreement. There are no cancellation, termination, or refund provisions in the Genentech Agreement that contain material financial consequences to the Company. Unless earlier terminated, the Genentech Agreement continues in full force and effect until the passing or expiration of all royalty payment obligations. Reciprocal termination rights under the agreement include termination for breach and termination for bankruptcy. Genentech may terminate the Genentech Agreement in its entirety, for convenience, upon thirty days' notice to the Company.

The Company evaluated the Genentech Agreement in accordance with the provisions of Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers* ("ASC 606"). The Company's obligations under the Genentech Agreement are the following promises: (i) exclusive license to certain intellectual property associated with a specific target, and (ii) technology and materials transfer related to the intellectual property underlying the licensed technology. The Company determined that the exclusive license is not distinct from the associated technology and materials transfer because the customer cannot benefit from, or utilize, the license without the technology and materials transfer. Specifically, the Company concluded that the exclusive license is not capable of being distinct from the associated technology and materials transfer because Genentech does not have the knowledge or expertise to fully exploit potential product candidates without the accompanying technology and materials provided pursuant to the transfer, and no other third party can perform the transfer due to the Company's proprietary knowledge and specialized expertise with respect to the licensed intellectual property. Accordingly, the Company concluded that these promises should be combined into a single performance obligation (the "License and Transfer Performance Obligation").

The Company measured the transaction price solely in reference to the \$5.0 million payment due upon receipt of notice from Genentech regarding the satisfactory completion of the technology and materials transfer. None of the variable consideration payable under the arrangement has been included in the transaction price. As of June 30, 2020, the Company has not achieved any research, development, regulatory, or commercial milestones, or earned any royalties under the Genentech Agreement. The Company utilizes "the most likely" amount method to estimate the amount of research, development, and regulatory milestone payments to be received. As part of the evaluation for the research and development milestone payments, the Company considers several factors including the stage of research and development of the compounds included in the arrangement, the risk associated with the remaining research and development work required to achieve the milestone, and the Company's level of involvement in the research and development activities.

Regulatory milestone payments are triggered upon the first commercial sale following receipt of regulatory approval from the FDA or other global regulatory authorities; therefore, such amounts will be excluded from the transaction price until the associated regulatory approval is received. The commercial milestone payments and royalties are subject to the royalty recognition constraint whereby such amounts will be recognized as revenue upon the later of: (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the payment has been allocated has been satisfied, or partially satisfied, because the exclusive license is deemed to be the sole or predominant item to which the payments relate. As all performance obligations are satisfied, the Company will recognize royalty revenue at the date the sales occur. The Company did not adjust the promised amount of consideration for the effects of a significant financing component because the Company expects that the period between when the promised goods and services are transferred and when the customer pays for those goods and services will be one year or less. There were no changes in the transaction price for the six months ended June 30, 2020.

The transaction price of \$5.0 million allocated to the combined performance obligation was recognized as revenue in February 2019 at the point in time that Genentech provided notice regarding the satisfactory completion of the technology and materials transfer. Upon that successful execution of the technology and materials transfer, control was deemed to be transferred for both the exclusive license and the technology and materials transfer promises, therefore the risks and rewards of ownership had been conveyed. As of June 30, 2020, the Company did not have any receivables or deferred revenue related to the Genentech Agreement because no payments under the arrangement became due, nor had the underlying performance obligation been satisfied.

## 10. Income Taxes

The Company did not record a federal or state income tax benefit for its losses for the three and six months ended June 30, 2020 and 2019, respectively, due to the conclusion that a full valuation allowance is required against the Company's deferred tax assets. All the Company's losses before income taxes were generated in the United States.

## 11. Net Loss per Share

Basic and diluted net loss per share was calculated as follows (in thousands, except share and per share amounts):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Numerator:				
Net loss	\$ (8,893)	\$ (20,018)	\$ (18,771)	\$ (34,436)
Denominator:				
Weighted average number of common shares outstanding—basic and diluted	52,147,656	51,097,456	52,147,145	51,037,514
Net loss per share—basic and diluted	\$ (0.17)	\$ (0.39)	\$ (0.36)	\$ (0.67)

The following common stock equivalents have been excluded from the computation of diluted weighted-average shares outstanding, because such securities had an antidilutive impact:

	June 30,	
	2020	2019
Options to purchase common stock	5,639,043	4,598,850
Restricted stock units	4,519	—
	5,643,562	4,598,850

## 12. Leases

The Company has an operating lease for office and laboratory space for its corporate headquarters in Boston, Massachusetts. The lease commenced in January 2018 and rent payments began in April 2018. This lease has a ten-year initial term with an option to extend for seven additional years.

The Company has the right to terminate the lease in the event of the inability to use the space due to substantial damage while the lessor has the right to terminate the lease if the Company defaults on the lease financial obligations. Per the terms of the lease agreement, the Company does not have any residual value guarantees. In calculating the present value of the lease payments, the Company utilized its incremental borrowing rate, which is based on rates that would be incurred to borrow on a collateralized basis over a term equal to the lease payments in a similar economic environment. The Company has allocated all the contract considerations to the one lease component. This may result in the initial and subsequent measurement of the balances of the right-of-use asset and lease liability for leases being greater than if the policy election was not applied. The Company's real estate lease in Boston is considered a net lease, as the non-lease components (i.e., common area maintenance) are paid separately from rent, based on actual costs incurred. Therefore, the variable non-lease components were not included in the right-of-use asset and liability and are reflected as an expense in the period incurred.

As of June 30, 2020, and December 31, 2019, assets under operating lease were \$12.0 million and \$12.6 million, respectively. The elements of lease expense were as follows (in thousands):

	<b>For the Three Months Ended June 30,</b>	
	<b>2020</b>	<b>2019</b>
<b>Lease cost</b>		
Operating lease cost	\$ 462	\$ 459
Variable lease cost (1)	158	179
<b>Total lease cost</b>	<b>\$ 620</b>	<b>\$ 638</b>
	<b>For the Six Months Ended June 30,</b>	
	<b>2020</b>	<b>2019</b>
<b>Lease cost</b>		
Operating lease cost	\$ 925	\$ 921
Variable lease cost (1)	261	316
<b>Total lease cost</b>	<b>\$ 1,186</b>	<b>\$ 1,237</b>
<b>Other information</b>		
Operating cash flows used for operating leases	\$ 859	\$ 836
Weighted-average remaining lease term	7.84 years	8.84 years
Weighted-average discount rate	4.50%	4.50%

(1) The variable lease costs for the three and six months ended June 30, 2020 and 2019 include common area maintenance charges.

Future lease payments under noncancelable leases as of June 30, 2020 (in thousands):

<b>Future Operating Lease Payments</b>	
2020	\$ 874
2021	1,780
2022	1,829
2023	1,880
2024	1,931
Thereafter	6,825
<b>Total lease payments</b>	<b>15,119</b>
Less: imputed interest	(2,486)
<b>Total operating lease liabilities</b>	<b>\$ 12,633</b>

## Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

*The following discussion and analysis of our financial condition and the results of operations should be read in conjunction with our financial statements and related notes thereto included elsewhere in this Quarterly Report on Form 10-Q, or Quarterly Report, and our audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2019 filed with the Securities and Exchange Commission, or the SEC, on March 10, 2020, or the Annual Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report, including information with respect to our plans and strategy for our business, includes forward looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section in our Annual Report and in this Quarterly Report, our actual results could differ materially from the results described, in or implied by, the forward-looking statements contained in the following discussion and analysis. Such factors may be amplified by the COVID-19 pandemic and its potential impact on our business and the global economy.*

### Overview

We are a clinical stage biopharmaceutical company committed to the discovery and development of novel therapeutics to treat CF through therotyping, or the process of matching modulators to individual response to treatment regardless of CFTR mutations. CF is a disease caused by defects in the function or abundance of CFTR protein. Although, CF is defined as a monogenic recessive genetic disorder caused by mutations in the CFTR gene, there is a broad range of disease activity for different organ systems in CF, including lung disease, meconium ileus, diabetes, and liver disease, even for CF patients who are homozygous for the most common mutation, F508del mutation. In summary, CF genotype does not always match CF phenotype.

CFTR modulators are compounds that affect the synthesis, folding, trafficking, function, and clearance of CFTR protein and are potentially disease modifying. However, these modulators are only available to certain patient subsets based on genotype or a classification based on the ways in which they affect CFTR protein. They have been found to substantially improve patient health outcomes compared to best supportive care, although these drugs have variable efficacy among individuals as has been observed for most drugs.

In a clinical setting, when treatment efficacy is uncertain for individuals and when high costs limit "trial and error" approaches to assessing potential benefit for a patient from a specific drug, the new focus has become matching individuals with drugs that are most likely to be effective. Thus, emerging evidence and increased use of CF patient-derived cells studied in a laboratory test, such as the organoid assay, have been shown to provide a patient-friendly and cost-effective approach to increasing access to treatment for patients with CF and to optimize the risk-benefit ratio and cost-effectiveness of CFTR modulators. Currently, in many geographies, access to CFTR modulators has been limited because the approved drugs failed to meet cost-effectiveness thresholds required by payors.

Our CF-focused pipeline consists of novel CFTR modulators including correctors, potentiators and amplifiers. Upon discovery of amplifiers, a novel class of CFTR modulators, we utilized their novel mechanism of action as a drug screening tool and subsequently identified correctors and potentiators that we are now developing as combination therapies. We have completed double blind, randomized, placebo-controlled Phase 2 clinical trials with the combination of all three of our investigational CFTR modulators (PTI-801, or posenacافتor, a third generation CFTR corrector; PTI-808, or dirocaفتor, a CFTR potentiator; and PTI-428, or nesolicaفتor, a CFTR amplifier) in patients with the most common F508del mutations. We are currently investigating combinations of posenacافتor, dirocaفتor, and nesolicaفتor in an *ex vivo* study to identify potential clinical responders among subjects with CF who have rare CFTR mutations. Based on the functional response to our investigational CFTR modulators in the *ex vivo* assay, we will invite select patients to participate in clinical trials with the drug candidates to validate the ability of the *ex vivo* response to predict clinical benefit. If approved, we intend to commercialize our combination therapy for CF patients with rare CF mutations and as well as those who have at least a single copy of the F508del mutation.

In February 2019, we joined the HIT-CF consortium, a pan-European strategic initiative which seeks to validate a personalized therapy approach for CF patients with rare genetic mutations and genotypes that make them ineligible for approved CFTR modulator therapies. As of February 2020, HIT-CF has collected rectal biopsies from over 500 subjects across European Cystic Fibrosis Society, or ECFS, Clinical Trial Network, or CTN, clinical sites out of a population of approximately 2,300 adults in Europe alone who have rare CFTR genotypes. These tissue samples from CF subjects with less-common genotypes are currently assayed as organoids and we are able to use these organoids to test responsiveness to our investigational CFTR modulators. We intend to initiate the CHOICES (Crossover trial based on Human Organoid Individual response in CF - Efficacy Study) trial, which we expect will be the first-ever personalized medicine-based trial in CF, in the second half of 2020. We plan to enroll patients in Europe with CF who are ineligible for current standard of care CFTR modulator therapies due to their genotype. This trial, which is financially supported by the European Commission, is contemplated to be a placebo-controlled, double blind, crossover study. Beyond HIT-CF, other groups in multiple regions have created repositories of patient-derived cells, including organoids, that offer additional pools of patients for *ex vivo* profiling for response to PTI compounds and possible confirmatory clinical trials that would mirror the CHOICES study design. We have completed scientific advice meetings with Medicines and Healthcare Products Regulatory Agency (MHRA), in the United Kingdom and the Dutch Medicines Evaluation Board (MEB) on the CHOICES program for the treatment of people living with CF. In addition to the positive scientific advice from the MHRA and MEB, we received a High Strategic Fit score from the Clinical Trials Network (CTN) for the HIT-CF – CHOICES protocol.

### ***Equity Financings and Research Funding***

In addition to our wholly owned CF programs, in December 2018, we entered into a Technology Transfer and License Agreement, or the Genentech Agreement, with Genentech, Inc., or Genentech. We granted Genentech a worldwide, exclusive license for technology and materials relating to potential therapeutic small molecule modulators of an undisclosed target within the proteostasis network. The rights do not include CFTR modulators and are unrelated to our investigational products or other ongoing research programs in cystic fibrosis. In connection with the Genentech Agreement, we received an upfront payment, and are eligible to receive additional milestone payments, which are approximately \$96.0 million in the aggregate, subject to the achievement of specified development, regulatory, and commercial milestones. In addition, Genentech is obligated to pay us tiered royalties in the low single-digits based on net sales of products covered by the licenses granted under the Genentech Agreement. As of June 30, 2020, we have not achieved any research, development, regulatory, or commercial milestones, or earned any royalties under the Genentech Agreement.

Since our inception in 2006, we have devoted substantially all our resources to organizing and staffing our company, business planning, raising capital, acquiring and developing product and technology rights, and conducting research and development activities for our product candidates. We do not have any products approved for sale and have not generated any revenue from product sales. We have funded our operations to date with proceeds received from equity offerings, the issuance of convertible promissory notes and, to a lesser extent, payments received in connection with collaboration agreements and a research grant.

In May 2019, we entered into a sales agreement with H.C. Wainwright & Co., LLC, or HCW, with respect to an at-the-market, or ATM, offering program, or the HCW ATM program, under which we may issue and sell, from time to time at our sole discretion, shares of our common stock, in an aggregate offering amount of up to \$56.6 million. HCW acts as our sales agent and will use commercially reasonable efforts to sell shares of common stock from time to time, based upon instruction from us. Common stock will be sold at prevailing market prices at the time of the sale, and as a result, prices may vary. We will pay HCW up to 3% of the gross proceeds from any common stock sold under the sales agreement. As of December 31, 2019, we had sold 987,653 shares of our common stock for total net proceeds of approximately \$3.5 million under the HCW ATM program. We did not sell any shares of our common stock under the ATM program during the six months ended June 30, 2020.

Since our inception, we have not generated significant revenue and have incurred significant operating losses. Our net losses were \$8.9 million and \$18.8 million for the three and six months ended June 30, 2020, respectively. As of June 30, 2020, we had an accumulated deficit of \$355.4 million. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We expect our expenses and capital requirements will increase substantially in connection with our development activities, as we:

- expand and/or advance our proprietary combination therapy candidates, posenaftor, dirocaftor, and nesolicaftor, into Phase 3 clinical trials;
- seek regulatory approval for our product candidates;
- seek support and approval from our collaboration partners, HIT-CF, the TDN, the CTN, and other interested parties;
- hire personnel to support our product development, manufacturing, commercialization, and administrative efforts;
- advance the research and development efforts of our CF and other product candidates, including, without limitation, back-up compounds; and
- scale up our manufacturing processes and capabilities to support our ongoing preclinical activities and clinical trials of our product candidates and commercialization of any of our product candidates for which we obtain marketing approval.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for our product candidates. If we obtain regulatory approval for any of our product candidates, we expect to incur significant expenses related to developing our internal commercialization capability to support product sales, marketing, and distribution. In addition, we will continue to incur additional costs associated with operating as a public company.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of public or private equity, debt financings, or other capital sources, including potential collaborations with other companies, or other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back, or discontinue the development and commercialization of one or more of our product candidates.

As of June 30, 2020, we had cash, cash equivalents and short-term investments of \$48.9 million. We believe that our existing cash, cash equivalents, and short-term investments are sufficient to fund our projected operating expenses and capital requirements for at least 12 months from the date of this filing. However, the expenditures that will be necessary to execute our business plan, and upon which our current liquidity and capital resources estimate is based, are subject to numerous uncertainties, which may adversely affect our liquidity and capital resources. Although we have been successful in raising capital in the past, there is no assurance that we will be successful in obtaining such additional financing on terms acceptable to us, if at all, nor is it considered probable under the accounting standards.

### ***Recent Developments***

In June 2020, we announced results from *in vitro* studies evaluating the use of PTI-129 as a treatment for COVID-19. PTI-129 is a pre-clinical, once-daily, oral small molecule originally designed to treat protein misfolding disorders involving the unfolded protein response, or UPR. In *in vitro* studies conducted at Calibr, the drug discovery division of Scripps Research, PTI-129 demonstrated the potential to reduce viral protein production in host cells by activating the adaptive branches of the UPR pathway and reducing the levels of misfolded proteins.

### ***COVID-19 Business Update***

With the global spread of the ongoing COVID-19 pandemic in the first half of 2020, we implemented business continuity plans designed to address and mitigate the impact of the COVID-19 pandemic on our employees and our business, including our clinical trials, supply chains, and third-party providers. We continue to closely monitor the COVID-19 situation as we evolve our business continuity plans and response strategy. In March 2020, the Governor of Massachusetts ordered all individuals living in the Commonwealth of Massachusetts to stay at their place of residence for an indefinite period of time (subject to certain exceptions to facilitate authorized necessary activities) to mitigate the impact of the COVID-19 pandemic so our workforce transitioned to working remotely. We are currently evaluating plans to reopen our office to allow employees to return to the office, which will be based on a phased approach that is principles-based and local in design, with a focus on patient continuity, employee safety and optimal work environment. While we are experiencing limited financial impacts at this time, given the global economic slowdown, the overall disruption of global healthcare systems and the other risks and uncertainties associated with the pandemic, our business, financial condition, results of operations, and growth prospects could be materially adversely affected.

### ***Clinical Development***

With respect to clinical development, we have taken measures to implement remote and virtual approaches, where possible, to maintain patient safety and trial continuity and to preserve study integrity. As the COVID-19 pandemic continues, we anticipate a potential impact on future patient enrollment. We could also see an impact on the ability to supply study drug, report trial results, or interact with regulators, ethics committees or other important agencies due to limitations in regulatory authority employee resources or otherwise. In addition, we rely on contract research organizations or other third parties to assist us with clinical trials and we cannot guarantee that they will continue to perform their contractual duties in a timely and satisfactory manner as a result of the COVID-19 pandemic. If the COVID-19 pandemic continues and persists for an extended period of time, we could experience significant disruptions to our clinical development timelines, which would adversely affect our business, financial condition, results of operations and growth prospects.

### ***Regulatory Activities***

With respect to regulatory activities, it is possible that we could experience delays in the timing of review and/or our interactions with the FDA or the European Commission, or EC, due to, for example, absenteeism by governmental employees, inability to conduct planned physical inspections related to regulatory approval, or the diversion of efforts of the FDA or EC and attention to approval of other therapeutics or other activities related to COVID-19, which could delay approval decisions with respect to the preparation and submission to the FDA of a new drug application, or NDA, or the preparation and submission to the EC of a Marketing Authorization Application, or MAA, and otherwise delay or limit our ability to make planned regulatory submissions or obtain new product approvals.

### ***Financial Impact***

The COVID-19 pandemic continues to rapidly evolve and has already resulted in a significant disruption of global financial markets. If the disruption persists and deepens, we may experience an inability to access additional capital, when and if needed. If we are unable to obtain funding, we would be forced to delay, reduce or eliminate our research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect our business prospects, or we may be unable to continue operations. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability.

## Components of our Results of Operations

### Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future. We did not recognize any revenue during the three and six months ended June 30, 2020. All our revenue during the six months ended June 30, 2019 was derived from our Genentech Agreement.

### Operating Expenses

#### Research and Development Expenses

Research and development expenses, which include costs of research services incurred in connection with our collaboration agreements and research grant, consist primarily of costs incurred in connection with the discovery and development of our product candidates, which include:

- employee-related expenses, including salaries, related benefits, travel, and stock-based compensation expense for employees engaged in research and development functions;
- expenses incurred in connection with the preclinical and clinical development of our product candidates under agreements with contract research organizations, or CROs, and contract manufacturing organizations, or CMOs;
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and supplies; and
- payments made under third-party licensing agreements.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our service providers.

