UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2022

OR

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

For the transition period from to

Commission File Number: 001-39527

PRELUDE THERAPEUTICS INCORPORATED
(Exact Name of Registrant as Specified in its Charter)

Delaware (State or other jurisdiction of incorporation or organization)	**81-1384762** (I.R.S. Employer Identification No.)
200 Powder Mill Road **Wilmington, Delaware** (Address of principal executive offices)	**19803** (Zip Code)

Registrant's telephone number, including area code: (302) 467-1280

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	PRLD	The Nasdaq Stock Market LLC

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

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

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

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

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

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

As of November 8, 2022, the registrant had 47,859,813 shares of voting and non-voting common stock, $0.0001 par value per share, outstanding.

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PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

PRELUDE THERAPEUTICS INCORPORATED

BALANCE SHEETS
(UNAUDITED)

(in thousands, except share data)	September 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 52,022	$ 31,828
Marketable securities	172,021	259,405
Prepaid expenses and other current assets	2,850	3,882
Total current assets	226,893	295,115
Restricted cash	4,044	4,044
Property and equipment, net	5,110	3,929
Right-of-use asset	1,354	1,707
Other assets	4,926	303
Total assets	$ 242,327	$ 305,098
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 10,250	$ 7,840
Accrued expenses and other current liabilities	9,922	9,621
Operating lease liability	1,388	1,740
Total current liabilities	21,560	19,201
Other liabilities	3,360	—
Total liabilities	24,920	19,201
Commitments (Note 8)		
Stockholders' equity:		
Voting common stock, $0.0001 par value: 487,149,741 shares authorized; 36,444,776 and 36,200,299 shares issued and outstanding at September 30, 2022 and December 31, 2021, respectively	4	4
Non-voting common stock, $0.0001 par value; 12,850,259 shares authorized; 11,402,037 and 11,402,037 shares issued and outstanding at September 30, 2022 and December 31, 2021, respectively	1	1
Additional paid-in capital	525,682	505,723
Accumulated other comprehensive income (loss)	(2,363)	(711)
Accumulated deficit	(305,917)	(219,120)
Total stockholders' equity	217,407	285,897
Total liabilities and stockholders' equity	$ 242,327	$ 305,098

See accompanying notes to unaudited interim financial statements.

PRELUDE THERAPEUTICS INCORPORATED

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS (UNAUDITED)

(in thousands, except share and per share data)	Three Months Ended September 30, 2022	Three Months Ended September 30, 2021	Nine Months Ended September 30, 2022	Nine Months Ended September 30, 2021
Operating expenses:				
Research and development	$ 22,889	$ 22,721	$ 67,020	$ 61,600
General and administrative	7,517	8,115	23,135	19,125
Total operating expenses	30,406	30,836	90,155	80,725
Loss from operations	(30,406)	(30,836)	(90,155)	(80,725)
Other income, net	448	149	3,358	1,873
Net loss	$ (29,958)	$ (30,687)	$ (86,797)	$ (78,852)
Per share information:				
Net loss per share of common stock, basic and diluted	$ (0.63)	$ (0.66)	$ (1.84)	$ (1.72)
Weighted average common shares outstanding, basic and diluted	47,449,811	46,330,794	47,265,712	45,841,049
Comprehensive loss				
Net loss	$ (29,958)	$ (30,687)	$ (86,797)	$ (78,852)
Unrealized gain (loss) on marketable securities, net of tax	(69)	(176)	(1,652)	(176)
Comprehensive loss	$ (30,027)	$ (30,863)	$ (88,449)	$ (79,028)

See accompanying notes to unaudited interim financial statements.

PRELUDE THERAPEUTICS INCORPORATED

STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (DEFICIT)
(UNAUDITED)

	Stockholders' equity (deficit)							
	Voting common stock		Non-voting common stock			Accumulated Other		
(in thousands, except shares)	Shares	Amount	Shares	Amount	Additional paid-in capital	Comprehensive Income (Loss)	Accumulated deficit	Total
Balance at January 1, 2022	36,200,299	$ 4	11,402,037	$ 1	$ 505,723	$ (711)	$ (219,120)	$ 285,897
Issuance of common stock upon exercise of stock options	93,032	—	—	—	153	—	—	153
Unrealized gain (loss) on marketable securities	—	—	—	—	—	(1,602)	—	(1,602)
Stock-based compensation expense	—	—	—	—	6,829	—	—	6,829
Net loss	—	—	—	—	—	—	(29,465)	(29,465)
Balance at March 31, 2022	36,293,331	$ 4	11,402,037	$ 1	$ 512,705	$ (2,313)	$ (248,585)	$ 261,812
Issuance of common stock upon exercise of stock options	31,253	—	—	—	59	—	—	59
Issuance of common stock under ESPP	68,080	—	—	—	300	—	—	300
Unrealized gain (loss) on marketable securities	—	—	—	—	—	19	—	19
Stock-based compensation expense, net of forfeitures of restricted stock awards	(23,416)	—	—	—	6,028	—	—	6,028
Net loss	—	—	—	—	—	—	(27,374)	(27,374)
Balance at June 30, 2022	36,369,248	$ 4	11,402,037	$ 1	$ 519,092	$ (2,294)	$ (275,959)	$ 240,844
Issuance of common stock upon exercise of stock options	75,528	—	—	—	148	—	—	148
Unrealized gain (loss) on marketable securities	—	—	—	—	—	(69)	—	(69)
Stock-based compensation expense, net of forfeitures of restricted stock awards	—	—	—	—	6,442	—	—	6,442
Net loss	—	—	—	—	—	—	(29,958)	(29,958)
Balance at September 30, 2022	36,444,776	$ 4	11,402,037	$ 1	$ 525,682	$ (2,363)	$ (305,917)	$ 217,407

See accompanying notes to unaudited interim financial statements.

PRELUDE THERAPEUTICS INCORPORATED

STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (DEFICIT) (CONTINUED) (UNAUDITED)

	Stockholders' equity (deficit)							
	Voting common stock		Non-voting common stock			Accumulated Other		
(in thousands, except shares)	Shares	Amount	Shares	Amount	Additional paid-in capital	Comprehensive Income (Loss)	Accumulated deficit	Total
Balance at January 1, 2021	32,595,301	$ 3	11,110,371	$ 1	$ 319,605	$ —	$ (107,426)	$ 212,183
Issuance of common stock upon exercise of stock options	210,274	—	—	—	386	—	—	386
Sale of common stock, net of offering costs of $739	2,583,334	1	291,666	—	161,411	—	—	161,412
Stock-based compensation expense	—	—	—	—	3,886	—	—	3,886
Net loss	—	—	—	—	—	—	(21,300)	(21,300)
Balance at March 31, 2021	35,388,909	$ 4	11,402,037	$ 1	$ 485,288	$ —	$ (128,726)	$ 356,567
Issuance of common stock upon exercise of stock options	247,786	—	—	—	422	—	—	422
Stock-based compensation expense	—	—	—	—	4,237	—	—	4,237
Net loss	—	—	—	—	—	—	(26,865)	(26,865)
Balance at June 30, 2021	35,636,695	$ 4	11,402,037	$ 1	$ 489,947	$ —	$ (155,591)	$ 334,361
Issuance of common stock upon exercise of stock options	153,064	—	—	—	711	—	—	711
Unrealized gain(loss) on marketable securities	—	—	—	—	—	(176)		(176)
Stock-based compensation expense	—	—	—	—	7,033	—	—	7,033
Net loss	—	—	—	—	—	—	(30,687)	(30,687)
Balance at September 30, 2021	35,789,759	$ 4	11,402,037	$ 1	$ 497,691	$ (176)	$ (186,278)	$ 311,242

See accompanying notes to unaudited interim financial statements.

PRELUDE THERAPEUTICS INCORPORATED

STATEMENTS OF CASH FLOWS
(UNAUDITED)

(in thousands)	Nine months ended September 30, 2022	2021
Cash flows used in operating activities:		
Net loss	$ (86,797)	$ (78,852)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	962	625
Noncash lease expense	1,281	928
Stock-based compensation	19,299	15,156
Amortization of premium and discount on marketable securities, net	2,770	356
Changes in operating assets and liabilities:		
Prepaid expenses and other current and long-term assets	(3,591)	(2,532)
Accounts payable	2,893	7,834
Accrued expenses and other liabilities	3,661	(393)
Operating lease liabilities	(1,280)	(951)
Net cash used in operating activities	(60,802)	(57,829)
Cash flows provided by (used in) investing activities:		
Purchases of marketable securities	(85,972)	(259,973)
Proceeds from maturities of marketable securities	168,934	—
Purchases of property and equipment	(2,626)	(2,026)
Net cash provided by (used in) investing activities	80,336	(261,999)
Cash flows provided by financing activities:		
Proceeds from the sale of common stock, net of offering costs	—	161,424
Proceeds from the issuance of common stock under ESPP	300	—
Proceeds from the issuance of common stock in connection with the exercise of stock options	360	1,519
Net cash provided by financing activities	660	162,943
Net increase in cash and cash equivalents	20,194	(156,885)
Cash, cash equivalents, and restricted cash at beginning of period	35,872	218,309
Cash, cash equivalents, and restricted cash at end of period	$ 56,066	$ 61,424
Supplemental disclosures:		
Operating lease right-of-use assets obtained in exchange for operating lease liabilities	$ 928	$ 567
Property and equipment in accounts payable	$ 323	$ 97
Unrealized loss on marketable securities	$ (1,652)	$ (176)

See accompanying notes to unaudited interim financial statements.

PRELUDE THERAPEUTICS INCORPORATED

NOTES TO UNAUDITED INTERIM FINANCIAL STATEMENTS

1. Background

Prelude Therapeutics Incorporated (the "Company") was incorporated in Delaware on February 5, 2016 and is a clinical-stage fully integrated oncology company built on a foundation of drug discovery excellence to deliver novel precision cancer medicines to underserved patients. Since beginning operations, the Company has devoted substantially all its efforts to research and development, conducting preclinical and clinical studies, recruiting management and technical staff, administration, and raising capital.

2. Risks and liquidity

The Company is subject to a number of risks common to early-stage companies in the biotechnology industry. Principal among these risks are the uncertainties in the development process, development of the same or similar technological innovations by competitors, protection of proprietary technology, dependence on key personnel, compliance with government regulations and approval requirements, and the need to obtain additional financing to fund operations. Product candidates currently under development will require significant additional research and development efforts, including extensive pre-clinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel infrastructure, and extensive compliance-reporting capabilities. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's technology will be obtained, that any products developed will obtain necessary government regulatory approval, or that any approved products will be commercially viable. The Company operates in an environment of rapid change in technology and substantial competition from pharmaceutical and biotechnology companies. In addition, the Company is dependent upon the services of its employees, consultants and contractors.

Since its inception, the Company has incurred operating losses and has an accumulated deficit of $305.9 million at September 30, 2022. The Company has no revenue to date and devotes its efforts to research and development. The Company anticipates incurring additional losses until such time, if ever, that it can generate significant sales of its product candidates currently in development.

The Company believes that its cash, cash equivalents, and marketable securities as of September 30, 2022 will be sufficient to fund its operating expenses and capital expenditure requirements into the fourth quarter of 2024.

To fund its operating expenses and capital expenditure requirements after that date, the Company plans to seek additional funding through public or private equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into strategic alliances or other arrangements on favorable terms, or at all. The terms of any financing may adversely affect the holdings or the rights of the Company's stockholders. If the Company is unable to obtain funding, the Company could be required to delay, reduce or eliminate research and development programs, product portfolio expansion or future commercialization efforts, which could adversely affect its business prospects.

On March 10, 2020, the World Health Organization characterized the novel COVID-19 virus as a global pandemic. There continues to be significant uncertainty as to the effects of this disease and emerging variants which may, among other things, materially impact the Company's planned clinical trials. This pandemic or outbreak could result in difficulty securing clinical trial site locations, contract research organizations ("CROs"), and/or trial monitors and other critical vendors and consultants supporting the trial. In addition, outbreaks or the perception of an outbreak near a clinical trial site location could impact the Company's ability to enroll patients. These situations, or others associated with the ongoing COVID-19 pandemic, could cause delays in the Company's clinical trial plans and could increase expected costs, all of which could have a material adverse effect on the Company's business and its financial condition. At the current time, the Company is unable to quantify the potential effects of this pandemic on its future financial statements.