Our direct research and development expenses are tracked on a program-by-program basis and consist primarily of external costs, such as fees paid to consultants, central laboratories, contractors, CROs, and CMOs in connection with our clinical trials and preclinical development activities. We do not allocate employee costs, costs associated with our platform technology, facility expenses, including depreciation, or other indirect costs, to specific product development programs because these costs are deployed across multiple product development programs and, as such, are not separately classified. We use internal resources to manage our preclinical development activities and perform data analysis for such activities. These employees work across multiple development programs and, therefore, we do not track their costs by program.

The table below summarizes our research and development expenses incurred by program (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
CF	\$ 2,080	\$ 12,606	\$ 5,611	\$ 24,462
UPR	11	100	13	212
Unallocated expenses:				
Employee-related	2,154	2,539	4,402	5,352
Facility-related	311	579	721	1,129
Other	28	1,101	355	1,917
Total research and development expenses	\$ 4,584	\$ 16,925	\$ 11,102	\$ 33,072

If our ongoing studies and clinical trials are successful, and if we can raise adequate funding, we expect that our expenses will increase substantially in connection with our ongoing and anticipated clinical trials, preclinical development, and commercialization activities. At this time, we cannot reasonably estimate the costs for completing the clinical development of posenacافت, dirocaftor, nesolicaftor, or our proprietary combination therapies for the treatment of CF, or the cost associated with the development of any of our other product candidates. The successful development and commercialization of our product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

- the scope, progress, outcome, and costs of our preclinical development activities, clinical trials, and other research and development activities;
- establishing an appropriate safety profile with IND and registration or approval-enabling studies;
- successful patient enrollment in, and the initiation and completion of, clinical trials;
- the cooperation and approval we receive from third parties including clinical investigators, HIT-CF, CROs, the TDN, and CTN;
- the timing, receipt, and terms of any marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining, maintaining, defending, and enforcing patent claims and other intellectual property rights;
- significant and changing government regulation;
- launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others; and
- maintaining a continued acceptable safety profile of the product candidates following approval.

Any changes in the outcome of any of these variables, or others identified within this filing, with respect to the development of our product candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if the FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect, or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate.

#### *General and Administrative Expenses*

General and administrative expenses consist primarily of salaries and related benefits, travel, and stock-based compensation for personnel in executive, finance, and administrative functions. General and administrative expenses also include facilities, which include direct and allocated expenses for rent and maintenance of facilities, depreciation, insurance, and supplies, as well as professional fees for legal, consulting, accounting, and audit services.

We anticipate that our general and administrative expenses will increase in the future to support our continued research activities and development of our product candidates. We also anticipate that we will continue to incur increased accounting, audit, legal, patent, regulatory, compliance, director and officer insurance costs, and director expenses, as well as investor and public relations expenses associated with being a public company.

#### *Interest Income*

Interest income consists of interest earned on cash equivalents and short-term investments held by us during the reporting periods.

#### *Interest Expense*

Interest expense consists of interest paid on our short-term borrowings during the reporting periods.

#### *Other Income (Expense), Net*

Other income (expense), net, primarily consists of the amortization of premiums and discounts on our short-term investments and the gains or losses associated with the changes in the fair values of our derivative liability. The derivative liability relates to a cash settlement option associated with the change of control provision in our CFF collaboration agreement. We remeasure the fair value of our derivative liability at each reporting period and record the change in fair value in other income (expense), net.

## Critical Accounting Policies and Significant Judgments and Estimates

Our financial statements are prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of our financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue, costs and expenses, and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions. These unaudited condensed financial statements should be read in conjunction with the audited financial statements, and notes thereto, which are contained in the Company's Annual Report on Form 10-K for the year ended December 31, 2019, filed with the SEC on March 10, 2020.

During the six months ended June 30, 2020, there were no material changes to our critical accounting policies. Our critical accounting policies are described under the heading, "Management's Discussion and Analysis of Financial Condition and Results of Operations— Critical Accounting Policies and Significant Judgments and Estimates," in our Annual Report on Form 10-K for the year ended December 31, 2019 and the notes to the financial statements appearing elsewhere in this Quarterly Report. We believe that of our critical accounting policies, the following accounting policies involve the most judgment and complexity:

- revenue recognition;
- accrued research and development expenses; and
- stock-based compensation.

Accordingly, we believe the policies set forth above are critical to fully understanding and evaluating our financial condition and results of operations. If actual results or events differ materially from the estimates, judgments and assumptions used by us in applying these policies, our reported financial condition and results of operations could be materially affected.

## Results of Operations

### Comparison of Three Months Ended June 30, 2020 and 2019

The following table summarizes our results of operations for the three months ended June 30, 2020 and 2019 (in thousands):

	Three Months Ended June 30,		Increase (Decrease)
	2020	2019	
Revenue	\$ —	\$ -	\$ -
Operating expenses:			
Research and development	4,584	16,925	(12,341)
General and administrative	4,366	3,682	684
Total operating expenses	8,950	20,607	(11,657)
Loss from operations	(8,950)	(20,607)	(11,657)
Interest income	54	297	(243)
Interest expense	(6)	—	(6)
Other income, net	9	292	(283)
Net loss	\$ (8,893)	\$ (20,018)	\$ (11,125)

### Revenue

There was no revenue for the three months ended June 30, 2020 or 2019.

### Research and Development Expenses

Research and development expenses were \$4.6 million for the three months ended June 30, 2020, compared to \$16.9 million for the three months ended June 30, 2019. The decrease of \$12.3 million was due to a decrease of approximately \$10.6 million in clinical-related research activities, \$1.0 million in professional fees, \$0.5 million in employee-related expenses, and \$0.2 million in facility expenses.

### General and Administrative Expenses

General and administrative expenses were \$4.4 million for the three months ended June 30, 2020, compared to \$3.7 million for the three months ended June 30, 2019. The increase of \$0.7 million in general and administrative expenses was primarily due to an increase of \$0.4 million in professional fees, \$0.2 million in insurance expenses, and \$0.1 million in facility expenses.

### Interest Income

Interest income was \$0.1 million for the three months ended June 30, 2020, compared to \$0.3 million for the three months ended June 30, 2019. The decrease of \$0.2 million in interest earned on cash equivalents and short-term investments is due to a decrease in average balance of invested cash held during the three months ended June 30, 2020, compared to the three months ended June 30, 2019.

### Interest Expense

Interest expense was less than \$0.1 million for the three months ended June 30, 2020 and consisted of interest paid on short-term borrowings. There was no interest expense for the three months ended June 30, 2019.

### Other Income, Net

Other income was less than \$0.1 million and \$0.3 million for the three months ended June 30, 2020 and 2019, respectively. The decrease of \$0.2 million in other income is primarily due to a decrease in net accretion of discounts on short-term securities in the three months ended June 30, 2020 compared to the three months ended June 30, 2019.

### Comparison of Six Months Ended June 30, 2020 and 2019

The following table summarizes our results of operations for the six months ended June 30, 2020 and 2019 (in thousands):

	Six Months Ended June 30,		Increase (Decrease)
	2020	2019	
Revenue	\$ -	\$ 5,000	\$ (5,000)
Operating expenses:			
Research and development	11,102	33,072	(21,970)
General and administrative	7,953	7,626	327
Total operating expenses	19,055	40,698	(21,643)
Loss from operations	(19,055)	(35,698)	(16,643)
Interest income	261	654	(393)
Interest expense	(9)	—	(9)
Other income, net	32	608	(576)
Net loss	\$ (18,771)	\$ (34,436)	\$ (15,665)

### Revenue

There was no revenue for the six months ended June 30, 2020, as compared to revenue of \$5.0 million related to the Genentech Agreement recognized in the six months ended June 30, 2019.

### Research and Development Expenses

Research and development expenses were \$11.1 million for the six months ended June 30, 2020, compared to \$33.1 million for the six months ended June 30, 2019. The decrease of \$22.0 million was due to a decrease of approximately \$19.4 million in clinical-related research activities, \$1.2 million in professional fees, \$1.1 million in employee-related expenses, and \$0.3 million in facility expenses.

### General and Administrative Expenses

General and administrative expenses were \$7.9 million for the six months ended June 30, 2020, compared to \$7.6 million for the six months ended June 30, 2019. The increase of \$0.3 million in general and administrative expenses was due to an increase of \$0.3 million in insurance expenses, an increase of \$0.2 million in facility expenses, and \$0.1 million in employee-related expenses, partially offset by a decrease of \$0.3 million in professional fees.

### Interest Income

Interest income was \$0.3 million for the six months ended June 30, 2020, compared to \$0.7 million for the six months ended June 30, 2019. The decrease of \$0.4 million in interest earned on cash equivalents and short-term investments is due to a decrease in average balance of invested cash held during the six months ended June 30, 2020, compared to the six months ended June 30, 2019.

### Interest Expense

Interest expense was less than \$0.1 million for the six months ended June 30, 2020 and consisted of interest paid on short-term borrowings. There was no interest expense for the six months ended June 30, 2019.

### Other Income, Net

Other income was less than \$0.1 million and \$0.6 million for the six months ended June 30, 2020 and 2019, respectively. The decrease of \$0.5 million in other income is primarily due to a decrease in net accretion of discounts on short-term securities in the six months ended June 30, 2020 compared to the six months ended June 30, 2019.

## Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We have generated limited revenue to date from our collaboration agreements and research grant. We have not yet commercialized any of our product candidates, which are in various phases of preclinical development and clinical trials and we do not expect to generate revenue from sales of any product for several years, if at all. We have funded our operations to date with proceeds received from equity offerings, the issuance of convertible promissory notes and, to a lesser extent, payments received in connection with collaboration agreements and a research grant.

As of June 30, 2020, we had cash, cash equivalents and short-term investments of approximately \$48.9 million and an accumulated deficit of \$355.4 million. During the six months ended June 30, 2020, we incurred a loss of \$18.8 million and used \$21.4 million of cash in operations. We expect that our cash, cash equivalents, and short-term investments as of June 30, 2020 will enable us to fund our operating expenses and capital requirements, based upon our current operating plan, for at least 12 months from the date of this filing. We will need additional financing to support our long-term plans for clinical trials, including the MORE trial. Further, while we have limited financial impact to date, it is difficult to assess or predict the future impact of COVID-19, and sustained economic uncertainty could negatively impact our liquidity. Our operation plans may change as a result of many factors, including as a result of COVID and otherwise, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, third-party funding, marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these approaches.

Until such time, if ever, as we can generate sufficient revenues to become profitable, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds. There can be no assurance that we will be able to obtain funding from any of these sources or, if obtained, what the terms of such funding(s) may be, or that any amount that we are able to obtain will be adequate to support our working capital requirements until we achieve profitable operations. We have no current committed sources of additional capital. In addition, we may elect to raise additional funds even before we need them if the conditions for raising capital are favorable. Although we have been successful in raising capital in the past, there is no assurance that we will be successful in obtaining such additional financing on terms acceptable to us, if at all. The ongoing COVID-19 pandemic is also impacting the global financial markets and could impair our ability to raise additional capital when and if needed. If we are unable to obtain funding, we could be forced to delay, reduce or eliminate some or all of our research and development programs, product portfolio expansion or commercialization efforts, which would adversely affect our business prospects, or we may be unable to continue operations.

### Cash Flows

The following table summarizes our sources and uses of cash for each of the periods presented (in thousands):

	<u>Six Months Ended June 30,</u>	
	<u>2020</u>	<u>2019</u>
Cash used in operating activities	\$ (21,389)	\$ (31,051)
Cash provided by investing activities	38,488	30,821
Cash provided by financing activities	761	56
Net increase in cash, cash equivalents and restricted cash	<u>\$ 17,860</u>	<u>\$ (174)</u>

### *Operating Activities*

Net cash used in operating activities was \$21.4 million during the six months ended June 30, 2020, primarily driven by our net loss of \$18.8 million and changes in operating assets and liabilities of \$4.6, partially offset by non-cash charges of \$2.0 million. Our net loss was primarily attributed to our research and development activities associated with the advancement of our clinical trials and preclinical studies. Changes in operating assets and liabilities were primarily related to a decrease of \$2.7 million in accrued expenses, a decrease of \$0.8 million in accounts payable, a decrease of \$0.6 million in operating lease liabilities, and an increase in prepaid and other current assets of \$0.5 million. Non-cash charges include \$1.3 million of stock-based compensation and \$0.7 million of depreciation and amortization.

Net cash used in operating activities was \$31.1 million during the six months ended June 30, 2019, primarily driven by our net loss of \$34.4 million, offset by non-cash charges of \$2.1 million and changes in operating assets and liabilities of \$1.3 million. Our net loss was primarily attributed to our research and development activities associated with the advancement of our preclinical studies and clinical trials. Non-cash charges include \$1.7 million of stock-based compensation, \$0.7 million of depreciation and amortization, \$0.3 million of stock issued for consulting services, partially offset by \$0.6 million of accretion of short-term investments. Changes in operating assets and liabilities were primarily related to an increase of \$1.3 million in accounts payable and an increase of \$1.2 million in accrued expenses, partially offset by a decrease of \$0.5 million in operating lease liabilities, an increase of \$0.6 million in prepaids and other current assets and an increase of \$0.1 million in other assets.

### *Investing Activities*

During the six months ended June 30, 2020, net cash provided by investing activities was \$38.5 million, consisting of proceeds received from maturities of short-term investments of \$49.7 million, partially offset by purchases of our short-term investments of \$11.2 million.

During the six months ended June 30, 2019, net cash provided by investing activities was \$30.8 million, consisting of proceeds received from maturities of short-term investments of \$74.0 million, partially offset by purchases of short-term investments of \$43.2 million.

### *Financing Activities*

During the six months ended June 30, 2020, net cash provided by financing activities was \$0.8 million, primarily related to proceeds from the issuance of short-term borrowings of \$1.2 million, offset by payments made on short-term borrowings of \$0.5 million.

During the six months ended June 30, 2019, net cash provided by financing activities was less than \$0.1 million, resulting from the issuance of common stock pursuant to our employee stock purchase plan as well as stock option exercises.

### **Future Funding Requirements**

Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, third-party clinical research and development services, clinical costs, legal and other regulatory expenses, and general overhead costs. We have based our estimates on assumptions that may prove to be incorrect, and we could use our capital resources sooner than we currently expect. Additionally, the process of testing product candidates in clinical trials is costly, and the timing of progress in these trials is uncertain. We cannot estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates or whether, or when, we may achieve profitability. We expect our expenses to increase substantially if we advance the preclinical and clinical trials of our product candidates in development.

Our expenses will also increase as we:

- continue to pursue the clinical development of our most advanced product candidates, including posenaftor, dirocaftor and nesolicaftor, as well as our combination therapies;
- seek support and approval from our collaboration partners, the TDN, HIT-CF, CTN, and other interested parties;
- continue the research and development of our other product candidates;
- seek to identify and develop additional product candidates;
- seek marketing approvals for any of our product candidates that successfully complete clinical development;
- develop and expand our sales, marketing, and distribution capabilities for our product candidates for which we obtain marketing approval;

- scale up our manufacturing processes and capabilities to support our ongoing preclinical activities, clinical trials of our product candidates, and commercialization of any of our product candidates for which we obtain marketing approval;
- maintain, expand, and protect our intellectual property portfolio;
- expand our operational, financial, and management systems, and increase personnel, including personnel to support our clinical development, manufacturing, and commercialization efforts, and our operations as a public company; and
- increase our product liability and clinical trial insurance coverage as we initiate additional clinical trials, expand our existing clinical trials, and launch commercialization efforts.

Because of the numerous risks and uncertainties associated with research, development, and commercialization of pharmaceutical drugs, we are unable to estimate the exact amount of our working capital requirements. Our future funding requirements will depend on many factors, including:

- the scope, initiation, progress, results, and costs of researching and developing our product candidates, and conducting preclinical studies and clinical trials;
- the outcome, timing of, and the costs involved in, obtaining regulatory approvals for any of our product candidates from the FDA, EC and comparable foreign regulatory authorities, including the potential for such authorities to require that we perform more trials than we currently expect;
- market acceptance of our drug candidates;
- the timing of, and costs involved in, manufacturing our drug candidates and any drugs we successfully commercialize;
- the cost of establishing sales, marketing and distribution capabilities for our drug candidates if either candidate receives regulatory approval and we determine to commercialize it ourselves;
- the costs of acquiring, licensing or investing in additional businesses, products, product candidates and technologies;
- our ability to establish and maintain strategic collaborations, licensing or other arrangements, and the financial terms of such agreements;
- delays that may be caused by changing regulatory requirements;
- diversion of healthcare resources away from the conduct of clinical trials as a result of the ongoing COVID-19 pandemic, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- the interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel, quarantines or social distancing protocols imposed or recommended by federal or state governments, employers and others in connection with the ongoing COVID-19 pandemic;
- cost and timing of hiring new employees to support our continued growth;
- the costs involved in preparing, filing, prosecuting, maintaining, defending, and enforcing patent claims, including litigation costs and the outcome of such litigation; and
- the timing, amount and receipt of sales of, or milestone payments related to or royalties on, our current or future product candidates, if any.

We have no products approved for commercial sale and have not generated any product revenues from product sales to date. Until such time, if ever, as we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements, or marketing and distribution arrangements. The COVID-19 pandemic continues to rapidly evolve and has already resulted in a significant disruption of global financial markets. If the disruption persists and deepens, we could experience an inability to access additional capital, which could in the future negatively affect our operations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise additional funds through other third-party funding, collaborations agreements, strategic alliances, licensing arrangements, or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts.

Based upon our current operating plan, we believe our existing cash, cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements, for at least 12 months from the date that these financial statements are issued. However, the expenditures that will be necessary to execute our business plan, and upon which our current liquidity and capital resources estimate is based, are subject to numerous uncertainties, which may adversely affect our liquidity and capital resources. These uncertainties primarily concern our clinical development efforts. We will require additional funding to fund our MORE trial, our CHOICES program, and to advance our proprietary combination therapy candidates through regulatory approval and into commercialization, if approved. Accordingly, we are in the process of considering various financing alternatives to support our operating and capital needs, including public or private equity or debt financings, third-party funding, marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these approaches. We are also considering strategic alternatives for our CF portfolio, including our proprietary combination therapy candidates posenacftor, dirocaftor, and nesolicaftor, with the goal of maximizing stockholder value of these assets. However, we do not currently have any commitments for future external funding and additional financing may not be available on a timely basis, on acceptable terms, or at all. Further, the COVID-19 pandemic continues to rapidly evolve and has already resulted in a significant disruption of global financial markets. If the disruption persists and deepens, we could experience an inability to access additional capital, which could in the future negatively affect our operations. If we are unable to implement any strategic or financing alternative and adequate funds are not available in the future, we may be required to delay, limit, reduce or terminate our clinical development or future commercialization efforts or obtain funds through arrangements with collaborators or others that may require us to relinquish rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

### ***Contractual Obligations and Commitments***

Under various agreements, we will be required to make milestone payments and pay royalties and other amounts to third parties.

We enter into contracts in the normal course of business with CROs for clinical trials, preclinical research studies, testing and other services, and products for operating purposes. These contracts generally provide for termination upon notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

### ***JOBS Act***

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

### ***Off-Balance Sheet Arrangements***

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

### **Item 3. Quantitative and Qualitative Disclosures About Market Risk**

We are a smaller reporting company as defined by Rule 12b-2 of the Securities Exchange Act of 1934 and are not required to provide the information under this item.