3. Summary of significant accounting policies

The summary of significant accounting policies included in the Company's financial statements for the year ended December 31, 2021 can be found in "Note 3. Summary of significant accounting policies" of the Company's Form 10-K filed with the Securities and Exchange Commission (the "SEC") on March 17, 2022. Those policies have not materially changed, except as set forth below.

Basis of presentation

The accompanying unaudited interim financial statements have been prepared in accordance with generally accepted accounting principles ("GAAP") for interim financial information, the instructions to Form 10-Q and Article 10 of Regulation S-X. They do not include all of the information and notes required by GAAP for complete financial statements. In the opinion of management, all adjustments (consisting of normal recurring accruals) considered necessary for a fair presentation have been included. Operating results for the three and nine months ended September 30, 2022 are not necessarily indicative of the results that may be expected for the year ending December 31, 2022. The accompanying unaudited interim financial statements should be read in conjunction with the annual audited financial statements and related notes as of and for the year ended December 31, 2021 found in the Form 10-K filed with the SEC on March 17, 2022. Any reference in these notes to applicable guidance is meant to refer to GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

Use of estimates

The preparation of the unaudited interim financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and contingent liabilities at the date of the unaudited interim financial statements and the reported amounts of expenses during the reporting period. Actual results could differ from those estimates.

Estimates and assumptions are periodically reviewed and the effects of the revisions are reflected in the accompanying unaudited interim financial statements in the period they are determined to be necessary. The most significant estimate relates to accrued clinical trial expenses.

Income taxes

Based upon the historical and anticipated future losses, management has determined that the deferred tax assets generated by net operating losses and research and development credits do not meet the more likely than not threshold for realizability. Accordingly, a full valuation allowance has been recorded against the Company's net deferred tax assets as of September 30, 2022 and December 31, 2021.

Cash, Cash Equivalents and Restricted cash

The Company's cash equivalents include short-term highly liquid investments with an original maturity of 90 days or less when purchased and are carried at fair value in the accompanying balance sheets.

Restricted cash comprises a letter of credit for the benefit of the landlord in connection with the Company's Chestnut Run Lease. See Note 8 for further details.

The following table provides a reconciliation of cash and cash equivalents and restricted cash reported within the balance sheet that total to the amounts shown in the statement of cash flows:

(in thousands)	**September 30, 2022**	**December 31, 2021**
Cash and cash equivalents	$ 52,022	$ 31,828
Restricted cash	4,044	4,044
Total cash, cash equivalents, and restricted cash shown in statement of cash flows	$ 56,066	$ 35,872

Marketable Securities

The Company's marketable securities consist of investments in corporate debt securities and United States, or U.S., government debt securities that are classified as available-for-sale. The securities are carried at fair value with the unrealized gains and losses, net of tax, included in accumulated other comprehensive income (loss), a component of stockholders' equity (deficit). Realized gains and losses as well as credit losses, if any, on marketable securities are included in the Company's statements of operations. The Company classifies marketable securities that are available for use in current operations as current assets on the balance sheets.

Net Loss Per Share

Basic net loss per share of common stock is computed by dividing net loss by the weighted-average number of shares of common stock outstanding during each period. The weighted-average number of shares of common stock outstanding used in the basic net loss per share calculation does not include unvested restricted stock awards as these instruments are considered contingently issuable shares until they vest. Diluted net loss per share of common stock includes the effect, if any, from the potential exercise of securities, such as stock options, and the effect from unvested restricted stock awards and restricted stock units which would result in the issuance of incremental shares of common stock. For diluted net loss per share, the weighted-average number of shares of common stock is the same for basic net loss per share due to the fact that when a net loss exists, dilutive securities are not included in the calculation as the impact is anti-dilutive. The Company's unvested restricted stock awards entitle the holder to participate in dividends and earnings of the Company, and, if the Company were to recognize net income, it would have to use the two-class method to calculate earnings per share. The two-class method is not applicable during periods with a net loss, as the holders of the unvested restricted stock awards have no obligation to fund losses.

The following potentially dilutive securities have been excluded from the computation of diluted weighted-average shares of common stock outstanding, as they would be anti-dilutive:

	September 30,	
	2022	**2021**
Unvested restricted stock awards	271,965	717,698
Unvested restricted stock units	170,000	25,000
Stock options	9,197,528	8,091,689
Employee stock purchase plan	46,560	8,742
	9,686,053	8,843,129

Amounts in the above table reflect the common stock equivalents.

Recently Issued Accounting Pronouncements

Emerging Growth Company Status

The Company is an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act, until such time as those standards apply to private companies. The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that it (i) is no longer an emerging growth company or (ii) affirmatively and irrevocably opts out of the extended transition period provided in the JOBS Act. As a result, these unaudited interim financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

Recently Adopted Accounting Pronouncements

In June 2016, the FASB issued ASU No. 2016-13, "*Financial Instruments-Credit Losses: Measurement of Credit Losses on Financial Instruments*" which has subsequently been amended by ASU No. 2019-04, ASU No. 2019-05, ASU No. 2019-10, ASU No. 2019-11, and ASU No. 2020-03 ("ASU 2016-03"). This guidance replaces the incurred loss impairment methodology under current U.S. GAAP with a methodology that reflects expected credit losses and requires consideration of a broader range of reasonable and supportable information to inform credit loss estimates. The Company early adopted this standard as of January 1, 2022 using a modified retrospective approach. It did not have a material impact on the Company's financial statements and related disclosures.

In November 2021, the FASB issued ASU No. 2021-10, *"Government Assistance: Disclosures by Business Entities about Government Assistance"*. The amendments in this Update improve financial reporting by requiring disclosures that increase the transparency of transactions with a government. The amendments require the following annual disclosures about transactions with a government that are accounted for by applying a grant or contribution accounting model by analogy (i) the type of transaction (ii) the accounting for the transaction, and (iii) the effect of the transaction on the entity's financial statements. The Company adopted this standard as of January 1, 2022 using a prospective approach and it did not have a material impact on the Company's financial statements and related disclosures.

4. Marketable Securities

The following is a summary of the Company's marketable securities.