### **Item 4. Management's Evaluation of our Disclosure Controls and Procedures.**

#### ***Management's Evaluation of our Disclosure Controls and Procedures***

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities and Exchange Act of 1934 is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our President and Chief Executive Officer, who is our principal executive officer and our interim principal financial officer, to allow timely decisions regarding required disclosure.

As of June 30, 2020, our management, with the participation of our principal executive officer, who is also our interim principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934). Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer, who is also

our interim principal financial officer, has concluded based upon the evaluation described above that, as of June 30, 2020, our disclosure controls and procedures were effective at the reasonable assurance level.

***Changes in Internal Control over Financial Reporting***

There were no changes in our internal control over financial reporting during the three months ended June 30, 2020 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

In the ordinary course of business, we are from time to time involved in lawsuits, claims, investigations, proceedings, and threats of litigation relating to intellectual property, commercial arrangements, employment and other matters. While the outcome of these proceedings and claims cannot be predicted with certainty, as of June 30, 2020, we were not party to any material pending legal proceedings, and we are not aware of any claims or actions pending or threatened against us that would have a material adverse impact on our financial position, results of operations or cash flows.

### Item 1A. Risk Factors

*Investing in our common stock involves a high degree of risk. You should carefully consider the following risks and uncertainties, together with all of the other information in this Quarterly Report on Form 10-Q, or this report, including our financial statements and related notes, before investing in our common stock. Any of the risks we describe below could adversely affect our business, financial condition or results of operations. The market price of our common stock could decline if one or more of these risks or uncertainties actually occur, causing you to lose all or part of your investment. The impact of COVID-19 may also exacerbate other risks discussed in this filing, any of which could have a material effect on us. This situation is changing rapidly and additional impacts may arise. Additional risks that we currently do not know about, or that we currently believe to be immaterial, may also impair our business. Certain statements below are forward-looking statements. See “Forward-Looking Statements” in this report.*

#### Risks Related to Our Business and Industry

***We are in the planning stages for a Phase 3 clinical trial of our triple combination of posenaftor, dirocaftor, and nesolicaftor in patients with the most common F508del mutation and if such trial fails to demonstrate safety and efficacy to the satisfaction of regulatory authorities or does not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our lead product candidates.***

Before obtaining marketing approval from regulatory authorities for the sale of our proprietary triple combination product candidates, we or a potential collaborator must conduct extensive trials to demonstrate the safety and efficacy of our proprietary triple combination in humans. We will not be able to submit an NDA or MAA unless and until we receive data demonstrating that a pivotal trial has achieved its primary endpoints.

Despite the results reported in our Phase 2 clinical trials, we do not know whether a potential Phase 3 clinical trial will demonstrate adequate efficacy and safety to result in regulatory approval to market our proprietary triple combination to address the treatment of rare CFTR mutations in any particular jurisdiction.

Clinical testing is expensive and difficult to design and implement, can take many years to complete and is inherently uncertain as to the outcome. A failure of one or more trials can occur at any stage of testing. The outcome of preclinical studies and early clinical trials may not accurately predict the success of later trials, and interim results of a trial do not necessarily predict final results. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced trials due to lack of efficacy or unacceptable safety profiles, notwithstanding promising results in earlier trials.

***We have incurred significant losses since our inception. We anticipate that we will continue to incur significant losses for the foreseeable future, and we may never achieve or maintain profitability.***

We are a drug research and development company focused primarily on developing our lead product candidates, PTI-801 or posenaftor, PTI-808 or dirocaftor and PTI-428 or nesolicaftor for the treatment of CF as part of our proprietary combination therapy candidates. We have incurred significant net losses in each year since our inception, including net losses of \$8.9 million and \$18.8 million for the three and six months ended June 30, 2020, respectively. As of June 30, 2020, we had an accumulated deficit of \$355.4 million.

To date, we have financed our operations primarily through the sale of equity securities and debt financings. We have devoted most of our financial resources to research and development, including our preclinical and clinical development activities. We have not completed the development of any of our product candidates. We expect to continue to incur significant and increasing losses and negative cash flows for the foreseeable future. The size of our losses will depend, in part, on the rate of future expenditures and our ability to generate revenues. In particular, we expect to incur substantial and increased expenses as we:

- continue the clinical development of our lead product candidates, posenaftor, dirocaftor and nesolicaftor, including, without limitation, as part of our proprietary combination therapy candidates, for the treatment of CF;
- seek to obtain regulatory approvals for our proprietary combination therapy candidates, and our other product candidates;
- seek cooperation and support from third parties, including clinical investigators, industry experts, therapeutic development networks of patient advocacy groups and clinical research organizations, as we enroll patients in our clinical trials;
- conduct our ongoing clinical trials and prepare for additional clinical trials and potential commercialization potential combination therapies, and our other product candidates;
- scale up contracted manufacturing processes and quantities to conduct our ongoing clinical trials and prepare for additional clinical trials and the commercialization of potential combination therapies, and our other product candidates for any indications for which we receive regulatory approval;
- establish outsourcing of the commercial manufacturing of posenaftor, dirocaftor and nesolicaftor and our other product candidates for any indications for which we may receive regulatory approval;
- establish an infrastructure for the sales, marketing and distribution of potential combination therapies, and our other product candidates for any indications for which we may receive regulatory approval;
- continue to advance our combination therapies as potential treatments for CF in clinical trials;
- prepare for Phase 3 trials, including, without limitation, trial design, conducting additional preclinical or nonclinical studies, manufacturing Phase 3 drug substance and drug product, analyzing Phase 2 data and other necessary work to support commencement of Phase 3 trials;
- expand our research and development activities and advance the discovery and development programs for other product candidates, including, without limitation, preclinical laboratory, animal and other testing and reports and the preparation of investigational new drug filings in the United States, and the equivalent in non-U.S. jurisdictions where we may seek to conduct clinical trials;
- maintain, expand and protect our intellectual property portfolio;
- continue our research and development efforts and seek to discover additional product candidates, including back-up candidates to existing product candidates; and
- add clinical, regulatory, operational, financial and management information systems to support our clinical development and commercialization efforts and operations as a public company.

We do not have any drugs that have received regulatory approval. Our business is dependent on our ability to successfully complete preclinical and clinical development of, obtain regulatory approval for, and, if approved, successfully commercialize our current and future drug candidates in a timely manner. An inability to effectively commercialize our current and future product candidates and to maximize their potential where possible through successful research and development activities, whether due to the impacts of the ongoing COVID-19 pandemic or otherwise, could have an adverse effect on our business, financial condition, results of operations and growth prospects.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. A decline in the value of our company could cause you to lose all or part of your investment.

***Our ability to generate future revenues from product sales is uncertain and depends upon our ability to successfully develop, obtain regulatory approval for and commercialize our product candidates, as well as the receipt and/or maintenance of regulatory approval of products and product candidates under development by third parties.***

Our ability to generate revenue and achieve profitability depends on our ability, alone or with collaborators, to successfully complete the development of, obtain the necessary regulatory approvals for, and commercialize, a product candidate or candidates. Our several development programs are currently focused on demonstrating their respective clinical benefit for CF patients. We do not anticipate generating revenues from sales of our proprietary combination therapy candidates, or any other product candidate for the foreseeable future, if ever. Our ability to generate future revenues from product sales depends heavily on:

- Vertex's continued compliance with regulatory requirements, the continued commercial availability of ivacaftor and lumacaftor, and ivacaftor and tezacaftor, with or without elxacaftor, the reimbursement of their cost to CF patients by insurers and their overall success in the market;
- obtaining favorable results for and advancing the development of posenaftor, dirocaftor, nesolicaftor, our proprietary combination therapy candidates, and our other product candidates, including successfully enrolling patients in and completing our ongoing clinical trials and initiating and completing additional clinical trials;
- obtaining regulatory approval in the United States of our proprietary combination therapy candidates, and our other product candidates for CF and equivalent foreign regulatory approvals;
- launching and commercializing our proprietary combination therapy candidates, and our other product candidates, including building a production infrastructure and a sales force, and collaborating with third parties;
- achieving broad market acceptance of our proprietary combination therapy candidates, and our other product candidates in the medical community and with third-party payors; and
- generating and advancing through clinical development, a pipeline of product candidates in addition to posenaftor, dirocaftor, nesolicaftor, our proprietary combination therapy candidates, and next-generation CFTR modulators.

Conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the data necessary to obtain regulatory approval and achieve product sales. Our anticipated development costs would likely increase if we do not obtain favorable results or if development of any product candidate is delayed. An inability to effectively commercialize our current and future drug candidates and to maximize their potential where possible through successful research and development activities, whether due to the impacts of the ongoing COVID-19 pandemic or otherwise, could have an adverse effect on our business, financial condition, results of operations and growth prospects.

Further, activities associated with the development and commercialization of our current and future drug candidates are subject to comprehensive regulation by the U.S. Food and Drug Administration, or FDA, and other regulatory agencies in the United States and similar regulatory authorities outside the United States. In particular, if we are required by the FDA and comparable regulatory authorities in other countries to perform studies or trials in addition to those that we currently expect to undertake, we would likely incur higher costs and it will likely take more time than we anticipate. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict the timing or amount of any increase in our anticipated development costs. Failure to obtain regulatory approval in the United States or other jurisdictions would prevent us from commercializing and marketing our current and future drug candidates.

Even if we obtain approval from the FDA and comparable foreign regulatory authorities for our current and future drug candidates, any approval might contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, or may be subject to burdensome post-approval study or risk management requirements. If we are unable to obtain regulatory approval, or any approval contains significant limitations, we may not be able to obtain sufficient funding or generate sufficient revenue to continue the development of that drug candidate or any other drug candidate that we may in-license, develop or acquire in the future.

Furthermore, even if we obtain regulatory approval for our current and future drug candidates, we will still need to develop a commercial organization, establish a commercially viable pricing structure and obtain approval for adequate reimbursement from third-party and government payors. If we are unable to successfully commercialize our current and future drug candidates, we may not be able to generate sufficient revenue to continue our business. As a result, we cannot assure you that we will be able to generate revenues from sales of any approved product candidates, or that we will achieve or maintain profitability even if we do generate sales.

***We will require additional capital to fund our operations. If we fail to obtain additional capital, we will be forced to delay, reduce or eliminate one or more of our product research and development programs, seek corporate partners for the development of our product development programs or relinquish or license on unfavorable terms our rights to technologies or product candidates.***

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete. We expect our research and development expenses to substantially increase in connection with our ongoing activities, particularly as we advance our clinical programs for posenacaftor, dirocaftor, nesolicaftor, which are our proprietary combination therapy candidates, and as we develop any other current or future product candidates.

Based upon our current operating plan, we believe that our existing cash, cash equivalents and short-term investments of \$48.9 million as of June 30, 2020 will enable us to fund our operating expenses and capital expenditure requirements for at least 12 months from the date that these financial statements are issued. However, the expenditures that will be necessary to execute our business plan, and upon which our current liquidity and capital resources estimate is based, are subject to numerous uncertainties, which may adversely affect our liquidity and capital resources. These uncertainties primarily concern our clinical development efforts. We will require additional funding to fund our MORE trial, our CHOICES program, and to advance our proprietary combination therapy candidates through regulatory approval and into commercialization, if approved. If we are unable to implement any strategic or financing alternative and adequate funds are not available in the future, we may be required to delay, limit, reduce or terminate our clinical development or future commercialization efforts or obtain funds through arrangements with collaborators or others that may require us to relinquish rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our actual cash requirements may vary materially from our current expectations. Should our operating plan change, we will be required to reassess our operating capital needs and there can be no assurance that we will have the cash resources to fund any changed operating plan or that additional funding will be available on terms acceptable to us, if at all. Changing circumstances including those beyond our control may cause us to consume capital more rapidly than we currently anticipate, and we may need additional funds sooner than planned. For example, our clinical trials may encounter technical, enrollment or other difficulties that could increase our development costs more than we expect, or the FDA may require us or we may choose to perform studies or trials in addition to those that we currently anticipate. We may need to raise additional funds to support our ongoing programs for posenacaftor, dirocaftor and nesolicaftor, our proprietary combination therapy candidates, and other clinical candidates, through regulatory approval and commercialization, or if we need or opt to seek to obtain regulatory approval for posenacaftor and/or nesolicaftor for administration with other CFTR modulators.

Securing additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates, including posenacaftor, dirocaftor and nesolicaftor, and our proprietary combination therapy candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. The impact of COVID-19 on global financial markets may increase the likelihood that we are unable to raise capital. If we are unable to raise additional capital when required or on acceptable terms, we may be required to:

- significantly delay, scale back or discontinue the research, development or commercialization of our product candidates, including posenacaftor, dirocaftor and nesolicaftor, our proprietary combination therapy candidates, and our other research or preclinical activities;
- seek corporate partners for our proprietary combination therapy candidates, or any of our other product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available; or
- relinquish, or license on unfavorable terms, our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves.

If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we will be prevented from pursuing our development and commercialization efforts, which will have a material adverse effect on our business, operating results and prospects and on our ability to develop our product candidates. In addition, if we are unable to raise capital, we will also need to implement cost reductions, and any failure to effectively do so will harm our business, results of operations and prospects.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs primarily through the sale of equity securities, debt financings and government and foundation grants. We may also seek to raise capital through third-party collaborations, strategic alliances and similar arrangements. We currently do not have any committed external source of funds.

In order to raise additional funds to support our operations, we may sell additional equity or debt securities, enter into collaborations, strategic alliances, or licensing arrangements or other marketing or distribution arrangements. As of August 6, 2020, an aggregate of approximately \$199.4 million of securities remain available for issuance under our effective universal shelf registration statements on Form S-3 pursuant to which we registered for sale up to \$100.0 million, and \$200.0 million, respectively, of any combination of our common stock, preferred stock, debt securities, warrants, rights, purchase contracts and/or units from time to time and at prices and on terms that we may determine. To the extent that we raise additional capital through the sale of equity or debt securities, the ownership interest of existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of common stockholders. For example, our board of directors has the right to issue previously-authorized shares of preferred stock with such preferences without stockholder approval. Debt financing, if available, may involve the right to convert any such debt into equity on favorable conversion terms, which conversion would dilute existing stockholders' ownership interest. Any such debt financing would also likely include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, and declaring dividends, and will impose limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business.

If we raise additional funds through collaborations, strategic alliances, or licensing arrangements or other marketing or distribution arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to expand our operations or otherwise capitalize on our business opportunities, our business, financial condition and results of operations could be materially adversely affected. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts, or grant others rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

The unpredictability of the capital markets may severely hinder our ability to raise capital within the time periods needed or on terms we consider acceptable, if at all. Furthermore, the impact of COVID-19 on global financial markets could make the terms of any available financing less attractive to us and more dilutive to our existing stockholders. Moreover, if we fail to advance one or more of our current product candidates to later-stage clinical trials, successfully commercialize one or more of our product candidates, or acquire new product candidates for development, we may have difficulty attracting investors that might otherwise be a source of additional financing.

***We have a limited operating history, which may make it difficult to evaluate the success of our business to date and to assess our future viability.***

We have not demonstrated an ability to perform the functions necessary for the successful commercialization of any product candidates. The successful commercialization of any product candidates will require us to perform a variety of functions, including:

- Continuing to undertake preclinical development and clinical trials;
- Participating in regulatory approval processes;
- Formulating and manufacturing products; and
- Conducting sales and marketing activities.

We were formed and began operations in December 2006. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing product and technology rights and conducting research and development activities for our product candidates. These operations provide a limited basis for you to assess our ability to commercialize our product candidates and the advisability of investing in our securities. We have not obtained regulatory approval for any of our product candidates. Consequently, any predictions about our future success, performance or viability may not be as accurate as they could be if we had a longer operating history, more experience with clinical development or approved products on the market.

***The failure to maintain our license agreement with Genentech, Inc., or the failure of Genentech, Inc. to perform their obligations under the agreement, could negatively impact our business.***

We are currently party to a technology transfer and license agreement with Genentech, Inc., or Genentech, in which we granted Genentech a worldwide, exclusive license for technology and materials relating to potential therapeutic small molecule modulators of an undisclosed target within the proteostasis network. We have limited control over the timing and amount of resources that Genentech will dedicate to this arrangement. In particular, we will not be entitled to receive milestone or royalty payments from Genentech absent further development and eventual commercialization of medicines resulting from this license agreement.

We are subject to a number of other risks associated with our dependence on our license agreement with Genentech, including:

- Genentech may not comply with applicable regulatory requirements with respect to developing or commercializing products under the license agreement, which could adversely impact development, regulatory approval and eventual commercialization of such products;
- we and Genentech could disagree as to future development plans and Genentech may delay initiation of clinical trials or stop a future clinical trial;
- there may be disputes between us and Genentech, including disagreements regarding the terms of the license agreement, that may result in the delay of or failure to achieve development, regulatory and commercial objectives that would result in milestone or royalty payments to us, the delay or termination of any future development or commercialization of licensed products using our technology, and/or costly litigation or arbitration that diverts our management's attention and resources;
- Genentech may not provide us with timely and accurate information regarding development progress and activities under the license agreement, which could adversely impact our ability to report progress to others, including our investors, and otherwise plan our own development of our product candidates;
- Genentech may fail to meet expected timelines, which could result in the delay of or failure to achieve development, regulatory and commercial objectives;
- business combinations or significant changes in Genentech's business strategy may adversely affect Genentech's ability or willingness to perform its obligations under the license agreement;
- our license partners and potential license partners may not properly maintain or defend our intellectual property rights in their licensed fields or territories or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential litigation;
- the royalties we are eligible to receive from Genentech may be reduced or eliminated based upon their and our ability to maintain or defend our intellectual property rights; and
- our license partners and potential license partners may be impacted by external business disruptions resulting from geopolitical actions, including war and terrorism, natural disasters including earthquakes, typhoons, floods and fires, or from economic or political instability, or public health emergencies, such as the novel COVID-19 coronavirus and related shelter-in-place orders, travel, social distancing and quarantine policies, boycotts, curtailment of trade and other business restrictions.

This license agreement is subject to early termination, including through Genentech's right to terminate without cause upon advance notice to us. If the agreement is terminated early, we may not be able to find another licensee for the technology and materials relating to potential therapeutic small molecule modulators of an undisclosed target within the proteostasis network, on acceptable terms, or at all, and we may otherwise be unable to pursue continued development on our own for these indications.

Furthermore, certain of the above risks and uncertainties may be amplified as a result of the impact of COVID-19. The extent to which COVID-19 may impact our license agreement with Genentech, or any other third-party partner, will depend on future developments, which are highly uncertain and cannot be predicted, including new information which may emerge concerning the severity of COVID-19 and the actions to contain COVID-19 or treat its impact, among others.