(in thousands)	Amortized Cost	Gross unrealized gain	Gross unrealized loss	Fair Value
September 30, 2022:				
Corporate debt securities	$ 154,536	$ 10	$ (2,378)	$ 152,168
U.S. government securities	19,848	5	—	$ 19,853
Total	$ 174,384	$ 15	$ (2,378)	$ 172,021
December 31, 2021				
Corporate debt securities	$ 193,798	$ 1	$ (696)	$ 193,103
Commercial paper	66,318	1	(17)	66,302
Total	$ 260,116	$ 2	$ (713)	$ 259,405

The Company's marketable securities generally have contractual maturity dates of 13 months or less. The Company believes that any unrealized losses associated with the decline in value of its securities is temporary, is primarily related to market factors and believes that it is more likely than not that it will be able to hold its debt securities to maturity. Therefore, the Company anticipates a full recovery of the amortized cost basis of its debt securities at maturity and an allowance for credit losses was not recognized.

5. Fair Value of Financial Instruments

Fair value is the price that could be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. Fair value determination in accordance with applicable accounting guidance requires that a number of significant judgments be made. Additionally, fair value is used on a nonrecurring basis to evaluate assets for impairment or as required for disclosure purposes by applicable accounting guidance on disclosures about fair value of financial instruments. Depending on the nature of the assets and liabilities, various valuation techniques and assumptions are used when estimating fair value. The Company follows the provisions of ASC 820, for financial assets and liabilities measured on a recurring basis. The guidance requires fair value measurements be classified and disclosed in one of the following three categories:

- *Level 1:* Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities.
- *Level 2:* Quoted prices in markets that are not active, or inputs which are observable, either directly or indirectly, for substantially the full term of the asset or liabilities.
- *Level 3:* Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e., supported by little or no market activity).

The following fair value hierarchy table presents information about the Company's assets and liabilities measured at fair value on a recurring basis:

	Fair value measurement at reporting date using		
(in thousands)	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
September 30, 2022:			
Assets:			
Cash equivalents (Money Market Funds)	$ 48,278	$ —	$ —
Marketable securities			
Corporate debt securities	—	152,168	—
U.S government securities		19,853	
Total	$ 48,278	$ 172,021	$ —
December 31, 2021:			
Assets:			
Cash equivalents (Money Market Funds)	$ 30,520	$ —	$ —
Marketable securities			
Corporate debt securities	—	193,103	—
Commercial paper	—	66,302	—
Total	$ 30,520	$ 259,405	$ —

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

(in thousands)	September 30, 2022	December 31, 2021
Compensation and related benefits	$ 5,741	$ 4,919
Research and development	4,006	4,615
Other	175	87
	$ 9,922	$ 9,621

7. Common Stock

Common Stock Offering

In January 2021, the Company sold 2,875,000 shares of its common stock at a public offering price of $60.00 per share. The Company received net proceeds of $161.4 million after deducting underwriting discounts, commissions, and other offering expenses paid by the Company.

The Company has two classes of common stock; "voting common stock" and "non-voting common stock." The holders of the voting common stock are entitled to one vote for each share of voting common stock held at all meetings of stockholders. Except as otherwise required by law, the holders of non-voting common stock shall not be entitled to vote at any meetings of stockholders (or written actions in lieu of meetings) and the shares of non-voting common stock shall not be included in determining the number of shares voting or entitled to vote on any matter. Unless required by law, there shall be no cumulative voting. Any holder of non-voting common stock may elect to convert each share of non-voting common stock into one fully paid and non-assessable share of voting common stock at any time by providing written notice to the Company; provided that as a result of such conversion, such holder, together with its affiliates and any members of a Schedule 13(d) group with such holder, would not beneficially own in excess of 9.99% of the Company's common stock immediately prior to and following such conversion, unless otherwise as expressly provided for in the Company's restated certificate of incorporation. However, this ownership limitation may be increased (not to exceed 19.99%) or decreased to any other percentage designated by such holder of non-voting common stock upon 61 days' notice to the Company.

8. Commitments

Leases

The Company leases office and laboratory space in Wilmington, Delaware under a noncancelable lease (the "Lease"). During the first quarter of 2022, the Lease was amended to allow the Company the option to renew the Lease for two 6-month periods and the Company exercised its option to renew the lease for an additional 6 months until June 30, 2023. The second option to extend the Lease for an additional 6 months was not recognized as part of the Company's measurement of the right-of-use asset and operating lease liability as of September 30, 2022. The discount rate used to account for the Company's operating lease under ASC 842 is the Company's estimated incremental borrowing rate of 6.0%.

Rent expense for both the three months ended September 30, 2022 and 2021 was $0.5 million. Rent expense for the nine months ended September 30, 2022 and 2021 was $1.6 million and $1.2 million, respectively.

Future minimum annual lease payments under the Lease at September 30, 2022 are as follows:

(in thousands)		
2022 (remaining)	$	459
2023		964
Total undiscounted lease payments		1,423
Less imputed interest		(35)
Current and noncurrent lease liability	$	1,388

In August 2022, we entered into an amendment (the "Lease Amendment") to the lease agreement for office and lab space at Chestnut Run Plaza in Wilmington, Delaware (the "Chestnut Run Lease"). The Chestnut Run Lease has a commencement date of the earlier of (i) the Landlord Work Substantial Completion Date (as such term is defined in the Chestnut Run Lease), or (ii) the date the Company takes possession of the premises for the conduct of the Company's business (the "Commencement Date"). The Chestnut Run Lease premises includes approximately 81,000 rentable square feet, located at Chestnut Run Plaza in Wilmington, Delaware (the Premises). Upon the Commencement Date, the Company will recognize a right-of-use asset and operating lease liability in accordance with ASC 842. The Chestnut Run Lease has an initial term of 162 months with 3 five-year extension options and certain expansion rights. The estimated rent payments related to the Chestnut Run Lease are as follows:

(in thousands)		
2022 (remaining)	$	—
2023		—
2024		2,125
2025		2,937
2026		3,010
2027		3,085
Thereafter		31,479

The Company paid a security deposit for the Chestnut Run Lease in the form of a letter of credit of $4.0 million, which is included in the balance sheet as restricted cash as of September 30, 2022. The security deposit may be reduced to $0.5 million over time in accordance with the terms of the Chestnut Run Lease.