#### **Risks Related to the Development and Regulatory Approval of Our Product Candidates**

***The effects of health epidemics, including the global coronavirus pandemic, in regions where we, or the third parties on which we rely, have business operations could have a material adverse impact on our business, including our clinical trials, preclinical studies, supply chain and manufacturing, as well as third-parties which whom we conduct business.***

Our business could be adversely affected by public health crises such as pandemics or similar outbreaks in regions where we have concentrations of clinical trial sites or other business operations, and could cause significant disruption in the operations of third party manufacturers and contract research organizations, or CROs, upon whom we rely. In December 2019, a novel strain of coronavirus, SARS-CoV-2, which causes coronavirus disease 2019 or COVID-19, surfaced in Wuhan, China. Since then, COVID-19 has spread to multiple countries, including the United States, Israel and many other European countries in which we have planned or ongoing clinical trials. Our company headquarters is located in Boston, and our CROs and CMOs are located in the United States and

abroad. In March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic, and the U.S. government imposed travel restrictions on travel between the United States, Europe and certain other countries. Further, the President of the United States declared the COVID-19 pandemic a national emergency, invoking powers under the Stafford Act, the legislation that directs federal emergency disaster response. In addition, on March 23, 2020, the Governor of Massachusetts ordered all individuals living in the Commonwealth of Massachusetts to stay at their place of residence for an indefinite period of time (subject to certain exceptions to facilitate authorized necessary activities) to mitigate the impact of the COVID-19 pandemic. The executive order exempts certain individuals needed to maintain continuity of operations of critical infrastructure sectors as determined by the federal government, and the Governor has clarified to MassBio that all biopharma research and development is essential and exempt.

In response to the spread of COVID-19 as well as public health directives and orders, we have implemented work-from-home policies to support the community efforts to reduce the transmission of COVID-19 and protect employees, complying with guidance from federal, state or municipal government and health authorities. We implemented a number of measures to ensure employee safety and business continuity. Our offices remain closed with our administrative employees continuing their work outside of our offices, restricted on-site staff to only those required to execute their job responsibilities and limited the number of staff in any given research and development laboratory. Business travel has been suspended, and online and teleconference technology is used to meet virtually rather than in person. We have taken measures to secure our research and development project activities, and work in has been minimized to reduce the risk of COVID-19 transmission.

The regions in which we operate are currently being affected by COVID-19. Further, timely enrollment in our clinical trials is dependent upon global clinical trial sites which may be adversely affected by COVID-19. We are currently planning for new clinical trials for our product candidates in countries, including the U.S. and throughout the E.U. Shutdowns or other restrictions related to COVID-19 or other infectious diseases could impact personnel at third-party manufacturing facilities in the United States and other countries, or the availability or cost of materials, which would disrupt our supply chain. Additionally, many of our clinical trials involve patients who have severe medical conditions and are at higher risk for COVID-19 and who are therefore more likely to avoid hospitals or other high-risk areas.

The effects of the executive orders and our work-from-home policies may negatively impact productivity, disrupt our business and delay our clinical programs and timelines (for example, our timelines for any of our product candidates), the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course.

Quarantines, shelter-in-place and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases could impact personnel at third-party manufacturing facilities in the United States and other countries, or the availability or cost of materials, which would disrupt our supply chain.

As a result of the COVID-19 outbreak, or similar pandemics, we may experience disruptions that could severely impact our business, clinical trials and preclinical studies, including:

- delays or difficulties in enrolling and maintaining patients in our clinical trials, including patients that may not be able or willing to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays or disruptions in non-clinical experiments and investigational new drug application-enabling good laboratory practice standard toxicology studies due to unforeseen circumstances in supply chain;
- delays or disruptions in our ability to manufacture our product candidates due to supply chain disruptions, lack of clinical staff or restrictions on the availability of shared hospital resources;
- increased rates of patients withdrawing from our clinical trials following enrollment as a result of contracting COVID-19, being forced to quarantine, or being unable to visit clinical trial locations;
- diversion or prioritization of healthcare resources away from the conduct of clinical trials and towards the COVID-19 pandemic, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials, and because, who, as healthcare providers, may have heightened exposure to COVID-19 and adversely impact our clinical trial operations;
- interruption of our key clinical trial activities, such as clinical assessments at pre-specified timepoints during the trial and clinical trial site data monitoring, due to limitations on travel imposed or recommended by governmental entities, employers and others or interruption of clinical trial subject visits and study procedures (particularly any procedures that may be deemed non-essential), which may impact the integrity of subject data and clinical study endpoints;

- interruption or delays in the operations of the FDA, European Medicines Agency, or EMA, and comparable foreign regulatory agencies or their refusal to accept data from clinical trials in affected geographies, which may impact approval timelines;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- limitations on employee resources that would otherwise be focused on the conduct of our clinical trials, including sickness of employees or their families, the desire of employees to avoid contact with large groups of people, an increased reliance on working from home or mass transit disruptions; and
- reduced ability to engage with the medical and investor communities due to the cancellation of conferences scheduled throughout the year.

To date, we have already experienced certain disruptions, including the temporary closure of certain facilities in Europe and delays in *ex vivo* testing of organoids. Such disruptions could lead to a delay in patient selection and recruitment. Such delay could result in broader impact to our contemplated timeline and clinical trial generally.

These and other factors arising from the COVID-19 pandemic could worsen in countries that are already afflicted with COVID-19, could continue to spread to additional countries, or could return to countries where the pandemic has been partially contained, each of which could continue to adversely impact our ability to conduct clinical trials and our business generally, and could have a material adverse impact on our operations and financial condition and results.

In addition, the trading price for our common stock and other biopharmaceutical companies, as well as the broader equity and debt markets, have been highly volatile as a result of the COVID-19 pandemic and the resulting impact on global financial markets. As a result, we may face difficulties raising capital when needed, and any such sales may be on unfavorable terms to us. Further, to the extent we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of existing shareholders will be diluted.

The global outbreak of the COVID-19 coronavirus continues to rapidly evolve. The extent to which the outbreak may impact our business, clinical trials and preclinical studies will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of COVID-19, the duration of the outbreak, travel restrictions and actions to contain the outbreak or treat its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

***We depend substantially on the success of our lead product candidates, posenaftor, diroaftor and nesoliftor, which are currently in clinical development. We cannot be certain that we will be able to successfully complete the clinical development of, obtain regulatory approval for, or successfully commercialize posenaftor, diroaftor and nesoliftor.***

We currently have no products on the market, and our most advanced product candidates, posenaftor, diroaftor and nesoliftor, are currently in clinical development.

Our business depends substantially on the successful clinical development, regulatory approval and commercialization of posenaftor, diroaftor and nesoliftor, and they will require substantial additional clinical development and regulatory approval efforts before we are permitted to commence commercialization, if ever. The clinical trials and manufacturing and marketing of posenaftor, diroaftor and nesoliftor and any other product candidates will be subject to extensive and rigorous review and regulation by numerous government authorities in the U.S., the E.U. and other jurisdictions where we intend to test and, if approved, market our product candidates. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through preclinical testing and clinical trials that the product candidate is safe and effective for use in each target indication, and potentially in specific patient populations, including the pediatric population. This process can take many years and may include post-marketing studies and surveillance, which would require the expenditure of substantial resources beyond the proceeds we have currently raised. Of the large number of drugs in development for approval in the United States and the European Union, only a small percentage successfully complete the FDA or EMA, regulatory approval processes, as applicable, and are commercialized. Accordingly, even if we are able to obtain the requisite financing to continue to fund our research, development and clinical programs, we cannot assure you that posenaftor, diroaftor, nesoliftor or any of our other product candidates will be successfully developed or commercialized.

***We also depend on the success of our proprietary combination therapies, including a double and a triple combination, which are currently in early clinical development. We cannot be certain that we will be able to successfully complete the clinical development of, obtain regulatory approval for, or successfully commercialize these combinations. Combination therapies involve additional complexity and risk that could delay or cause our programs to stall or fail; development of such programs may be more costly, may take longer to achieve regulatory approval and may be associated with unanticipated adverse events.***

Our business depends on the successful clinical development, regulatory approval and commercialization of combination therapies, including potential proprietary double and triple combinations that will require substantial additional clinical development and regulatory approval efforts before we are permitted to commence commercialization, if ever. The clinical trials and manufacturing and marketing of these combinations will be subject to extensive and rigorous review and regulation by numerous government authorities in the United States, the European Union and other jurisdictions where we intend to test and, if approved, market them. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through preclinical testing and clinical trials that the product candidate is safe and effective for use in each target indication, and potentially in specific patient populations, including the pediatric population. This process can take many years and may include post-marketing studies and surveillance, which would require the expenditure of substantial resources beyond the proceeds we have currently raised. Of the large number of drugs in development for approval in the United States and the European Union, only a small percentage successfully complete the FDA or European Medicines Agency, or EMA, regulatory approval processes, as applicable, and are commercialized. Accordingly, even if we are able to obtain the requisite financing to continue to fund our research, development and clinical programs, we cannot assure you that our proprietary combination therapies or any of our other product candidates will be successfully developed or commercialized.

Clinical development and commercialization of combination therapies, such as our potential proprietary double and triple combinations, involve additional complexity and risk, including without limitation, those involving preclinical studies, drug-drug interactions, dose selection, unanticipated adverse events, clinical design and approvals of regulatory bodies and therapeutic development networks of patient advocacy groups. For example, if we or regulatory bodies identify concerns in preclinical and/or combination toxicology studies, we may need to run additional studies before commencing or continuing clinical development. Combination therapy clinical development may also involve more restrictive inclusion criteria based on the profiles of multiple investigational products, which could delay enrollment. We have limited experience developing and commercializing combination therapies and are competing with industry players with greater resources than us. If we are unable to manage the additional complexities and risks of the development and commercialization of combination therapies, our proposed combination program could be delayed, halted or otherwise fail to receive approval.

***The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. Agency requirements that differ from our assumptions or change can result in delays in starting, conducting and finishing clinical trials that are needed before we can apply for the next phase of development and, if successful, marketing approvals. If we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.***

We are not permitted to market posenaftor, dirocaftor, nesolicaftor, our potential combination therapies, or any of our other product candidates in the United States or the European Union until we receive approval of a New Drug Application, or NDA, from the FDA or a Marketing Authorization Application, or MAA, from the European Commission, respectively. Prior to submitting an NDA to the FDA or an MAA to the EMA for approval of any of our product candidates for a specific indication, we will need to complete preclinical and toxicology studies, as well as Phase 1, Phase 2 and Phase 3 clinical trials.

Successfully initiating and completing our clinical program and obtaining approval of an NDA or an MAA is a complex, lengthy, expensive and uncertain process, and the FDA, the EMA or other comparable foreign regulatory authorities may delay, limit or deny approval of any of our candidates for many reasons, including, among others:

- we may not be able to demonstrate that our product candidates are safe and effective to the satisfaction of the FDA or the EMA;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or the EMA for marketing approval;
- the FDA or the EMA may disagree with the number, design, size, conduct or implementation of our clinical trials or the requirements for or adequacy of the information and data needed to support the next phase of development (including, without limitation, Phase 3) for one or more of our product candidates, such as our combination therapy candidates;
- the FDA or the EMA may require that we conduct additional clinical trials or cohorts or run cohorts sequentially, all of which could delay our trial completion timelines;
- the FDA or the EMA may not approve the formulation, labeling or specifications of posenaftor, dirocaftor, nesolicaftor, or our other product candidates;

- the clinical research organizations, or CROs, that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials;
- the FDA or the EMA may find the data from preclinical studies and clinical trials insufficient to demonstrate that posenaftor, dirocaftor, nesolicaftor, our potential combination therapies, and/or our other product candidates' clinical and other benefits outweigh their safety or other risks, including, without limitation, the potential for drug-drug interaction;
- the FDA or the EMA may disagree with our interpretation of data from our preclinical studies and clinical trials, including our characterization of observed toxicities;
- the FDA or the EMA may not accept data generated at our clinical trial sites;
- if our NDAs or MAAs, if and when submitted, are reviewed by the FDA or the EMA, as applicable, the regulatory agency may have difficulties scheduling the necessary review meetings in a timely manner, may recommend against approval of our application or may recommend that the FDA or the EMA, as applicable, require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;
- the FDA may require development of a Risk Evaluation and Mitigation Strategy as a condition of approval or post-approval, and the EMA may grant only conditional approval or impose specific obligations as a condition for marketing authorization, or may require us to conduct post-authorization safety studies;
- the FDA or the EMA may find deficiencies with or not approve the manufacturing processes or facilities of third-party manufacturers with which we contract; or
- the FDA or the EMA may change their approval policies or adopt new regulations.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain regulatory approval for and successfully market posenaftor, dirocaftor, nesolicaftor, our potential combination therapies, or any of our other product candidates. Any such setback in our pursuit of regulatory approval would have a material adverse effect on our business and prospects.

Disruptions at the FDA and any comparable agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, including in 2018 and 2019, the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. Separately, in response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products through April 2020. On March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities and provided guidance regarding the conduct of clinical trials. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

In addition to the United States and the European Union, we intend to market our product candidates, if approved, in other international markets. Such marketing will require separate regulatory approvals in each market and compliance with numerous and varying regulatory requirements. The approval procedures vary from country-to-country and may require additional testing. Moreover, the time required to obtain approval may differ from that required to obtain FDA or EMA approval. In addition, in many countries, a product candidate must be approved for reimbursement before it can be approved for sale in that country. Approval by the FDA or the EMA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA or the EMA. The regulatory approval process in other international markets may include all of the risks associated with obtaining FDA or EMA approval.

***Our lead product candidates are designed to be administered with other CF therapies. Developing product candidates for administration with other therapies may lead to unforeseen side effects or failures in our clinical trials that could delay or prevent their regulatory approval or limit the commercial profile of an approved label.***

We are exploring proprietary combination therapies consisting of combinations of posenaftor and dirocaftor, as a double combination, and posenaftor, dirocaftor and nesolicaftor, as a triple combination. We anticipate that if one or more of our product candidates is approved for marketing, it may be approved to be administered with other therapies. Our development programs and planned studies carry all the risks inherent in drug development activities, including the risk that they will fail to demonstrate meaningful efficacy or acceptable safety. In addition, our development programs are subject to additional regulatory, commercial, manufacturing and other risks because of the potential use of other therapies in combination with our product candidates. Testing product candidates in combination with other therapies may increase the risk of significant adverse effects or test failures, or impact from drug-drug interactions. The timing, outcome and cost of developing products to be used in combination with other therapies is difficult to predict and dependent on a number of factors that are outside our reasonable control. If we experience safety or toxicity issues in our clinical trials or with any approved products, we may not receive approval to market any products, which could prevent us from ever generating revenues or achieving profitability.

If the data from our existing, ongoing and planned preclinical studies and clinical trials of posenaftor, dirocaftor and nesolicaftor as part of a proprietary combination therapy, regarding the safety or efficacy of these combinations are not favorable, the FDA and comparable foreign regulatory authorities may not approve these combination therapies and we may be forced to delay or terminate the development of any of these combination therapies, which would materially harm our business. Further, even if we gain marketing approvals for any of these combination therapies from the FDA and comparable foreign regulatory authorities in a timely manner, we cannot be certain that they will be commercially successful. If the results of the anticipated or actual timing of marketing approvals for these combination therapies, or the market acceptance of these combination therapies, if approved, including treatment reimbursement levels agreed to by third-party payors, do not meet the expectations of investors or public market analysts, the market price of our common stock would likely decline. Government and other third-party payors seek to contain costs of health care through legislative and other means. If they fail to provide coverage and adequate reimbursement rates for these products, it could increase the cost of our trials in such jurisdictions and decrease the possible market for any approved combination therapy that includes these co-administered drugs.

***Failures or delays in the commencement, progress or completion of our clinical trials of our product candidates, including due to competition from competing trials for CF patients, amended or additional trials or cohorts, lack of sufficient approvals including from the FDA, local regulatory and ethics bodies and those of therapeutic development networks of patient advocacy groups, or trial holds or stoppage due to interim results or safety concerns, could result in increased costs to us and could delay, prevent or limit our ability to generate clinical trial data, advance our product candidates in the clinic, submit an NDA (or foreign equivalent) for any of our product candidates for U.S. or foreign marketing approval, derive revenue and continue our business.***

Successful completion of the clinical trials for posenaftor, dirocaftor, nesolicaftor, our proprietary combination therapy candidates, and our other candidates is a prerequisite to submitting an NDA to the FDA or a MAA to the EMA and, consequently, the ultimate approval and commercial marketing of posenaftor, dirocaftor, nesolicaftor, our proprietary combination therapy candidates, and our other candidates in the United States and the European Union. Similar prerequisites apply in other foreign jurisdictions and for all of our product candidates in any jurisdiction. Clinical trials are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. A product candidate can unexpectedly fail at any stage of clinical development. The historical failure rate for product candidates is high due to scientific feasibility, safety, tolerability, toxicology, efficacy, changing standards of medical care and other variables. If the FDA requires us to complete, or we choose to implement, amended or additional studies beyond what we currently expect or assume, or to run additional cohorts or conduct cohorts sequentially, we may be delayed in completing our clinical trials and our expenses will increase. Conducting our trials in Europe and other ex-U.S. jurisdictions has and will continue to require IND-equivalent submissions to, and the approval of, local regulatory and ethics bodies, and we cannot assure you we will receive these approvals, or receive them in a timely manner. If therapeutic development networks of CF patient advocacy groups in the United States and/or other jurisdictions such as Europe do not timely sanction or highly rate or score our trials, or prioritize trials of other sponsors over our trials, we may not be able to enroll sufficient patients to conduct our trials at their member sites, or it may take longer to conduct these trials and we may need to look to other jurisdictions where we can more efficiently run our trials. Many CF clinical trial sites place importance on the review, ranking and sanctioning of therapeutic development networks of CF patient advocacy groups. In the U.S., we believe many sites consider sanctioning from the Protocol Review Committee, or PRC, of the Therapeutic Development Network of the U.S.-based Cystic Fibrosis Foundation, or the TDN, when deciding whether and when to participate in a trial or which trials to prioritize. For example, the TDN deferred sanctioning of nesolicaftor, which we believe contributed to a delay in our now completed nesolicaftor Phase 2 trial. There is also a large number of CF programs in clinical development at this time, including numerous corrector and combination trials from Vertex, and other companies with greater resources and experience than us. We face intense competition for eligible CF patients, which has and could continue to hamper our recruitment efforts. We do not know whether all of our clinical trials will begin or be completed on schedule, if at all, as the commencement and completion of clinical trials can be delayed or prevented for a number of reasons, including, among others:

- delays in reaching or failing to reach agreement on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- inadequate quantity or quality of or access to a product candidate or other materials, necessary to conduct clinical trials;
- difficulties obtaining institutional review board, or IRB, or ethics committee, or EC, approval to conduct a clinical trial at a prospective site or sites;
- challenges in recruiting and enrolling patients to participate in clinical trials, including the size and nature of the patient population, the proximity of patients to clinical sites (including, without limitation, if U.S. trial sites include international subjects coming to the U.S. on a visa), eligibility criteria for the clinical trial, the nature of the clinical trial protocol (including, without limitation, patient factors such as the time commitment involved in the required number of trial-related visits and procedures and the inability to take certain existing therapies during the trial), risks included in the signed informed consent and any new or amended consents required by each study participant, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications;

- unfavorable review of or a decision to defer sanctioning or not to sanction one or more of our clinical trials by the TDN, or the CTN, each of which may not sanction our trials for conduct at prospective trial sites, may change or alter any approval it may grant, or may provide a ranking or revised ranking of an amended protocol that adversely impacts recruitment in our clinical trials compared with other investigational new drugs in CF; while the TDN approved and favorably ranked our proprietary triple combination (for posenaftor, dirocaftor and nesolicaftor), proprietary double combination (for posenaftor and dirocaftor), posenaftor protocols as well as our posenaftor and nesolicaftor trials in patients on background Symdeko, we cannot assure you that it will sanction any of our other trials; the CTN has approved and favorably ranked the protocols for our posenaftor, nesolicaftor and triple combination trials and we are actively working to continue to expand into Europe with its member sites, subject to regulatory and ethics approvals in local jurisdictions, but we cannot assure you that such expansion will be successful
- severe or unexpected drug-related side effects experienced by patients in our clinical trials or by individuals using drugs similar to our product candidates;
- reports from preclinical or clinical testing of other similar therapies that raise safety or efficacy concerns; or
- difficulties retaining and/or obtaining data from patients who have enrolled in a clinical trial but may be prone to withdraw due to lack of efficacy, side effects, personal issues, loss of interest, difficulty travelling to the trial site or returning for required check-ins, or other factors, some of which are out of our control.

There are an unprecedented number of CF clinical trials ongoing in the United States and in other countries. As a result of this and other factors described above, the activation of clinical trial sites for our ongoing trials, and securing our target subject enrollment for these clinical trials, has been delayed from what we had originally planned. If we are unable to increase our enrollment, we will not have a substantially complete data set for these trials by our target dates.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended, placed on clinical hold or terminated by us, the FDA, other regulatory authorities or the IRBs/ECs at the sites where the IRBs/ECs are overseeing a clinical trial, or a data safety monitoring board, or DSMB, may recommend that the sponsor suspend or terminate a trial, due to a number of factors, including, among others:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA, the EMA or other regulatory authorities that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a clinical hold;
- unforeseen safety issues, including any that could be identified in our ongoing toxicology studies, adverse side effects or lack of effectiveness, including as part of ambiguous or negative interim results;
- changes in government regulations or administrative actions;
- problems with clinical supply materials; and
- lack of adequate funding to continue the clinical trial.

***Positive results from preclinical or in vitro, in vivo and ex vivo testing of our product candidates are not necessarily predictive of the results of our ongoing and future clinical trials of these candidates. If we cannot achieve positive results in our clinical trials for our proprietary candidates, or our other candidates, we may be unable to successfully develop, obtain regulatory approval for and commercialize our proprietary candidates.***

Positive results from our preclinical testing of posenaftor, dirocaftor, nesolicaftor, our proprietary combination therapy candidates, and our other candidates *in vitro*, *in vivo* and *ex vivo* may not necessarily be predictive of the results from our clinical trials in humans (including, without limitation, as part of any predicted correlation between *in vitro* CFTR protein activity as measured by an Ussing Chamber Assay and lung function improvement measured by FEV<sub>1</sub> improvement in clinical trials). Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical trials after achieving positive results in preclinical *in vitro* and *in vivo* studies, and we may face similar setbacks in our *ex vivo* organoid studies. For example, CFTR mRNA levels in target tissues of rats and monkeys exposed to nesolicaftor were observed to increase proportionally with exposure to nesolicaftor. Additionally, preliminary exploratory biomarker nasal CFTR mRNA and protein data from the SAD and MAD cohorts in our Phase 1 clinical trial for nesolicaftor in healthy volunteers and nesolicaftor as an add-on agent to Symdeko confirm target engagement. However, later clinical trials may not show that this biomarker is predictive of clinical efficacy or we may not be able to successfully obtain sufficient biomarker data to analyze. Preclinical and clinical data are often susceptible to varying interpretations and analyses, and the FDA or other regulatory agencies may require changes to our protocols or other aspects of our clinical trials or require additional studies. Additionally, many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or EMA approval. If we fail to produce positive results in our clinical trials of one or more of our product candidates, the development timeline and regulatory approval and commercialization prospects for those product candidates, and, correspondingly, our business and financial prospects, would be materially adversely affected. These risks could also impair our ability to successfully commence, progress or complete studies of our proprietary combination therapy candidates.

***Even if we obtain positive clinical results for our proprietary candidates in early-stage clinical trials (including, without limitation, those involving a relatively short duration in a small number of subjects, with the publication of interim, initial, preliminary or final results), those positive results may not be repeated in later-stage clinical trials.***

Before obtaining regulatory approval for the sale of our product candidates, including posenaftor, dirocaftor, nesolicaftor, and any proprietary combination therapy candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Successful completion of such clinical trials is a prerequisite to submitting an NDA to the FDA and, consequently, the ultimate approval and commercial marketing of posenaftor, dirocaftor and nesolicaftor and any proprietary combination therapy candidates in the United States. Similar requirements apply in the European Union and other foreign jurisdictions. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and preliminary, initial or interim results of a clinical trial do not necessarily predict final results. Our current CF trials involve relatively short duration in a small number of patients, resulting in limited data sets. From time to time, we may publish or report interim, initial or preliminary data from our clinical trials. Interim, initial or preliminary data from clinical trials that we may conduct may not be indicative of the final results of the trial and are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Interim, initial or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the interim, initial or preliminary data. We may also experience delays in analyzing or an inability to analyze samples, including, without limitation, biomarker data, due to insufficient sample size, errors in collection procedures at one or more sites, or other factors. As a result, interim, initial or preliminary data should be viewed with caution until the final data are available.

Negative or inconclusive results of our clinical trials of posenaftor, dirocaftor or nesolicaftor, any proprietary combination therapy candidates, or any other clinical trials we conduct, could mandate repeated or additional clinical studies. We do not know whether our clinical trials of any product candidate will demonstrate adequate efficacy and safety to result in regulatory approval to market such product candidate. Even if early-stage clinical results are favorable, if later-stage clinical trials (including, without limitation, those for longer duration with greater numbers of patients) do not produce favorable results, our ability to obtain regulatory approval for our product candidates, including posenaftor, dirocaftor and nesolicaftor, and any proprietary combination therapy candidates, may be adversely impacted.

***Our product candidates may cause adverse effects or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance.***

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. It is possible that, during the course of the development of posenaftor, dirocaftor, nesolicaftor, our proprietary combination therapy candidates, or our other product candidates, results of our studies and clinical trials could reveal an unacceptable severity and prevalence of side effects and/or drug-drug interactions. For example, in preclinical testing of nesolicaftor we observed reduced platelet counts in the animals we tested following administration at doses in excess of the doses we expect to administer in our clinical trials. As a result of this or any other side effects, our clinical trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development, or deny approval, of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims or result in delays in the trials due to requirements to provide new informed consents to patients to disclose new or changed risks or side effects. Even if approved for marketing, our product candidates could face label restrictions based on the above factors or others.

Additionally, if one or more of our product candidates receive 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 or impose restrictions on its distribution in a form of a modified Risk Evaluation and Mitigation Strategy;
- regulatory authorities may require additional labeling, such as warnings or contraindications;
- we may be required to change the way the product is administered or to conduct additional clinical studies;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

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

***If we cannot demonstrate an acceptable safety and toxicity profile for our product candidates in our clinical studies, we will not be able to continue our clinical trials or obtain approval for our product candidates.***

In order to obtain approval of a product candidate, we must demonstrate safety in various nonclinical and clinical tests. At the time of initiating human clinical trials, we may not have conducted or may not conduct the types of nonclinical testing ultimately required by regulatory authorities, or future nonclinical tests may indicate that our product candidates are not safe for use. Nonclinical testing and clinical testing are both expensive and time-consuming and have uncertain outcomes. For example, results of an earlier laboratory study of PTI-130, a former amplifier candidate, in non-rodent species suggested potential hematologic and reproductive toxicology issues that we believe are specific to the non-rodent species. We cannot predict whether future safety and toxicology studies may produce these same problems or cause other undesirable effects. We also observed certain undesired hematological (including reduced platelet count) side effects in animals dosed at levels of nesolicaftor that are higher than those intended for our clinical studies. We plan to complete additional toxicity studies of reproductive toxicity, carcinogenicity and long-term side effects prior to or concurrent with any Phase 3 clinical trials of our product candidates, and we cannot exclude the possible occurrence of these or other side effects in future nonclinical or clinical studies. In addition, success in initial tests does not ensure that later testing will be successful. We may experience numerous unforeseen events during, or as a result of, the testing process, which could delay or prevent our ability to develop or commercialize our product candidates, including:

- our preclinical and nonclinical testing may produce inconclusive or negative safety results, which may require us to conduct additional nonclinical testing or to abandon product candidates;
- our product candidates may have unfavorable pharmacology or toxicity characteristics or suggest possible drug-drug interaction;
- our product candidates may cause undesirable side effects; and
- the FDA or other regulatory authorities may determine that additional safety testing is required.

Any such events would increase our costs and could delay or prevent our ability to commercialize our product candidates, which could adversely impact our business, financial condition and results of operations.

***Nesolicaftor is based on a novel technology, which may raise development issues we may not be able to resolve, regulatory issues that could delay or prevent approval, or personnel issues that may keep us from being able to develop our product candidates.***

Our product candidate nesolicaftor is based on our novel amplifier technology. We are not aware of other drugs that work in a manner that we believe our amplifier technology does. We cannot assure you that development problems related to our novel technology will not arise in the future that could cause significant delays or that we are not able to resolve.

Clinical development and regulatory approval of novel product candidates such as ours can be more expensive and take longer than other, more well-known or extensively studied pharmaceutical product candidates due to our, investigators' and regulatory agencies' lack of experience with them. These factors also apply to patient advocacy groups and sanctioning by their affiliated therapeutic development center arms, such as the TDN. To our knowledge, there are no other amplifiers in clinical development and none have been approved to date. The novelty of our technology may lengthen the clinical development timeline and regulatory review process, require us to conduct additional studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. For example, the FDA could require additional studies or characterization that may be difficult or impossible to perform.

In addition, if we are unable to hire and retain the necessary personnel, the rate and success at which we can develop and commercialize product candidates will be limited. Any such events would increase our costs and could delay or prevent our ability to commercialize our product candidates, which could adversely impact our business, financial condition and results of operations.

***Even if we meet safety and efficacy endpoints in clinical trials, we cannot predict whether or when we will obtain regulatory approval to commercialize our product candidates and we cannot, therefore, predict the timing of any future revenue from posenacaftor, dirocaftor, nesolicaftor, our proprietary combination therapy candidates or any of our other product candidates.***

We cannot commercialize our product candidates, including posenacaftor, dirocaftor, nesolicaftor, and our proprietary combination therapy candidates, until the appropriate regulatory authorities, such as the FDA, have reviewed and approved the product candidate. The regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval for posenacaftor, dirocaftor, nesolicaftor, proprietary combination therapy candidates, or our other product candidates at all. Additional delays may result if posenacaftor, dirocaftor, nesolicaftor, proprietary combination therapy candidates, or any other product candidate is brought before an FDA advisory committee or an analogous foreign body, which could recommend

restrictions on approval or recommend non-approval of the product candidate. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical studies and the review process. As a result, we cannot predict when, if at all, we will receive any future revenue from commercialization of any of our product candidates, including posenaftor, dirocaftor, nesolicaftor, and proprietary combination therapy candidates.

***Even if we obtain regulatory approval for our proprietary candidates and/or our other product candidates, we will still face extensive regulatory requirements and our products may face future development and regulatory difficulties.***

Even if we obtain regulatory approval in the United States, the FDA may still impose significant restrictions on the indicated uses or marketing of our product candidates, including posenaftor, dirocaftor and nesolicaftor and our proprietary combination therapy candidates, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance, including Phase 4 clinical trials. For example, the labeling, if approved for our product candidates, including posenaftor, dirocaftor and nesolicaftor and our proprietary combination therapy candidates, will likely include restrictions on use due to the specific patient population and manner of use in which the drug was evaluated and the safety and efficacy data obtained in those evaluations.

Posenaftor, dirocaftor, nesolicaftor, our proprietary combination therapy candidates and our other product candidates will also be subject to additional ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, record-keeping and reporting of safety and other post-market information. The holder of an approved NDA is obligated to monitor and report adverse events and any failure of a product to meet the specifications described in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, manufacturers of drug products and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practice, or cGMP, requirements and adherence to commitments made in the NDA. If we, or a regulatory agency, discover previously unknown problems with a product, such as quality issues or adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requesting a recall or requiring withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of our product candidate, a regulatory agency may:

- issue an untitled or warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or supplements to an NDA submitted by us; or
- request a recall and/or seize product.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize posenaftor, dirocaftor, nesolicaftor, our proprietary combination therapy candidates and our other product candidates and inhibit our ability to generate revenues.

***Even if we obtain regulatory approval for our proprietary candidates or any of our other product candidates in the one geographical area, we may never obtain approval for or commercialize these candidates or any of our other product candidates outside of that area, which would limit our ability to realize their full market potential.***

In order to market any products in the United States or European Union, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy. Approval by the FDA or EMA does not ensure approval by regulatory authorities in other countries or jurisdictions. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Successful approval by one jurisdiction does not necessarily guarantee approval in any other jurisdiction. Further, the disparate impact of COVID-19 across the United States and the European Union could result in yet further differences in their respective regulatory regimes, and an unwillingness for the FDA or EMA to accept data from clinical trials conducted in certain geographies.

Seeking foreign regulatory approval could result in difficulties and costs for us and require additional preclinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our product candidates in those countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our product candidates will be unrealized.

***If we are not able to obtain or maintain orphan product status for our product candidates for which we seek this status, we will not be able to claim the tax credits for our clinical trials of such products provided by this status or potentially take advantage of other benefits of orphan drug status.***

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a disease or condition that fewer than 200,000 individuals in the United States have been diagnosed as having at the time of the submission of the request for orphan drug designation. Under Regulation No. (EC) 141/2000 on Orphan Medicinal Products, a medicinal product may be designated as an orphan medicinal product if, among other things, it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people in the European Union when the application is made. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of market exclusivity. This exclusivity precludes the EMA or the FDA, as applicable, from approving another marketing application for the same or, in the European Union, a similar drug for the same indication for that time period, unless, among other things, the later product is clinically superior. The exclusivity period is seven years in the United States and ten years in the European Union following marketing approval. The EU exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation, for example if the drug is sufficiently profitable so that market exclusivity is no longer justified.

In the United States, orphan drug exclusivity may be lost if the FDA withdraws or revokes the orphan-drug designation as permitted by law, we withdraw the marketing application for the drug, we consent to another's marketing application for approval of the same use or indication as the designated orphan drug, or we fail to assure a sufficient quantity of the drug as required by law. Similarly, in the European Union, exclusivity may be lost if we request the removal of the orphan-drug designation or the drug no longer meets any of the criteria that made it eligible for orphan-drug status at the outset. Even after an orphan drug is approved, the same or, in the European Union, a similar drug can subsequently be approved for the same condition if the competent regulatory agency concludes that the later drug is clinically superior to the original orphan drug by providing a significant therapeutic advantage over and above that drug.

If we do not obtain orphan drug exclusivity or if our competitors obtain orphan drug exclusivity for other rare diseases or conditions we are targeting before we do, we may be delayed in obtaining marketing authorization or we may lose out on the potential benefits of market exclusivity associated with the orphan drug designation. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee. If we do not obtain orphan designation for posenaftor or our other product candidates (and maintain such designation as to nesolicaftor), we will lose out on such benefits associated with orphan designation.

#### ***Use of social media platforms presents new risks.***

Social media increasingly is being used to communicate about our product candidates and the diseases our therapies are designed to treat. We believe that members of the CF community may be more active on social media as compared to other patient populations. Social media practices in the pharmaceutical and biotechnology industries are evolving, which creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media platforms to comment on the effectiveness of, or adverse experiences with, a drug candidate, which could result in reporting obligations. In addition, there is a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face restrictive regulatory actions or incur other harm to our business.

#### **Risks Related to Our Dependence on Third Parties**

***If third parties on which we depend to conduct our preclinical studies or any ongoing or future clinical trials do not perform as contractually required, fail to satisfy regulatory or legal requirements or miss expected deadlines, our development program could be delayed with materially adverse effects on our business and prospects.***

We rely on clinical research organizations, clinical data management organizations and consultants, collectively referred to as CROs, to design, conduct, supervise and monitor preclinical and clinical studies of our product candidates and plan to do the same for our ongoing and future clinical trials for posenaftor, dirocaftor, nesolicaftor, proprietary combination therapy candidates and any other clinical trials. We and our CROs are required to comply with various regulations, including Good Clinical Practice, or GCP, requirements, which are enforced by the FDA, and guidelines of the Competent Authorities of the Member States of the European

Economic Area, and comparable foreign regulatory authorities to ensure that the health, safety and rights of patients are protected in clinical development and clinical trials, and that trial data integrity is assured. Regulatory authorities ensure compliance with these requirements through periodic inspections of trial sponsors, principal investigators and trial sites, as well as third party contractors. If we or any of our CROs fail to comply with applicable requirements, or the CRO does not perform its contractually required obligations (or makes errors or mistakes), the clinical data, including, without limitation, biomarker data, generated in our clinical trials may not be collected or may be collected but be deemed unreliable, and the FDA, the EMA or other comparable foreign regulatory authorities may require us (or we may choose ourselves) to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with such requirements. In addition, our clinical trials must be conducted with products produced under cGMP requirements, which mandate the methods, facilities and controls used in manufacturing, processing and packaging of a drug product to ensure its safety and identity. Failure to comply with these regulations may require us to delay or repeat preclinical and clinical trials, which would delay the regulatory approval process.

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 ongoing clinical and preclinical programs. We generally represent a small percentage of these firms' overall business, which could limit our ability to receive priority allocation of their resources. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

We also rely on clinical investigators and clinical research organizations, as well as therapeutics development arms of patient advocacy groups, such as the HIT-CF, TDN and CTN, to assist in the design and review of our clinical trials, including supporting the enrollment of qualified patients. If these third parties do not approve or sanction our trial protocols to facilitate enrollment, our ability to conduct clinical trials may be impeded. Because we have relied on third parties, our internal capacity to perform these functions is limited. Outsourcing these functions involves risk that third parties may not perform to our standards, may not produce results in a timely manner or may fail to perform at all. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated or inadvertently be made publicly-available. We currently have a small number of employees, which limits the internal resources we have available to identify and monitor our third-party providers. To the extent we are unable to identify and successfully manage the performance of third-party service providers in the future, our business may be adversely affected. Though we carefully manage our relationships with our CROs, and other third parties, there can be no assurance that we will not encounter similar 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.

In addition, our CROs and collaborators have been and may continue to be affected by the COVID-19 pandemic. Clinical site closure and other activities that require visits to clinical sites, have been and may continue to be delayed due to prioritization of hospital resources toward the COVID-19 pandemic or concerns among patients about participating in clinical trials during a pandemic. This is particularly true of our European-based collaborators, in which we are aware of certain disruptions and potential delays in *ex vivo* in testing of organoids due to the research personal transitioning to working in shifts to reduce the number of people gathered together at one time in any given laboratory or temporary closures of research laboratories. Disruption of our collaborators' and CRO's business as a result of COVID-19 could increase the likelihood that they are unable to perform as contractually required, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. The FDA and the EMA require clinical trials to be conducted in accordance with GCP, including for conducting, recording and reporting the results of preclinical studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Any such event could have a material adverse effect on our business, financial condition, results of operations and prospects.

***We rely on third-party manufacturers and suppliers and we intend to rely on third parties to produce preclinical, clinical and commercial supplies of posenacافت, dirocaفت, nesolicaفت and any future product candidates. These third parties may not perform as contractually required or expected and issues may arise that could delay the commencement or completion of clinical trials.***

We rely on third parties to supply the materials and components for our research and development, preclinical and clinical trial supplies. We do not own manufacturing facilities or supply sources for such components and materials. There can be no assurance that our supply of research and development, preclinical and clinical development drugs and other materials will not be limited, interrupted, restricted in certain geographic regions or of satisfactory quality or continue to be available at acceptable prices. Any replacement of these third parties could require significant effort and expertise because there may be a limited number of qualified replacements.