In connection with the Company's expansion of operations in the State of Delaware, the Company was approved for a grant from the State of Delaware in 2021 that will provide up to $5.5 million in reimbursements over three years for the development of lab space in addition to increasing jobs in Delaware to meet specific targeted levels through 2023. During the third quarter of 2022, the Company was approved for an additional grant from the State of Delaware for the development of lab space in the amount of $1.0 million. In 2022, the Company received cash of $3.4 million from the grants for the development of lab space. The Company has deferred the recognition of these grant funds as they relate to capitalized costs and has classified them as long-term liabilities on the balance sheet. The Company will recognize the grant funds in other income as grant income over the useful life of the related assets. If, after two years from the disbursement date, the incurred costs for lab space are less than the $3.4 million received, the Company is required to pay back the difference between total funds received and allowable costs incurred. Additionally, if the Company leaves the State of Delaware within five years of the disbursement, the Company is required to return an amount equal to the amount of grant funds disbursed on a pro-rated basis. During the first quarter of 2022, the Company also received cash of $0.3 million for satisfying the first performance benchmark measurement. The Company recognized this in other income, net on the statement of operations and comprehensive loss. To the extent the Company's employee headcount is fewer than the performance benchmark, the Company is required to repay the amount of grant funds received for the number of employees below the benchmark.

Employment Agreements

The Company entered into employment agreements with key personnel providing for compensation and severance in certain circumstances, as defined in the respective employment agreements.

401(k) Defined Contribution Plan

The Company sponsors a 401(k) defined-contribution plan covering all employees. Participants are permitted to contribute up to 100% of their eligible annual pretax compensation up to an established federal limit on aggregate participant contributions. The Company provides a match of a maximum amount of 3% of the participant's compensation. For both the three months ended September 30, 2022 and 2021, the Company made matching contributions of $0.1 million. For both the nine months ended September 30, 2022 and 2021, the Company made matching contributions of $0.4 million.

Research Collaboration Agreement

In September 2021, the Company entered into a research collaboration agreement estimated to last for approximately one year (the "Darwin Health Agreement") with Darwin Health, Inc. ("DarwinHealth"). Under the terms of the Darwin Health Agreement, DarwinHealth will utilize their drug discovery technologies and certified methodologies in precision oncology to advance and accelerate clinical development for certain of the Company's programs across a broad range of tumor subtypes. The Company will pay DarwinHealth a total of $3.0 million in three equal installments over the one-year term (the "Research Term") to fund the research and, if the Company adopts any of DarwinHealth's development ideas, the Company will be responsible for the development, manufacturing, and commercialization of any such products. In addition to research funding, DarwinHealth is eligible to receive future research, development and regulatory milestones of up to $3.0 million for each product candidate and is also eligible to receive tiered royalties in the low single digits on net sales of each product developed using DarwinHealth's development technologies or methods. However, within eighteen-months following the Research Term, the Company, in its sole discretion, may notify DarwinHealth that it will not utilize its development ideas and will be entitled to receive a refund of $0.5 million.

Other Research and Development Arrangements

The Company enters into agreements with "CROs" to assist in the performance of research and development activities. Expenditures to CROs will represent a significant cost in clinical development for the Company.

9. Stock-Based Compensation

The Company has two equity incentive plans: the 2016 Equity Incentive Plan, as amended, and the 2020 Equity Incentive Plan. New awards can only be granted under the 2020 Equity Incentive Plan (the "Plan") and as of September 30, 2022, 5,347,757 shares were available for future grants. The number of shares of the Company's common stock that may be issued pursuant to rights granted under the Plan shall automatically increase on January 1st of each year, commencing on January 1, 2021, and continuing for ten years, in an amount equal to five percent of the total number of shares of the Company's common stock outstanding on December 31st of the preceding calendar year, subject to the discretion of the board of directors or compensation committee to determine a lesser number of shares shall be added for such year. The Plan provides for the granting of common stock, incentive stock options, nonqualified stock options, restricted stock awards, restricted stock units and/or stock appreciation rights to employees, directors, and other persons, as determined by the Company's board of directors. The Company's stock options vest based on the terms in each award agreement, generally over four-year periods with 25% of options vesting after 1 year and then monthly thereafter, and have a term of ten years.

The Company measures stock-based awards at their grant-date fair value and records compensation expense on a straight-line basis over the vesting period of the awards. The Company recorded stock-based compensation expense in the following expense categories in its accompanying statements of operations:

	Three Months Ended September 30,		Nine Months Ended September 30,	
(in thousands)	**2022**	**2021**	**2022**	**2021**
Research and development	$ 3,214	$ 3,262	$ 8,886	$ 7,305
General and administrative	3,228	3,771	10,413	7,851
	$ 6,442	$ 7,033	$ 19,299	$ 15,156

Stock Options

The following table summarizes stock option activity for the periods indicated:

	Number of shares		Weighted average exercise price per share	Weighted average remaining contractual term (years)
Outstanding at January 1, 2022	7,179,482	$	15.36	8.66
Granted	3,257,993	$	7.92	
Exercised	(202,578)	$	1.77	
Forfeited	(1,037,369)	$	18.10	
Outstanding at September 30, 2022	9,197,528	$	12.72	8.45
Exercisable at September 30, 2022	3,199,699	$	12.05	7.61

At September 30, 2022, the aggregate intrinsic value of outstanding options and exercisable options was $12.1 million and $7.1 million, respectively.

The following table summarizes information about stock options outstanding at September 30, 2022 under the Plan:

	Options Outstanding				Options Exercisable		
Range of Exercise Prices	**Number Outstanding**	**Weighted Average Remaining Contractual Life (in years)**		**Weighted Average Exercise Price**	**Number Exercisable**		**Weighted Average Exercise Price**
$0.31 - $3.05	2,012,240	7.00	$	1.79	1,468,921	$	1.76
$3.06 - $10.34	1,620,577	9.72		5.21	6,750		10.09
$10.35 - $11.72	1,410,778	9.37		10.58	—		0.00
$11.73 - $13.04	2,159,338	7.92		12.85	1,090,003		12.85
$13.05 - $88.98	1,994,595	8.80		31.21	634,025		34.55
	9,197,528				3,199,699		

The weighted-average grant date fair value of options granted was $5.72 and $24.88 per share for the nine months ended September 30, 2022 and 2021, respectively. The aggregate intrinsic value of options exercised was $1.1 million for the nine months ended September 30, 2022. The Company recorded stock-based compensation expense of $6.1 million and $6.7 million for the three months ended September 30, 2022 and 2021, respectively, related to stock options. The Company recorded stock-based compensation expense of $18.3 million and $14.4 million for the nine months ended September 30, 2022 and 2021, respectively, related to stock options. As of September 30, 2022, the total unrecognized compensation expense related to unvested stock option awards was $56.5 million, which the Company expects to recognize over a weighted-average period of 2.58 years.