The manufacturing process for a product candidate is subject to FDA, EMA and other foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities to comply with regulatory standards such as cGMP. In the event that any of our suppliers or manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, our regulatory filings may be delayed, our preclinical studies or clinical trials may be delayed or suspended, and we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills or technology to another third party and a feasible alternative may not exist; even if it exists, it may be cost-prohibitive and time-prohibitive to engage in technology transfer to switch vendors for drug substance and/or product candidate manufacturing. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our drug substance and/or product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget. Drug formulation is an inherently uncertain process with numerous steps, some of which may need to be repeated, to ensure quality, accuracy and yield; unexpected variances may occur, which could delay our manufacturing efforts and delay commencement or completion of preclinical studies and/or clinical trials.

Additionally, our third-party manufacturers and suppliers have been impacted and may continue to be impacted by the COVID-19 pandemic. We depend on personnel at third-party manufacturing facilities in the United States and other countries to manufacture products used in our preclinical studies and clinical trials. Quarantines, shelter-in-place and similar government orders, or the expectation that such orders, shutdowns or other restrictions could occur, whether related to COVID-19 or other infectious diseases, could impact personnel at third-party manufacturing facilities in the United States, European Union and other countries, or the availability or cost of materials, which could disrupt our supply chain.

If our relationships with our manufacturers, suppliers or other vendors are terminated or scaled back as a result of the COVID-19 pandemic or other health epidemics, we may not be able to enter into arrangements with alternative suppliers or vendors or do so on commercially reasonable terms or in a timely manner. Further, if the COVID-19 pandemic persists for an extended period of time and begins to impact essential distribution systems such as FedEx and postal delivery, we could experience disruptions to our supply chain and operations, and associated delays in the manufacturing and supply of our product candidates. Switching or adding additional suppliers or vendors involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new supplier or vendor commences work. As a result, delays may occur, which could adversely impact our ability to meet our desired clinical development and any future commercialization timelines. Although we carefully manage our relationships with our suppliers and vendors, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not harm our business.

We expect to continue to rely on third-party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements could adversely affect our business in a number of ways, including:

- preventing us from initiating or continuing preclinical studies or clinical trials of product candidates under development;
- delaying our trials and/or delaying submissions of regulatory applications or receipt of regulatory approvals for product candidates;
- preventing a collaborator from cooperating with us;
- subjecting our product candidates to additional inspections by regulatory authorities;
- requiring us to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, preventing us from meeting commercial demands for our products.

***If a current or future collaborative partner terminates or fails to perform its obligations under an agreement with us, or if research does not produce viable lead candidates or meet specified criteria during the applicable research term, the development and commercialization of the product candidates could be delayed or terminated.***

If one of our collaborative partners, such as Genentech, does not devote sufficient time and resources to a collaboration arrangement with us, we may not realize the potential commercial benefits of the arrangement, and our results of operations may be materially adversely affected.

Much of the potential revenue from our collaboration consists of contingent payments, such as payments for achieving scientific or regulatory milestones or royalties payable on sales of drugs. The milestone and royalty revenue that we may receive under collaborations will depend upon our collaborators' ability to successfully develop, introduce, market and sell new products. Our collaboration partners may fail to develop or effectively commercialize their products using our products or technologies or otherwise discontinue their research activities because they:

- exercise their unilateral right to terminate the collaboration agreement including, without limitation, if research does not produce a viable lead candidate or meet specified criteria during the applicable research term;
- decide not to devote the necessary resources due to internal constraints, such as limited personnel with the requisite expertise, limited cash resources or specialized equipment limitations, or the belief that other drug development programs may have a higher likelihood of obtaining marketing approval or may potentially generate a greater return on investment;
- decide to pursue other technologies or develop other product candidates, either on their own or in collaboration with others, including our competitors, to treat the same diseases targeted by our own collaborative programs;
- do not have sufficient resources necessary to carry the product candidate through clinical development, marketing approval and commercialization; or
- cannot obtain the necessary marketing approvals.

Competition may negatively impact a partner's focus on and commitment to our relationship and, as a result, could delay or otherwise negatively affect the commercialization of our products, which would have a material adverse effect on our operating results and financial condition. Terminated collaborations include the risk that the former partner maintains rights to exploit certain co-developed technology, and the risk that, to the extent the program is desired to continue, funding formerly provided by the partner will need to come from alternative sources such as us or a new partner and such funding may not be available on terms acceptable to us, if at all. These factors can cause a delay or abandonment of technology programs and could negatively affect commercialization of our products, which would have a material adverse effect on our operating results and financial condition.

We face a number of challenges in seeking future collaborations. Collaborations are complex and any potential discussions may not result in a definitive agreement for many reasons. For example, whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of a number of factors, such as the design or results of our clinical trials, the potential market for our product candidates, the costs and complexities of manufacturing and delivering our product candidates to patients, the potential of competing products, the existence of uncertainty with respect to ownership or the coverage of our intellectual property, and industry and market conditions generally. If we determine that additional collaborations for our product candidates are necessary and are unable to enter into such collaborations on acceptable terms, we might elect to delay or scale back the development or commercialization of our product candidates in order to preserve our financial resources or to allow us adequate time to develop the required physical resources and systems and expertise ourselves.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. If a current or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

## Risks Related to Commercialization of Our Product Candidates

***The commercial success of posenaftor, dirocaftor, nesolicaftor, any proprietary combination therapy candidates and our other product candidates will depend upon the acceptance of those products, if approved, by the medical community, including physicians, patients and health care payors.***

Even if posenaftor, dirocaftor, nesolicaftor, any proprietary combination therapy candidates or our other product candidates are approved for sale, they may not achieve sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. If these product candidates, if approved, do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of any of our product candidates, including posenaftor, dirocaftor and nesolicaftor and any proprietary combination therapy candidates, will depend on a number of factors, including:

- demonstration of safety and efficacy in our clinical trials and in any post-marketing studies;
- the relative convenience, ease of administration and acceptance by physicians, patients and health care payors;
- the prevalence and severity of any adverse effects;
- limitations or warnings contained in the FDA-approved label for the relevant product candidate;
- availability of alternative treatments;
- pricing and cost-effectiveness;
- the effectiveness of our or any future collaborators' sales and marketing strategies; and
- our ability to obtain and maintain healthcare payor approval and reimbursement, which may vary from country to country and within a country.

If any of our product candidates, including posenaftor, dirocaftor and nesolicaftor and any proprietary combination therapy candidates, is approved but does not achieve an adequate level of acceptance by physicians, patients and health care payors, we may not generate sufficient revenue and we may not become or remain profitable.

***If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing our product candidates if and when they are approved.***

We do not have a sales or marketing infrastructure, and we have limited experience in the sales, marketing or distribution of pharmaceutical products. Our commercialization strategy will target key prescribing physicians and advocacy groups, as well as provide patients with support programs, and seek to ensure product access and secure reimbursement. Outside of the United States, Canada, Europe and Australia, we may seek a partner to commercialize our products. In the future, we may choose to build a focused sales and marketing infrastructure to market or co-promote our product candidates if and when they are approved, which would be expensive and time-consuming. Alternatively, we may elect to outsource these functions to third parties. Either approach carries significant risks. For example, recruiting and training a sales force is expensive and time-consuming and, if done improperly, could delay a product launch and result in limited sales. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- inability to recruit, manage and retain adequate numbers of effective sales and marketing personnel;
- the inability of marketing personnel to develop effective marketing materials;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

We may also not be successful in entering into additional arrangements with third parties to sell and market our product candidates or doing so on terms that are favorable to us. Even if we do enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product candidates are likely to be lower than if we were to market and sell our products ourselves. In addition, we likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

***If our competitors develop technologies or product candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize our products may be adversely affected. Competitive products for treatment of CF may reduce or eliminate the commercial opportunity for our product candidates.***

The clinical and commercial landscape for CF is highly competitive and subject to rapid and significant technological change. New data from clinical-stage products continue to emerge. It is possible that these data may alter the current standard of care, completely precluding us from further developing posenaftor, dirocaftor, nesolicaftor, our proprietary combination therapy candidates or our other product candidates for CF. Further, it is possible that we may advance our clinical trials only to find that data from competing products make it impossible for us to complete enrollment in these trials, resulting in our inability to file for marketing approval with regulatory agencies. Even if posenaftor, dirocaftor, nesolicaftor, proprietary combination therapy candidates or our other product candidates are approved for marketing, they may have limited sales due to particularly intense competition in the CF market.

Competitive therapeutic treatments include those that are currently in development and any new treatments that enter the market. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may try to develop product candidates. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. Examples include Vertex Pharmaceuticals Incorporated, AbbVie Inc., F. Hoffmann-LaRoche Ltd., Novartis AG, Gilead Sciences, Inc., Laurent Pharmaceuticals Inc., Pfizer Inc., AstraZeneca, Translate Bio Inc., Sanofi Genzyme, Bayer AG, Corbus Pharmaceuticals Holdings, Inc., Eloxx Pharmaceuticals, Verona Pharma plc, Spirovant Sciences, Enterprise Therapeutics Ltd. and several other companies.

Vertex or other competitors could develop other drugs or combinations that may obviate the applicability of posenaftor, dirocaftor and nesolicaftor. Changes in standard of care or use patterns could also make our combination therapy obsolete. For example, Vertex has developed tezacaftor and ivacaftor as a combination therapy on its own, and with another corrector, elexacaftor, and was recently granted marketing approval for both combinations under the names Symdeko and Trikafta, respectively. Also, if gene therapy is able to successfully cure CF, the clinical need for our product candidates would diminish.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products.

Many of our competitors have greater financial, technical, manufacturing, clinical development, marketing, sales and supply resources, technical and human resources or experience than us and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of product candidates and the commercialization of those products. Accordingly, our competitors may be more successful than we may be in obtaining FDA and other regulatory approvals for therapies and achieving widespread market acceptance. Our competitors' products may be more effective, or more effectively marketed and sold, than any product candidate we may commercialize and may render our therapies obsolete or non-competitive before we can recover development and commercialization expenses.

If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the efficacy, safety and tolerability of our products, the ease with which our products can be administered, the extent to which physicians and patients accept combination therapies and, for nesolicaftor, new classes of modulators, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including being more effective, safer, or less expensive, or could be marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop, or products with which we are approved for use in combination, obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a small number of competitors.

We also compete with other clinical-stage companies and institutions for clinical trial participants, which could reduce our ability to recruit participants for our clinical trials. For example, actual or perceived risks of our product candidates, such as posenaftor, dirocaftor, nesolicaftor, or our proprietary combination therapy candidates, or actual or perceived benefits of product candidates of our competitors, may negatively affect potential clinical trial participants or patients when deciding whether to participate in our clinical trials, and could result in patients seeking alternative clinical trials or commercial therapies from our competitors. Delay in recruiting clinical trial participants could adversely affect our ability to bring a product to market. Further, research and discoveries by others may result in breakthroughs that render our product candidates obsolete even before they begin to generate any revenue.

In addition, our competitors may obtain patent protection or FDA approval and commercialize products more rapidly than we do, which may impact future sales of any of our product candidates that receive marketing approval. If the FDA approves the commercial sale of any of our product candidates, we will also be competing with respect to marketing capabilities and manufacturing efficiency, areas in which we have limited or no experience. We expect competition among products will be based on product efficacy and safety, the timing and scope of regulatory approvals, availability of supply, marketing and sales capabilities, product price, reimbursement coverage by government and private third-party payors, and patent position. Our profitability and financial position will suffer if we cannot compete effectively in the marketplace, even if our products receive regulatory approval.

***Payor approval and reimbursement may not be available for posenaftor, dirocaftor, nesolicaftor, any proprietary combination therapy candidates and our other product candidates, or third-party therapies taken with our drugs, which could make it difficult or impossible for us to sell our products profitably.***

Market acceptance and sales of posenaftor, dirocaftor or nesolicaftor, any proprietary combination therapy candidates, or any other product candidates that we develop, will depend in part on the extent to which reimbursement for these products and related third party treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers, health maintenance organizations and pharmacy benefit management organizations, decide which medications they will pay for, at what tier level and establish reimbursement levels. In the United States, non-governmental payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. A primary trend in the United States healthcare industry and elsewhere is cost containment. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Even if we are successful in gaining reimbursement in one country, that does not mean we will achieve reimbursement at the same levels or at all in any other country. Reimbursement may impact the demand for, or the price of, any product for which we obtain marketing approval. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with products administered under the supervision of a physician. Reimbursement levels may be impacted by factors including, without limitation, the perceived safety and efficacy of our products relative to the cost (and relative to the perceived safety and efficacy and cost for available competitive products), the views of independent research organizations on drug pricing and the political climate, many of which factors we cannot control. Also, reimbursement amounts may reduce the demand for, or the price of, our products. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize posenaftor, dirocaftor, nesolicaftor, any proprietary combination therapy candidates, or any other product candidates that we develop. We will also be required to establish systems and programs that assist patients in determining the reimbursement level and in some instances establishing patient economic support programs to alleviate the economic burden of co-pays and/or co-insurance. These patient support programs are complex, costly and require knowledge and expertise that we currently do not possess.

There have been a number of legislative and regulatory proposals to change the healthcare system in the United States and in some foreign jurisdictions that could affect our ability to sell any future products profitably. For example, the Trump administration's budget proposal for fiscal year 2021 includes a \$135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Further, the Trump administration previously released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contained additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services, or HHS, has solicited feedback on some of these measures and has implemented others under its existing authority. On July 24, 2020, the Trump administration announced four executive orders related to prescription drug pricing that attempt to implement several of the administration's proposals, including a policy that would tie Medicare Part B drug prices to international drug prices; one that directs HHS to finalize the Canadian drug importation proposed rule previously issued by HHS and makes other changes allowing for personal importation of drugs from Canada; one that directs HHS to finalize the rulemaking process on modifying the anti-kickback law safe harbors for plans, pharmacies, and pharmaceutical benefit managers; and one that reduces costs of insulin and epipens to patients of federally qualified health centers. Although a number of these and other

measures may require additional authorization to become effective, Congress and the Trump administration have both stated that they will continue to seek new legislative and/or administrative measures to control drug costs. These legislative and regulatory changes may negatively impact the reimbursement for any future products, following approval. The availability of generic treatments may also substantially reduce the likelihood of reimbursement for any future products, including posenaftor, dirocaftor and nesolicaftor or any proprietary combination therapy candidates. The application of user fees to generic drug products will likely expedite the approval of additional generic drug treatments. We expect to experience pricing pressures in connection with the sale of posenaftor, dirocaftor, nesolicaftor, any proprietary combination therapy candidates, and any other product candidate that we develop, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes.

In addition, there may be significant delays in obtaining reimbursement for approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or regulatory authorities in other countries. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the product and the clinical setting in which it is used, may be based on payments allowed for lower cost products that are already reimbursed, and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, however reimbursement and levels of reimbursement may also vary within a country based on the individual decisions of private payors.

Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any of our product candidates, including posenaftor, dirocaftor and nesolicaftor and any proprietary combination therapy candidates, could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

***We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

The success of our business depends primarily on our ability to identify, develop and commercialize product candidates. Because we have limited financial and managerial resources, we focus on research programs and product candidates for the indications that take advantage of our deep expertise and knowledge and that we believe are the most scientifically and commercially promising. Our resource allocation decisions may cause us to fail to capitalize on viable scientific or commercial products or profitable market opportunities. In addition, we may spend valuable time and managerial and financial resources on research programs and product candidates for specific indications that ultimately do not yield any scientifically or commercially viable products. If we do not accurately evaluate the scientific and commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in situations where it would have been more advantageous for us to retain sole rights to development and commercialization.

#### **Risks Related to Government Regulation**

***We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws and health information privacy and security laws. Some of these laws were recently amended, and their interpretation following such amendments remains unclear. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.***

Our current and future operations may be directly, or indirectly through our customers, subject to various federal and state fraud and abuse laws, including, without limitation, the federal anti-kickback statute. These laws may impact, among other things, our research, proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal anti-kickback statute which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward 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 federal healthcare programs such as Medicare and Medicaid;
- the federal false claims laws, including civil whistleblower or qui tam actions, and civil monetary penalties, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent or from knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which, among other things, imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly or willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statement using or making any false or fraudulent document, in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, and as amended by the final HIPAA omnibus rule, Modifications to the HIPAA Privacy, Security, Enforcement, and Breach Notification Rules Under HITECH and the Genetic Information Nondiscrimination Act; Other Modifications to HIPAA, published in January 2013, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information on entities subject to the rule, such as health plans, clearinghouses and certain healthcare providers and their business associates that create, use or disclose individually identifiable health information on their behalf;
- the Federal Food, Drug, and Cosmetic Act, or FDCA, which prohibits, among other things, the distribution of adulterated or misbranded drugs or medical devices;
- the federal Physician Payments Sunshine Act, enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively referred to herein as the Affordable Care Act, or the ACA, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologicals and medical supplies to report to CMS information related to payments and other transfers of value made to physicians, as defined by such law, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by state governmental and non-governmental third-party payors, including private 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; state laws and regulations that require manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws that require the registration of pharmaceutical sales representatives.

Further, the ACA, among other things, amends the intent requirement of the federal anti-kickback and criminal health care fraud statutes. A person or entity can now be found guilty of fraud or false claims under ACA without actual knowledge of the statute or specific intent to violate it. In addition, ACA provides 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 statutes.

Possible sanctions for violation of these laws include significant monetary fines, civil and criminal penalties, exclusion from Medicare, Medicaid and other government programs, forfeiture of amounts collected in violation of such prohibitions, imprisonment, and integrity oversight and ongoing monitoring. 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.

In addition, regulators globally are also imposing greater monetary fines for privacy violations. For example, in 2016, the E.U. adopted a new regulation governing data practices and privacy called the General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR applies to any company established in the E.U. as well as to those outside the E.U. if they collect and use personal data in connection with the offering goods or services to individuals in the E.U. or the monitoring of their behavior. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, expanded disclosures about how personal information is to be used, limitations on retention of information, mandatory data breach notification requirements and onerous new obligations on services providers. Non-compliance with the GDPR may result in monetary penalties of up to €20 million or 4% of worldwide revenue, whichever is higher. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of personal data, such as healthcare data or other sensitive information, could greatly increase our cost of providing our products and services or even prevent us from offering certain services in jurisdictions that we operate in.

The scope and enforcement of these laws is uncertain and subject to change in the current environment of health care reform, especially in light of the lack of applicable precedent and regulations. Such changes are impossible to predict. It is possible that some of our business activities could be subject to challenge by federal or state regulatory authorities under one or more of these laws. Any such challenge could have a material adverse effect on our reputation, business, results of operations, and financial condition. Any state or federal regulatory review of us, regardless of the outcome, would be costly and time-consuming, and could have a material adverse effect on our business, financial condition and results of operations.

***Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading, which could have a material adverse effect on our business.***

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent misconduct 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. 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.

***Health care reform measures could adversely affect our business.***

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs. The ACA, which includes measures to significantly change the way health care is financed by both governmental and private insurers, was enacted in March 2010. Among the provisions of the ACA of greatest importance to the pharmaceutical and biotechnology industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs;
- new requirements to report certain financial arrangements with physicians, as defined by thereunder, and teaching hospitals, including reporting any “transfer of value” made or distributed to physicians and teaching hospitals and reporting any ownership interests held by physicians and their immediate family members;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

At this time, the full effect that the ACA would have on our business remains unclear. There remain judicial, Congressional and efforts by the current administration to challenge certain aspects of the ACA. Legislation has been drafted and enacted to repeal and replace parts of the ACA, but no comprehensive ACA replacement law has been enacted. However, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseparable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case, and has allotted one hour for oral arguments, which are expected to occur in the fall. It is unclear how such litigation and other efforts to repeal and replace the ACA will impact the ACA and our business. We cannot predict any initiatives that may be adopted in the future.

Individual states 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 designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce ultimate demand for our products or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

In addition, given recent federal and state government initiatives directed at lowering the total cost of healthcare, Congress and state legislatures will likely continue to focus on healthcare reform, the cost of prescription drugs and biologics and the reform of the Medicare and Medicaid programs. While we cannot predict the full outcome of any such legislation, it may result in decreased reimbursement for drugs and biologics, which may further exacerbate industry-wide pressure to reduce prescription drug prices. This could harm our ability to generate revenues. Increases in importation or re-importation of pharmaceutical products from foreign countries into the United States could put competitive pressure on our ability to profitably price our products, which, in turn, could adversely affect our business, results of operations, financial condition and prospects. We might elect not to seek approval for or market our products in foreign jurisdictions in order to minimize the risk of re-importation, which could also reduce the revenue we generate from our product sales. It is also possible that other legislative proposals having similar effects will be adopted.

Furthermore, regulatory authorities' assessment of the data and results required to demonstrate safety and efficacy can change over time and can be affected by many factors, such as the emergence of new information, including on other products, changing policies and agency funding, staffing and leadership. We cannot be sure whether future changes to the regulatory environment will be favorable or unfavorable to our business prospects. For example, average review times at the FDA for marketing approval applications can be affected by a variety of factors, including budget and funding levels and statutory, regulatory and policy changes.

Additionally, it is possible that additional governmental action is taken to address the COVID-19 pandemic. For example, on April 18, 2020, CMS announced that Qualified Health Plan issuers under the ACA may suspend activities related to the collection and reporting of quality data that would have otherwise been reported between May and June 2020 given the challenges healthcare providers are facing responding to the COVID-19 virus.

***The withdrawal of the United Kingdom, or U.K., from the European Union, or E.U., commonly referred to as “Brexit,” may adversely impact our ability to obtain regulatory approvals of our product candidates in the E.U., result in restrictions or imposition of taxes and duties for importing our product candidates into the E.U., and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the E.U.***

Following the result of a referendum in 2016, the U.K. left the E.U. on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the U.K. and the E.U., the U.K. will be subject to a transition period until December 31, 2020, or the Transition Period, during which E.U. rules will continue to apply. Negotiations between the U.K. and the E.U. are expected to continue in relation to the customs and trading relationship between the U.K. and the E.U. following the expiry of the Transition Period.

Since a significant proportion of the regulatory framework in the U.K. applicable to our business and our product candidates is derived from E.U. directives and regulations, Brexit, following the Transition Period, could materially impact the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the U.K. or the E.U. For example, as a result of the uncertainty surrounding Brexit, the European Medicines Agency (the “EMA”) relocated to Amsterdam from London. Following the Transition Period, the U.K. will no longer be covered by the centralized procedures for obtaining E.U.-wide marketing authorization from the EMA and, unless a specific agreement is entered into, a separate process for authorization of drug products, including our product candidates, will be required in the U.K., the potential process for which is currently unclear. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the U.K. or the E.U. and restrict our ability to generate revenue and achieve and sustain profitability. In addition, we may be required to pay taxes or duties or be subjected to other hurdles in connection with the importation of our product candidates into the E.U., or we may incur expenses in establishing a manufacturing facility in the E.U. in order to circumvent such hurdles. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the U.K. or the E.U. for our product candidates, or incur significant additional expenses to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the U.K. It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the E.U.

## Risks Related to Protecting Our Intellectual Property

***It is difficult and expensive to protect our intellectual property rights and we cannot ensure that they will prevent third parties from competing against us. If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents that are sufficient to protect our product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.***

Our success will depend, in part, on our ability to obtain and maintain intellectual property rights, both in the United States and other countries, successfully defend this intellectual property against third-party challenges and successfully enforce this intellectual property to prevent third-party infringement. We rely upon a combination of patents, trade secret protection and confidentiality agreements.

Our ability to protect any of our product candidates and technologies from unauthorized or infringing use by third parties depends in substantial part on our ability to obtain and maintain valid and enforceable patents in both the United States and other countries. Patent matters in the biotechnology and pharmaceutical industries can be highly uncertain and involve complex legal and factual questions. Changes in the patent laws, their implementing regulations or their interpretations may diminish the value of our patent rights.

There can be no assurance that we will discover or develop patentable products or processes or that patents will issue from any pending patent applications owned or licensed by us, or if issued, the breadth of such patent coverage. We currently have two issued U.S. patents relating to our product candidate PTI-428, one issued U.S. patent to our product candidate PTI-801, one issued U.S. patent to our product candidate PTI-808, and pending patent applications directed to our other product candidates, PTI-801, PTI-808, PTI-428, our combination therapies and our technologies. Many of our patent applications related to our CF program are in the earliest stages, including provisional patent applications, although we do have six (6) issued patents covering early CFTR modulator compounds not currently in development. We cannot provide any assurances that any of our pending patent applications will lead to issued patents and, if they do, that such patents will include claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage. Even if issued, we cannot guarantee that claims of issued patents owned or licensed to us are or will be held valid or enforceable by the courts or, even if unchallenged, will provide us with exclusivity or commercial value for our product candidates or technology or any significant protection against competitive products or prevent others from designing around our claims. Further, if we encounter delays in regulatory approvals, the period of time during which we could market our product candidates under patent protection could be reduced. Our patent rights also depend on our compliance with technology and patent licenses upon which our patent rights are based and upon the validity of assignments of patent rights from consultants and other inventors that were, or are, not employed by us.

The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any patent claims that we may obtain cannot be predicted with certainty. Patents, if issued, may be challenged, deemed unenforceable, invalidated, or circumvented. U.S. patents and patent applications may also be subject to derivation or adversarial proceedings, ex parte reexamination, or inter partes review proceedings, supplemental examination and challenges in district court. Patents may be subjected to opposition, post-grant review, or comparable proceedings lodged in various foreign, both national and regional, patent offices. These proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such proceedings may be costly. Thus, any patents, should they issue, that we may own or exclusively license may not provide any protection against competitors.

Patent applications are generally maintained in confidence until publication. In the United States, for example, patent applications are maintained in secrecy for up to 18 months after their filing. Similarly, publication of discoveries in scientific or patent literature often lags behind actual discoveries. Consequently, we cannot be certain that we were the first to file patent applications on our product candidates. There is also no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which could be used by a third party to challenge validity of our patents, should they issue, or prevent a patent from issuing from a pending patent application.

In addition, even if patents do successfully issue, third parties may challenge any such patent we own or license through adversarial proceedings in the issuing offices, which could result in the invalidation or unenforceability of some or all of the relevant patent claims. If a third party asserts a substantial new question of patentability against any claim of a U.S. patent we own or license, the U.S. Patent and Trademark Office, or USPTO, may grant a request for reexamination, which may result in a loss of scope of some claims or a loss of the entire patent. The adoption of the Leahy-Smith America Invents Act, or the Leahy-Smith Act, on September 16, 2011, established additional opportunities for third parties to invalidate U.S. patent claims, including *inter partes* review and post-grant review, on the basis of a lower legal standards than reexamination and additional grounds.

We will incur significant ongoing expenses in maintaining our patent portfolio. Should we lack the funds to maintain our patent portfolio or to enforce our rights against infringers, we could be adversely impacted. Moreover, the failure of any patents that may issue to us or our licensors to adequately protect our product candidates or technology could have an adverse impact on our business.

***We will not be able to seek and obtain protection for our intellectual property in all jurisdictions throughout the world, and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.***

Filing, prosecuting and defending patents on all of our product candidates throughout the world would be prohibitively expensive. Competitors may manufacture and sell our potential products in those foreign countries where we do not file for and obtain patent protection or where patent protection may be unavailable, not obtainable or ultimately not enforceable. 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 and, further, may be able to export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as that 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.

The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications. For posenacafator, dirocaftor and nesolicaftor, all of the statutory deadlines have passed. For certain patent applications related to our CFTR modulators, their use, and related technology, the relevant statutory deadlines have not yet expired. Thus, for each of these patent families, particularly those that we believe provide coverage for these product candidates, we will need to decide whether and where to pursue protection outside the United States by the relevant deadlines, and we will only have the opportunity to obtain patent protection in those jurisdictions where we file for protection, and prosecute and obtain issued claims.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The scope and available coverage thus may vary significantly. Outside of the United States, patents we own or license, if issued, may become subject to patent opposition in the European Patent Office or similar proceedings, which may result in loss of scope of some claims or loss of the entire patent. Participation in adversarial proceedings is very complex and expensive, and may divert our management's attention from our core business and may result in unfavorable outcomes that could adversely affect our ability to prevent third parties from competing with us.

The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. 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. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

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. For example, an April 2014 report from the Office of the United States Trade Representative identified a number of countries, including India and China, where challenges to the procurement and enforcement of patent rights have been reported. Several countries, including India and China, have been listed in the report every year since 1989. If we encounter difficulties in protecting our intellectual property rights in foreign jurisdictions, our business prospects could be substantially harmed.

Proceedings to enforce our patent rights, if obtained, in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

***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 any patents, should they issue, that we own or have exclusively licensed.
- We or our licensors or strategic collaborators might not have been the first to make the inventions covered by any issued patent or pending patent application that we own or have exclusively licensed.
- We or our licensors or strategic collaborators might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- Our pending patent applications may not lead to issued patents.
- Patents, should they issue, that we own or that we have exclusively licensed, if any, 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 additional proprietary technologies that are patentable.
- 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.

***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.***

The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business, our current and pending patent portfolio and future intellectual property strategy. 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.

***Obtaining and maintaining our 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.***

Periodic maintenance fees on any issued patent are due to be paid to the USPTO, the European Patent Office and other foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign national or international patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, 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. Non-compliance events that could result in abandonment or lapse of patent rights include, but are not limited to, failure to file non-provisional applications claiming priority to our provisional applications by the statutory deadlines, failure to timely file national and regional stage patent applications based on an international patent application, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, our competitors might be able to enter the market, which would have a material adverse effect on our business.

***The patent protection and patent prosecution for some of our product candidates is dependent or may be dependent in the future on third parties.***

While we normally seek and gain the right to fully prosecute the patents relating to our product candidates, there may be times when platform technology patents or product-specific patents that relate to our product candidates are controlled by our licensors or collaboration partners. In addition, our licensors and/or licensees and/or collaboration partners may have back-up rights to prosecute patent applications in the event that we do not do so or choose not to do so, and our licensees and/or collaboration partners may have the right to assume patent prosecution rights after certain milestones are reached. If any of our licensing partners fails to appropriately prosecute and maintain patent protection for patents covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products.

***We have entered into and may in the future enter into licenses to licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing a product candidate, if approved, that relied on such licensed intellectual property.***

We are currently a party to and may in the future be party to license agreements under which we are or will be granted rights to intellectual property that are important to our business. Certain of our existing and terminated license agreements impose, and we expect that future license agreements will impose on us, various diligence obligations, payment of milestones and/or royalties and other obligations, including, without limitation, patent prosecution, research and development and efforts to meet milestones under mutually-agreed development plans. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to continue to use the rights granted under the license, or develop or market products covered by the license. Our business could suffer, for example, if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms.

We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we cannot provide any assurances that third-party patents do not exist that might be enforced against our current product candidates or future products in the absence of such a license. We may fail to obtain any of these licenses on commercially reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business, and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation.

Licensing of intellectual property involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we license now or in the future prevent or impair our ability to maintain our licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

***We may be subject to litigation alleging that we are infringing the intellectual property rights of third parties or litigation or other adversarial proceedings seeking to invalidate our patents or other proprietary rights, and we may need to resort to litigation to protect or enforce our patents or other proprietary rights, all of which will be costly to defend, uncertain in its outcome and may prevent or delay development and commercialization efforts or otherwise harm our business.***

Our success also will depend, in part, on our refraining from infringing patents or otherwise violating intellectual property owned or controlled by others. Numerous patents and pending applications are owned by third parties in the fields in which we are developing product candidates, both in the United States and elsewhere. It is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to our product candidates and technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning and scope of patent claims. Moreover, because some patent applications are maintained in secrecy until the patents publish, we cannot be certain that third parties have not filed patent applications that cover our products and technologies. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale, importation or use of a current or future product candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications can, subject to certain limitations, be later amended in a manner that could cover our technologies, our future products or the manufacture or use of our future products. Pharmaceutical companies, biotechnology companies, universities, research institutions and others may have filed patent applications or have received, or may obtain, issued patents in the United States or elsewhere relating to aspects of our technology, including our products, processes for testing, manufacture, formulation or methods of use, including combination therapy. It is uncertain whether the issuance of any third-party patents will require us to alter our product candidates or processes, obtain licenses, or cease certain activities.

If patents issued to third parties contain blocking, dominating or conflicting claims we may choose to or, if such claims are ultimately determined to be valid, be required to obtain licenses to these patents or to develop or obtain alternative non-infringing technology and cease practicing those activities, including, potentially, the manufacture or marketing of any products deemed to infringe those patents. If any licenses are required, there can be no assurance that we will be able to obtain any such licenses on commercially favorable terms, if at all, and if these licenses are not obtained, we might be prevented from pursuing the development and commercialization of certain of our potential products entirely or for certain indications. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. Our failure to obtain a license to any technology that we may require to commercialize our products on favorable terms may have a material adverse impact on our business, financial condition and results of operations.

We may be exposed to, or threatened with, future litigation by third parties, including our competitors, having patent or other intellectual property rights alleging that our technologies, including our products, processes for manufacture or methods of use, including combination therapy, or other proprietary technologies infringe, either literally or under the doctrine of equivalents, their intellectual property rights. Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further 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. In the event of a successful infringement or other intellectual property claim against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our affected products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Parties making successful claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. We cannot provide any assurances that third-party patents do not exist which might be enforced against our products or product candidates, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties. Any of those occurrences would have a material adverse impact on our business.

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 or any other patent litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

***We may be involved in lawsuits to protect or enforce our intellectual property, which could be time consuming, expensive and unsuccessful, and issued patents covering our product candidates could be found invalid or unenforceable if challenged in court.***

Competitors may infringe our patents or the patents of our licensors, assuming patents issue from patent applications we own or license. Litigation, which could result in substantial costs to us (even if determined in our favor), may also be necessary to enforce any patents issued or licensed to us. The cost to us in initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management's attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question.

If we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates or our technology, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States and in most European countries, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, 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 USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of our products or certain aspects of our platform technology. Such a loss of patent protection could have a material adverse impact on our business. Patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without legally infringing our patents or other intellectual property rights.

An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing. Any of these outcomes would not only have an adverse effect on our patent portfolio but may also have an adverse effect on our business if we are unable to prevent the competitive activities of third parties.

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 or any other patent litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

***If we are not able to adequately prevent disclosure of trade secrets and other proprietary information, the value of our technology and products could be significantly diminished.***

We rely on trade secrets to protect technology especially where patent protection is not believed to be appropriate or obtainable or where patents have not issued. We attempt to protect our proprietary technology and processes, in part, with confidentiality agreements and assignment of invention agreements with our employees and confidentiality agreements with our consultants and certain contractors. There can be no assurance that these agreements will not be breached, that we would have adequate remedies for any breach, or that our trade secrets will not otherwise become known or be independently discovered by competitors. We may fail in certain circumstances to obtain the necessary confidentiality agreements, or their scope or term may not be sufficiently broad to protect our interests.

If our trade secrets or other intellectual property become known to our competitors, it could result in a material adverse effect on our business, financial condition and results of operations. To the extent that we or our consultants or research collaborators use intellectual property owned by others in work for us, disputes may also arise as to the rights to related or resulting know-how and inventions.

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

We enter into confidentiality and intellectual property assignment agreements with our employees, consultants, outside scientific advisors, and sponsored researchers. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. Moreover, we may not obtain these agreements in all circumstances.

Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

***We may be subject to claims that we or our employees or consultants have wrongfully used or disclosed alleged trade secrets of our employees' or consultants' former employers or their clients. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages and may lose valuable intellectual property rights or personnel.***

Many of our employees and consultants were previously or concurrently employed at universities or biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees, consultants or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could compromise our ability to commercialize, or prevent us from commercializing, our product candidates, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

### **Risks Related to Our Business Operations and Industry**

***Our future success depends on our ability to retain executives and to attract, retain and motivate key personnel in a competitive environment for skilled biotechnology personnel.***

Because of the specialized scientific nature of our business and the unique properties of our technology, our success is highly dependent upon our ability to attract and retain qualified scientific and technical personnel, consultants and advisors. We are dependent on the principal members of our scientific and management staff, particularly Ms. Meenu Chhabra, Ms. Sheila Wilson, Drs. Geoffrey Gilmartin, Benito Munoz and Marija Zecevic, who have extensive knowledge of and experience developing our technology. The loss of any of their services might significantly delay or prevent the achievement of our research, development and business objectives.

We may need to recruit a significant number of additional personnel in order to achieve our operating goals. In order to pursue our product development and marketing and sales plans, we may need to hire additional qualified scientific personnel to perform research and development, and preclinical studies, as well as personnel with expertise in clinical operations, clinical testing, government regulation, compliance, manufacturing, marketing and sales, which may strain our existing managerial, operational, regulatory compliance, financial and other resources. We also rely on consultants and advisors to assist in formulating our research and development strategy and adhering to complex regulatory requirements. We face strong competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities and other research institutions, many of which have greater financial and other resources than us. There can be no assurance that we will be able to attract and retain such individuals on acceptable terms, if at all. Additionally, our facilities are located in Massachusetts, which may make attracting and retaining qualified scientific and technical personnel from outside of Massachusetts difficult. The failure to attract and retain qualified personnel, consultants and advisors could have a material adverse effect on our business, financial condition and results of operations.

***As our product candidates advance through clinical trials we may experience difficulties in managing our growth and expanding our operations, including, without limitation, managing international clinical trials.***

We have limited experience in drug development. As our product candidates advance through preclinical studies and clinical trials, we will need to expand our development, regulatory and manufacturing capabilities or contract with other organizations to provide these capabilities for us. In the future, we expect to have to manage additional relationships with collaborators or partners, suppliers and other organizations, including, without limitation, international clinical trials. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

***We are exposed to potential product liability or similar claims, and insurance against these claims may not be sufficient to cover our liabilities, or may not be available to us at a reasonable rate in the future or at all.***

Our business exposes us to potential liability risks that are inherent in the testing, manufacturing and marketing of human therapeutic products. Clinical trials involve the testing of product candidates on human subjects or volunteers under a research plan, and carry a risk of liability for personal injury or death to patients due to unforeseen adverse side effects, improper administration of the product candidate, or other factors. Many of these patients are already seriously ill and are therefore particularly vulnerable to further illness or death. Our trials may include third party drugs taken with ours that could injure trial subjects for whose damages we would be liable and, even if we were not, we nevertheless may not be able to show or prove that our product was not a cause of the injury.

We carry clinical trial and product liability insurance. However, there can be no assurance that we will be able to obtain the amount of insurance necessary to cover potential claims or liabilities. We could be materially and adversely affected if we were required to pay damages or incur defense costs in connection with a claim outside the scope of indemnity or insurance coverage, if the indemnity is not performed or enforced in accordance with its terms, or if our liability exceeds the amount of applicable insurance. In addition, there can be no assurance that insurance, if obtained, will continue to be available on terms acceptable to us. Similar risks would exist upon the commercialization or marketing of any products by us or our collaborators.