The fair value of each option was estimated on the date of grant using the weighted average assumptions in the table below:

	Nine months ended September 30,	
	2022	**2021**
Expected volatility	84.91%	88.50%
Risk-free interest rate	2.52%	0.87%
Expected life (in years)	6.02	6.03
Expected dividend yield	—	—

Restricted Stock Awards and Units

The Company issues restricted stock awards (“RSA”) to employees that generally vest over a four-year period with 25% of awards vesting after one year and then monthly thereafter. Any unvested shares will be forfeited upon termination of services. The fair value of an RSA is equal to the fair market value price of the Company’s common stock on the date of grant. RSA expense is recorded on a straight-line basis over the vesting period.

The following table summarizes activity related to RSA stock-based payment awards:

	Number of shares	Weighted-average grant date fair value
Unvested balance at January 1, 2022	611,608	$ 2.29
Vested	(316,227)	$ 1.96
Forfeited	(23,416)	$ 1.89
Unvested balance at September 30, 2022	271,965	$ 2.71

The Company recorded stock-based compensation expense of $0.2 million and $0.3 million for the three months ended September 30, 2022 and 2021, respectively, related to RSAs. The Company recorded stock-based compensation expense of $0.6 million and $0.7 million for the nine months ended September 30, 2022 and 2021, respectively, related to RSAs. As of September 30, 2022, the total unrecognized expense related to all RSAs was $0.7 million, which the Company expects to recognize over a weighted-average period of 1.25 years.

The Company granted restricted stock units ("RSU") to employees that generally vest over a four-year period with 25% of awards vesting after one year and then quarterly thereafter. Any unvested units will be forfeited upon termination of services.

The following table summarizes activity related to RSU stock-based payment awards:

	Number of shares	Weighted-average grant date fair value
Unvested balance at January 1, 2022	20,000	$ 18.32
Granted	150,000	$ 4.86
Unvested balance at September 30, 2022	170,000	$ 6.44

The Company recorded stock-based compensation expense of $74 thousand and $156 thousand for the three and nine months ended September 30, 2022, respectively, related to RSUs. At September 30, 2022, the total unrecognized expense related to the RSUs was $0.9 million, which the Company expects to recognize over 3.36 years.

Employee Stock Purchase Plan

The Company has an Employee Stock Purchase Plan (the "ESPP"), which, as of September 30, 2022, had 1,342,050 shares of common stock reserved for future issuance. The number of shares of the Company's common stock that may be issued pursuant to rights granted under the ESPP shall automatically increase on January 1st of each year and continuing for ten years beginning in 2021, in an amount equal to one percent of the total number of shares of all classes of the Company's common stock outstanding on December 31st of the preceding calendar year, subject to the discretion of the board of directors or compensation committee to determine a lesser number of shares shall be added for such year. On January 1, 2022, 476,023 shares were added to the ESPP.

Under the ESPP, eligible employees can purchase the Company's common stock through accumulated payroll deductions at such times as are established by the compensation committee. Eligible employees may purchase the Company's common stock at 85% of the lower of the fair market value of the Company's common stock on the first day of the offering period or on the last day of the offering period. Eligible employees may contribute up to 15% of their eligible compensation. Under the ESPP, a participant may not accrue rights to purchase more than $25,000 worth of the Company's common stock for each calendar year in which such right is outstanding.

The ESPP is considered compensatory under the FASB stock compensation rules. Accordingly, share-based compensation expense is determined based on the option's grant-date fair value as estimated by applying the Black Scholes option-pricing model and is recognized over the withholding period. The Company recognized share-based compensation expense of $0.1 million and $0.3 million for the three and nine months ended September 30, 2022, respectively, related to the ESPP. The Company recognized share-based compensation expense of $0.1 million for both the three and nine months ended September 30, 2021 related to the ESPP.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes and other financial information included elsewhere in this Quarterly Report on Form 10-Q. In addition to historical financial information, this discussion contains forward-looking statements based upon current expectations that involve risks and uncertainties, such as statements of our plans, objectives, expectations, intentions and belief. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth in the section titled "Risk Factors" under Part II, Item 1A below. These forward-looking statements may include, but are not limited to, statements regarding our future results of operations and financial position, the impact of the ongoing COVID-19 pandemic, business strategy, market size, potential growth opportunities, preclinical and clinical development activities, efficacy and safety profile of our product candidates, use of net proceeds from our offerings, our ability to maintain and recognize the benefits of certain designations received by product candidates, the timing and results of preclinical studies and clinical trials, commercial collaborations with third parties and the receipt and timing of potential regulatory designations, approvals and commercialization of product candidates. The words "believe," "may," "will," "potentially," "estimate," "continue," "anticipate," "predict," "target," "intend," "could," "would," "should," "project," "plan," "expect," and similar expressions that convey uncertainty of future events or outcomes are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These statements are based upon information available to us as of the date of this Quarterly Report on Form 10-Q, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely upon these statements.

Overview

We are a clinical-stage fully integrated oncology company built on a foundation of drug discovery excellence to deliver novel precision cancer medicines to underserved patients. By leveraging our core competencies in cancer biology and medicinal chemistry, combined with our target class- and technology platform-agnostic approach, we have built an efficient, fully-integrated drug discovery engine to identify compelling biological targets and create new chemical entities, or NCEs, that we rapidly advance into clinical trials. We believe our approach could result in better targeted cancer therapies. Our discovery excellence has been validated by our rapid progress in creating a wholly-owned, internally developed pipeline. Since our inception in 2016, we have received clearance from the U.S. Food and Drug Administration, or the FDA, for investigational new drug applications, or INDs, and successfully advanced five programs into clinical trials. In addition, we have other unique programs in various stages of preclinical development.