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

- decreased demand for our product;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial volunteers or subjects;
- costs of litigation;
- distraction of management; and
- substantial monetary awards to plaintiffs.

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

***We may become involved in securities class action litigation that could divert management's attention and adversely affect our business and could subject us to significant liabilities.***

The stock markets in general and the market for pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. 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, including limited trading volume and impact of COVID-19 on market performance. In addition to the risks described in this "Risk Factors" section of this Annual Report, market and industry factors may cause the market price and demand for our common stock to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from selling their shares at or above the price paid for the shares and may otherwise negatively affect the liquidity of our shares.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies generally experience significant stock price volatility. We may become involved in this type of litigation in the future. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms.

Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our business practices. Defending against litigation is costly and time-consuming, and could divert our management's attention and our resources. Furthermore, during the course of litigation, there could be negative public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a negative effect on the market price of our stock.

***We must comply with environmental laws and regulations, and failure to comply with these laws and regulations could expose us to significant liabilities.***

We use hazardous chemicals and biological materials in certain aspects of our business and are subject to a variety of U.S. federal, state and local laws and regulations governing the use, generation, manufacture, distribution, storage, handling, treatment and disposal of these materials. Although we believe our safety procedures for handling and disposing of these materials and waste products comply with these laws and regulations, we cannot eliminate the risk of accidental injury or contamination from the use, manufacture, distribution, storage, handling, treatment or disposal of hazardous materials. In the event of contamination or injury, or failure to comply with environmental, occupational health and safety and export control laws and regulations, we could be held liable for any resulting damages and any such liability could exceed our assets and resources, including any available insurance.

***Our business and operations would suffer in the event of system failures.***

Our internal computer systems and those of our current and future contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we are not aware of any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture our product candidates and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

***We might not be able to utilize all or a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.***

Our net operating loss, or NOL, carryforwards could expire unused and be unavailable to offset future income tax liabilities because of their limited duration or because of restrictions under U.S. tax law. Our NOLs generated in tax years beginning on or before December 31, 2017 are only permitted to be carried forward for 20 years under applicable U.S. tax law. Under the Tax Cuts and Jobs Act, or the Tax Act, our federal NOLs generated in tax years beginning after December 31, 2017 are permitted to be carried forward indefinitely under applicable U.S. tax law. Also under the Tax Act, as modified by the CARES Act, the deductibility of federal NOLs, particularly for tax years beginning after December 31, 2020, may be limited. It is uncertain if and to what extent various states will conform to the Tax Act and the CARES Act. As of December 31, 2019, we had federal and state NOL carryforwards of \$308.8 million and \$295.4 million, respectively, of which less than \$0.1 million and \$10.7 million begin to expire in 2026 and 2030, respectively. As of December 31, 2019, we also had federal and state research and development tax credit carryforwards of \$11.6 million and \$4.1 million, respectively, of which less than \$0.1 million begin to expire in 2027 and 2025, respectively.

These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an “ownership change,” which is generally defined as a greater than 50% change, by value, in its equity ownership over a 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. We have not determined if we have experienced Section 382 ownership changes in the past and if a portion of our net operating loss and tax credit carryforwards are subject to an annual limitation under Section 382. In addition, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If we determine that an ownership change has occurred and our ability to use our historical net operating loss and tax credit carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations. We have a full valuation allowance against our net deferred tax assets.

Accordingly, there is a risk that due to changes under the Tax Act, the CARES Act, an ownership change, regulatory changes or other unforeseen reasons, our existing NOLs could expire or otherwise be unavailable to offset future income tax liabilities.

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

As of June 30, 2020, we had 41 full-time employees. We may need to substantially expand our managerial, commercial, financial, manufacturing and other personnel resources in order to manage our operations and prepare for the commercialization of our triple combination product, if approved. Our management and personnel systems and facilities currently in place may not be adequate to support this future growth. In addition, we may not be able to recruit and retain qualified personnel in the future, particularly for sales and marketing positions, due to competition for personnel among pharmaceutical businesses, and the failure to do so could have a significant negative impact on our future product revenues and business results. Our need to effectively manage our operations, growth and various projects requires that we:

- continue the hiring and training of an effective commercial organization in anticipation of the potential approval of our triple combination product, and establish appropriate systems, policies and infrastructure to support that organization;
- ensure that our consultants and other service providers successfully carry out their contractual obligations, provide high quality results, and meet expected deadlines;
- continue to carry out our own contractual obligations to our licensors and other third parties; and

- continue to improve our operational, financial and management controls, reporting systems and procedures.
- We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our development and commercialization goals.

***We may not be able to manage our business effectively if we are unable to attract and retain key personnel.***

We may not be able to attract or retain qualified management and commercial, scientific and clinical personnel due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. If we are not able to attract and retain necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the skills and leadership of our management team, including Meenu Chhabra, our Chief Executive Officer. Our senior management may terminate their employment with us at any time. If we lose one or more members of our senior management team, our ability to successfully implement our business strategy could be seriously harmed. Replacing these employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate additional key personnel. We do not maintain “key person” insurance for any of our executives or other employees.

**Risks Related to the Ownership of Our Common Stock**

***Our stock price has been and will likely continue to be volatile and an active, liquid and orderly trading market may not develop for our common stock. As a result, you may not be able to resell your shares at or above your purchase price.***

The market price of our common stock may fluctuate substantially as a result of many factors, some of which are beyond our control. These fluctuations could cause you to lose all or part of the value of your investment in our common stock. Factors that could cause fluctuations in the market price of our common stock include the following:

- the development status of our product candidates and when our products receive regulatory approval or are granted special regulatory designations, or lose such designations;
- the results, and the timing of results, of our preclinical studies and clinical trials, including, without limitation, the publication or delay in publication of preliminary, interim or final results, adverse events, side effects, safety or efficacy data or other information;
- the support and approval, if any, that we receive from our collaboration partners, the TDN, CTN, HIT-CF and other interested parties;
- performance of third parties on whom we rely to conduct preclinical studies, manage our clinical trials, and manufacture our products, product components and product candidates, including their ability to comply with regulatory requirements;
- the success of, and fluctuation in, the sales of our product candidates, if approved;
- our execution of our sales and marketing, manufacturing and other aspects of our business plan;
- results of operations that vary from those of our competitors and the expectations of securities analysts and investors;
- changes in expectations as to our future financial performance, including financial estimates by securities analysts and investors;
- changes in expectations as to our future preclinical or clinical results or prospects, including those of securities analysts and investors;
- our announcement of significant licensing or collaboration arrangements, or the termination of such arrangements;
- our announcement of significant contracts, acquisitions, or capital commitments;
- announcements by our competitors of competing products, clinical data, or other initiatives, including, without limitation, those that lead to the development of a new standard of care;
- announcements by third parties of significant claims or proceedings against us;
- regulatory and reimbursement developments in the United States and abroad;

- changes in the structure of healthcare payment systems;
- future sales of our common stock or debt securities;
- ability to meet minimum listing requirements of the Nasdaq Stock Market;
- additions or departures of key personnel; and
- general domestic and international economic conditions unrelated to our performance.

The stock market in general, and the Nasdaq Global Market and life sciences companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance these companies, including very recently in connection with the ongoing COVID-19 pandemic, which has resulted in decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. Broad market and industry factors, including potentially worsening economic conditions and other adverse effects or developments relating to the ongoing COVID-19 pandemic, may negatively. These broad market factors may adversely affect the market price of our common stock, regardless of our actual operating performance. In the past, following periods of volatility in the market price of a company's securities, securities class action litigation has often been instituted. A securities class action suit against us could result in significant liabilities and, regardless of the outcome, could result in substantial costs and the diversion of our management's attention and resources.

Although our common stock is listed on The Nasdaq Global Market, trading volume in our common stock has been limited and an active trading market for our shares may never develop or be sustained. If an active market for our common stock does not develop, you may be unable to sell your shares when you wish to sell them or at a price that you consider attractive or satisfactory. The lack of an active market may also adversely affect our ability to raise capital by selling securities in the future or impair our ability to license or acquire other product candidates, businesses or technologies using our shares as consideration.

***Although we have regained compliance with the requirements for continued listing on The Nasdaq Global Market, we could in the future fail to satisfy the Nasdaq continued listing requirements and our common stock could be delisted from trading, which would adversely affect the liquidity of our common stock and our ability to access the capital markets.***

Our common stock is listed on the Nasdaq Global Market. If we fail to satisfy the continued listing requirements of The Nasdaq Stock Market, or Nasdaq, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock. Such a delisting would have a negative effect on the price of our common stock and would impair the ability to sell or purchase our common stock when persons wish to do so.

On August 26, 2019, we received a letter from the Listing Qualification Department of The Nasdaq Stock Market, or the Staff, notifying us that, for the last 30 consecutive business days, our common stock had not maintained the minimum bid price requirement of \$1.00 per share pursuant to Nasdaq Listing Rule 5450(a)(1).

We were provided an initial period of 180 calendar days, or until February 24, 2020, to regain compliance. On December 2, 2019, we issued a press release announcing that we received a letter dated November 27, 2019 from the Staff notifying us that we had regained compliance with the requirement of The Nasdaq Global Market to maintain a minimum bid price of \$1.00 per share.

Although we have regained compliance with the Nasdaq listing requirements, Nasdaq will continue to monitor our ongoing compliance. No assurance can be given that we will meet applicable Nasdaq continued listing standards. Failure to meet applicable Nasdaq continued listing standards could result in a delisting of our common stock, which could materially reduce the liquidity of our common stock and result in a corresponding material reduction in the price of our common stock. In addition, delisting could harm our ability to raise capital through alternative financing sources on terms acceptable to us, or at all, and may result in the inability to advance our drug development programs, potential loss of confidence by investors and employees, and fewer business development opportunities.

***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 depend in part on the research and reports that securities or industry analysts or investors publish about us or our business. We do not have any control over these analysts or investors. If one or more of the analysts who covers us downgrades our stock or analysts or investors publish inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, demand for our stock could decrease, which could cause our stock price and trading volume to decline.

***A significant portion of our total outstanding shares may be sold into the market. This could cause the market price of our common stock to drop significantly, even if our business is doing well.***

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market believes that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly. All of our outstanding shares of common stock are available for sale in the public market, subject only to the restrictions of Rule 144 under the Securities Act in the case of our affiliates.

In addition, we have filed registration statements on Form S-8 registering the issuance of shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under these registration statements are available for sale in the public market subject to vesting arrangements and exercise of options, as well as Rule 144 in the case of our affiliates.

In addition, a holder of our common stock, or their transferee, has rights, subject to some conditions, to require us to file one or more registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If we were to register the resale of these shares, they could be freely sold in the public market. If these additional shares are sold, or if it is believed that they will be sold, in the public market, the trading price of our common stock could decline.

***Raising additional funds by issuing securities may cause dilution to existing stockholders and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights.***

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, grants and license and development agreements in connection with any collaborations. We do not have any committed external source of funds. To the extent that we raise additional capital by issuing equity securities, our existing stockholders' ownership will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. Any debt financing that we enter into may involve covenants that restrict our operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of our assets as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

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

We are an emerging growth company and we are taking advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We will remain an emerging growth company until December 31, 2021.

Even following the termination of our status as an emerging growth company, we will be able to take advantage of the reduced disclosure requirements applicable to smaller reporting companies (as that term is defined in Rule 12b-2 of the Exchange Act) and, in particular, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. To the extent that we are no longer eligible to use exemptions from various reporting requirements, we may be unable to realize our anticipated cost savings from these exemptions, which could have a material adverse impact on our operating results.

***If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.***

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, the Sarbanes-Oxley Act of 2002 and the rules and regulations of The Nasdaq Global Market. Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to perform system and process evaluation and testing of our internal control over financial reporting to allow our management to report on the effectiveness of our internal control over financial reporting in this Form 10-Q. However, while we remain an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. When we cease to be an emerging growth company, we will be required to incur substantial additional professional fees and internal costs to expand our accounting and finance functions in order to include such attestation report.

We may in the future discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all error and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system’s objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected. If we identify one or more material weaknesses in our internal controls, investors could lose confidence in the reliability of our financial statements, the market price of our stock could decline and we could be subject to sanctions or investigations by The Nasdaq Global Market, the SEC or other regulatory authorities.

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

We are subject to the periodic reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably ensure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management and 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 as well as 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 and will be 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.

***Operating as a public company has significantly increased our costs and requires our management to devote substantial time to compliance efforts.***

As a public company, we are incurring and will continue to incur significant legal, accounting, insurance and other expenses that we did not incur as a private company. The Dodd-Frank Act and the Sarbanes-Oxley Act, as well as related rules implemented by the SEC and The Nasdaq Stock Market, have required changes in corporate governance practices of public companies. In addition, rules that the SEC is implementing or is required to implement pursuant to the Dodd-Frank Act are expected to require additional changes. We expect that compliance with these and other similar laws, rules and regulations, including compliance with Section 404 of the Sarbanes-Oxley Act, will substantially increase our expenses, including our legal and accounting costs, and make some activities more time-consuming and costlier. We also expect these laws, rules and regulations to make it more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage, which may make it more difficult for us to attract and retain qualified persons to serve on our board of directors or as officers. Additionally, we are currently searching for a new senior financial officer, and we expect that we may need to hire additional accounting, finance and other personnel in connection with our efforts to comply with the requirements of being a public company, and our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements may increase our legal and financial compliance costs and may make some activities more time-consuming and costlier. Although the JOBS Act may for a limited period of time somewhat lessen the cost of complying with these additional regulatory and other requirements, we nonetheless expect a continued increase in legal, accounting, insurance and certain other expenses in the future, which may negatively impact our business, results of operations and financial condition.

***Anti-takeover provisions in our charter documents could discourage, delay or prevent a change in control of our company and may affect the trading price of our common stock.***

Our amended and restated certificate of incorporation and amended and restated by-laws and the Delaware General Corporation Law contain provisions that may enable our board of directors to resist a change in control of our company even if a change in control were to be considered favorable by you and other stockholders. These provisions:

- provide that directors can be removed only for cause, and then only by a supermajority stockholder vote;
- establish advance notice requirements for nominating directors and proposing matters to be voted on by stockholders at stockholder meetings;

- require majority stockholder voting to effect certain amendments to our certificate of incorporation and by-laws;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors;
- prohibit stockholder action by written consent;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorize our board of directors to modify, alter or repeal our amended and restated by-laws, subject to any limitations set forth therein;
- require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation; and
- require supermajority votes of the holders of our common stock to amend our amended and restated by-laws, unless such amendments have been recommended to the stockholders, in which case only a majority vote is necessary.

In addition, we are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A “business combination” includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An “interested stockholder” is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation’s voting stock.

A Delaware corporation may “opt out” of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or by-laws resulting from a stockholders’ amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

***We do not expect to pay any dividends on our common stock for the foreseeable future.***

We currently expect to retain all future earnings, if any, for future operations, expansion and repayment of debt and have no current plans to pay any cash dividends to holders of our common stock for the foreseeable future. Any decision to declare and pay dividends in the future will be made at the discretion of our board of directors and will depend on, among other things, our results of operations, financial condition, cash requirements, contractual restrictions and other factors that our board of directors may deem relevant. As a result, you may not receive any return on an investment in our common stock unless you sell our common stock for a price greater than that which you paid for it.

*Our by-laws provide that the Court of Chancery of the State of Delaware will be 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, employees or stockholders.*

Our by-laws provide that the Court of Chancery of the State of Delaware is the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our by-laws, 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, other employees or stockholders (including beneficial owners), which may discourage such lawsuits against us and our directors, officers, other employees or stockholders (including beneficial owners). Alternatively, if a court were to find the choice of forum provision contained in our by-laws 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.

**Item 2. Unregistered Sales of Equity Securities and Use of Proceeds**

None.

**Item 3. Defaults Upon Senior Securities**

None.

**Item 4. Mine Safety Disclosures**

Not applicable.

**Item 5. Other Information**

None.

**Item 6. Exhibits**

Exhibit No.	Exhibit Description	Incorporated by Reference			
		Form	File No.	Exhibit No.	Filing Date
3.1	<a href="#">Fifth Amended and Restated Certificate of Incorporation of the Registrant.</a>	S-3	333-228529	3.1	November 23, 2018
3.2	<a href="#">Second Amended and Restated By-laws of the Registrant.</a>	S-1/A	333-208735	3.4	February 1, 2016
4.1	<a href="#">Specimen Common Stock Certificate.</a>	S-1/A	333-208735	4.1	February 1, 2016
4.2	<a href="#">Third Amended and Restated Stockholders' Agreement of the Registrant.</a>	S-1/A	333-208735	4.2	February 1, 2016
4.3	<a href="#">Form of Preferred Stock Warrant.</a>	S-1	333-208735	4.3	December 23, 2015
4.4	<a href="#">Form of Senior Indenture</a>	S-3	333-228529	4.6	November 23, 2018
4.5	<a href="#">Form of Subordinated Indenture</a>	S-3	333-228529	4.7	November 23, 2018
31.1	<a href="#">Certification of Principal Executive Officer and Interim Financial Officer pursuant to Exchange Act rules 13a-14 or 15d-14 under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</a>				Filed herewith
32.1*	<a href="#">Certification of Principal Executive Officer and Interim Financial Officer and Principal Accounting Officer pursuant to 18 U.S.C. Section 1350., as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</a>				Furnished herewith
101.INS	XBRL Instance Document.				Filed herewith
101.SCH	XBRL Taxonomy Extension Schema Document.				Filed herewith
101.CAL	XBRL Taxonomy Extension Calculation Document.				Filed herewith
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.				Filed herewith
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document.				Filed herewith
101.PRE	XBRL Taxonomy Extension Presentation Link Document.				Filed herewith
104	Cover Page Interactive Data File—the cover page interactive data is embedded within the XBRL document or included within the Exhibit 101 attachments.				Filed herewith

\*This certification is being furnished herewith and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing of the Registrant under the Securities Act of 1933, as amended, or Securities Exchange Act of 1934, as amended, whether made before or after the date hereof, regardless of any general incorporation language 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.

### **PROTEOSTASIS THERAPEUTICS, INC.**

Date: August 6, 2020

By: /s/ Meenu Chhabra  
Meenu Chhabra  
President and Chief Executive Officer  
(Principal Executive Officer and Interim Principal Financial Officer)

## Certification

I, Meenu Chhabra, certify that:

1. I have reviewed this quarterly report on Form 10-Q for the period ended June 30, 2020 of Proteostasis Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 6, 2020

/s/ Meenu Chhabra

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Meenu Chhabra  
President and Chief Executive Officer  
(Principal Executive Officer and Interim Principal Financial Officer)

**CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350,  
AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the quarterly report on Form 10-Q of Proteostasis Therapeutics, Inc. (the "Company") for the period ended June 30, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Meenu Chhabra, President and Chief Executive Officer (Principal Executive Officer and Interim Principal Financial Officer) hereby certify, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350, that to my knowledge:

- 1) the Report which this statement accompanies fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and
- 2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 6, 2020

/s/ Meenu Chhabra

Meenu Chhabra  
President and Chief Executive Officer  
(Principal Executive Officer and Interim Principal Financial Officer)

In connection with the quarterly report on Form 10-Q of Proteostasis Therapeutics, Inc. (the "Company") for the period ended June 30, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Michael L. Alfieri, Head of Finance (Principal Accounting Officer) hereby certify, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350, that to my knowledge:

- 3) the Report which this statement accompanies fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and
- 4) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 6, 2020

/s/ Michael L. Alfieri

Michael L. Alfieri  
Head of Finance  
(Principal Accounting Officer)