By focusing on developing agents using broad mechanisms that have multiple links to oncogenic driver pathways in select patients, we have developed a diverse pipeline consisting of multiple distinct programs spanning methyltransferases, kinases, protein-protein interactions and targeted protein degraders. Our pipeline is geared towards serving patients with high unmet medical need where there are limited or no treatment options. We believe we can best address these diseases by developing therapies that target primary and secondary resistance mechanisms.

We have two clinical candidates that are designed to be oral, potent and selective inhibitors of protein arginine methyltransferase 5, or PRMT5. The potency and selectivity of our product candidates is supported by preclinical data demonstrating nanomolar inhibition of PRMT5 and no inhibition of related enzymes at 1,000 times higher concentration of our product candidates. Our PRMT5 candidates are currently being studied in Phase 1 clinical trials in solid tumors and myeloid malignancies. In November 2022, we announced that we will discontinue the internal development of our PRMT5 program and focus our efforts on our CDK9, MCL1, CDK4/6 and SMARCA2 programs. In the Phase 1 trials for PRT543 and PRT811, both molecules were generally well tolerated. We saw two complete responses with PRT811. While encouraging, these results did not meet our criteria necessary to continue to develop the PRMT5 program internally.

PRT1419, our next clinical candidate, is designed to be a potent and selective inhibitor of the anti-apoptotic protein, MCL1. The potency and selectivity of PRT1419 is supported by preclinical data demonstrating nanomolar inhibition of MCL1 and no inhibition of related enzymes at 200 times higher concentration of our product candidate.

The IV formulation of PRT1419 has demonstrated a desirable pharmacokinetic, pharmacodynamic and safety profile with potential for differentiation from competitor compounds. We are enrolling patients in a Phase 1 solid tumor dose escalation and confirmation study, including a significant number of patients at the recommended expansion dose of 80 mg/m^2. In this study, PRT1419 has been well tolerated, with no cardiotoxicity observed in these patients to date. Cardiovascular parameters including troponin levels and ejection fraction changes were evaluated, in addition to standard safety, pharmacokinetics and target engagement metrics. The clinical pharmacodynamic profile of PRT1419 demonstrates the desired level of target engagement, as measured by caspase activation in peripheral mononuclear cells and reduction of CD14+ monocytes to levels associated with tumor regressions in preclinical models of hematological cancers. We intend to evaluate PRT1419 in hematology malignancies in monotherapy and combinations therapies, with the goal of establishing safety, clinical activity and a recommended Phase 2 dose in hematology malignancies in 2023.

PRT2527 is designed to be a potent and selective Cyclin-dependent kinase 9, or CDK9, inhibitor. In preclinical studies, PRT2527 was shown to reduce MCL1 and MYC protein levels and was highly active in preclinical models at well-tolerated doses. PRT2527 has demonstrated high potency and kinase selectivity which may offer improved efficacy and safety compared to less selective CDK9 inhibitors. Preclinical data demonstrated that treatment with PRT2527 depleted oncogenic drivers with short half-lives, such as MYC and MCL1, and effectively induced apoptosis. PRT2527 treatment demonstrated efficacy in both hematological malignancies and solid tumor models with MYC dysregulation. A phase one trial is underway evaluating escalating IV doses of PRT2527 as a monotherapy in patients with selected solid tumors, including sarcoma, prostate cancer, lung cancer, and other cancers with genomic alterations that lead to MYC dependence. Dose dependent increases in exposure and target engagement were observed as evidenced by MYC and MCL1 depletion to levels associated with tumor regression in preclinical models. No adverse events leading to dose reduction or discontinuation have been reported. We remain on track to select a recommended Phase 2 dose in solid tumor by year-end. We will use these safety data to continue the cohort expansion in solid tumors, as well as to inform and rapidly progress PRT2527 in a hematology malignancies clinical trial.

In July 2022, we received clearance for an investigational new drug application, or an IND application, for PRT3645, a brain penetrant molecule that potently and selectively targets CDK4/6. We remain on track to initiate a clinical trial for PRT3645 by year end.

We completed IND-enabling studies and received IND clearance in October 2022 for PRT3879, a SMARCA protein degrader. We plan to dose the first patient in the first quarter of 2023. SMARCA2 inhibition has the greatest potential in patients with SMARCA4 deficient cancers.

We were incorporated in February 2016 under the laws of the State of Delaware. Since inception, we have devoted substantially all of our resources to developing product and technology rights, conducting research and development, organizing and staffing our company, business planning and raising capital. We have incurred recurring losses, the majority of which are attributable to research and development activities, and negative cash flows from operations. We have funded our operations primarily through the sale of convertible preferred stock and common stock. Our net loss was $86.8 million and $78.9 million for the nine months ended September 30, 2022 and 2021, respectively. As of September 30, 2022, we had an accumulated deficit of $305.9 million. Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures, and to a lesser extent, general and administrative expenditures. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our current or future product candidates. We expect to continue to incur significant expenses and operating losses for the foreseeable future as we advance our product candidates through all stages of development and clinical trials and, ultimately, seek regulatory approval. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Furthermore, we expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and our expenditures on other research and development activities.

We will need to raise substantial additional capital 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 plan to finance our operations through the sale of equity, debt financings or other capital sources, which may include collaborations with other companies or other strategic transactions. There are no assurances that we will be successful in obtaining an adequate level of financing as and when needed to finance our operations on terms acceptable to us or at all. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to secure adequate additional funding, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more product candidates or delay our pursuit of potential in-licenses or acquisitions.

As of September 30, 2022, we had $224.0 million in cash, cash equivalents, and marketable securities. We expect our existing cash, cash equivalents and marketable securities will enable us to fund our operating expense and capital expenditures into the fourth quarter of 2024.

COVID-19 Impact

We are continuing to proactively monitor and assess the ongoing COVID-19 pandemic. Since early March 2020 we have been monitoring the potential impact on our business that may result from this rapidly evolving crisis and to avoid any unnecessary potential delays to our programs. At this time, our lead programs and research activities remain on track. The safety and well-being of employees, patients and partners is our highest priority. See the Risk Factor "*The ongoing COVID-19 pandemic could adversely impact our business, including our clinical trials and clinical trial operations*" in Part II, Item 1A. "Risk Factors" below.

Components of Results of Operations

Revenue

To date, we have not recognized any revenue from any sources, including from product sales, and we do not expect to generate any revenue from the sale of products in the foreseeable future. If our development efforts for our product candidates are successful and result in regulatory approval, or license agreements with third parties, we may generate revenue in the future from product sales. However, there can be no assurance as to when we will generate such revenue, if at all.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred in connection with the discovery and development of our product candidates. We expense research and development costs as incurred, including:

- expenses incurred to conduct the necessary discovery-stage laboratory work, preclinical studies and clinical trials required to obtain regulatory approval;
- personnel expenses, including salaries, benefits and stock-based compensation expense for our employees engaged in research and development functions;
- costs of funding research performed by third parties, including pursuant to agreements with contract research organizations, or CROs, that conduct our clinical trials, as well as investigative sites, consultants and CROs that conduct our preclinical and nonclinical studies;
- expenses incurred under agreements with contract manufacturing organizations, or CMOs, including manufacturing scale-up expenses and the cost of acquiring and manufacturing preclinical study and clinical trial materials;
- fees paid to consultants who assist with research and development activities;
- expenses related to regulatory activities, including filing fees paid to regulatory agencies; and
- allocated expenses for facility costs, including rent, utilities, depreciation and maintenance.

We track outsourced development costs and other external research and development costs to specific product candidates on a program-by-program basis, fees paid to CROs, CMOs and research laboratories in connection with our preclinical development, process development, manufacturing and clinical development activities. However, we do not track our internal research and development expenses on a program-by-program basis as they primarily relate to compensation, early research and other costs which are deployed across multiple projects under development.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect our research and development expenses to increase significantly over the next several years as we increase personnel costs, including stock-based compensation, conduct our clinical trials, including later-stage clinical trials, for current and future product candidates and prepare regulatory filings for our product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel expenses, including salaries, benefits and stock-based compensation expense, for employees and consultants in executive, finance and accounting, legal, operations support, information technology and human resource functions. General and administrative expense also includes corporate facility costs not otherwise included in research and development expense, including rent, utilities, depreciation and maintenance, as well as legal fees related to intellectual property and corporate matters and fees for accounting and consulting services.

We expect that our general and administrative expense will increase in the future to support our continued research and development activities and potential commercialization efforts. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, legal support and accountants, among other expenses. If any of our current or future product candidates obtains U.S. regulatory approval, we expect that we would incur significantly increased expenses associated with building a sales and marketing team.

Other Income, Net

Other income, net consists primarily of interest earned on our cash equivalents and marketable securities and grant income received from the State of Delaware. We anticipate re-applying for grants from the State of Delaware from time to time as long as we maintain qualifying headcount levels in the State of Delaware.

Income Taxes

Since our inception, we have not recorded any income tax benefits for the net operating losses, or NOLs, we have incurred or for our research and development tax credits, as we believe, based upon the weight of available evidence, that it is more likely than not that all of our NOLs and tax credits will not be realized.

Results of Operations

Comparison of the Three Months Ended September 30, 2022 and 2021

The following table sets forth our results of operations for the three months ended September 30, 2022 and 2021.

(in thousands)	Three months ended September 30, 2022	Three months ended September 30, 2021	Change
Operating expenses:			
Research and development	$ 22,889	$ 22,721	$ 168
General and administrative	7,517	8,115	(598)
Total operating expenses	30,406	30,836	(430)
Loss from operations	(30,406)	(30,836)	430
Other income, net	448	149	299
Net loss	$ (29,958)	$ (30,687)	$ 729

Research and Development Expenses

Research and development expenses increased by $0.2 million to $22.9 million for the three months ended September 30, 2022 from $22.7 million for the three months ended September 30, 2021. Included in research and development expenses for the quarter ended September 30, 2022, was $3.2 million of non-cash expense related to stock-based compensation expense, including employee stock options, compared to $3.3 million for the three months ended September 30, 2021. Research and development expense remains steady as our clinical pipeline advances into clinical trials.

Research and development expenses by program are summarized in the table below:

(in thousands)	Three months ended September 30, 2022	Three months ended September 30, 2021
PRT543	$ 2,868	$ 2,797
PRT811	864	2,588
PRT1419 (Oral and IV)	1,396	2,013
PRT2527	611	832
Discovery programs	6,227	4,979
Internal costs, including personnel related	10,923	9,512
	$ 22,889	$ 22,721

General and Administrative Expenses

General and administrative expenses decreased by $0.6 million to $7.5 million for the three months ended September 30, 2022 from $8.1 million for the three months ended September 30, 2021. Included in the general and administrative expenses for the quarter ended September 30, 2022, was $3.2 million of non-cash expense related to stock-based compensation expense, including employee stock options, as compared to $3.8 million for the same period in 2021. The decrease in general and administrative expense was primarily due to non-cash stock-based compensation expense and prudent management of expenses.

Other Income, net

Other income, net increased by $0.3 million to $0.4 million for the three months ended September 30, 2022 from $0.1 million for the three months ended September 30, 2021, primarily due to interest earned on the investment of our cash proceeds.

Comparison of the Nine Months Ended September 30, 2022 and 2021

The following table sets forth our results of operations for the nine months ended September 30, 2022 and 2021.

(in thousands)	Nine months ended September 30, 2022	Nine months ended September 30, 2021	Change
Operating expenses:			
Research and development	$ 67,020	$ 61,600	$ 5,420
General and administrative	23,135	19,125	4,010
Total operating expenses	90,155	80,725	9,430
Loss from operations	(90,155)	(80,725)	(9,430)
Other income, net	3,358	1,873	1,485
Net loss	$ (86,797)	$ (78,852)	$ (7,945)

Research and Development Expenses

Research and development expenses increased by $5.4 million to $67.0 million for the nine months ended September 30, 2022 from $61.6 million for the nine months ended September 30, 2021. Included in research and development expenses for the nine months ended September 30, 2022, was $8.9 million of non-cash expense related to stock-based compensation expense, including employee stock options, compared to $7.3 million for the nine months ended September 30, 2021. The increase in research and development expense was primarily due to an increase in discovery-stage program expenses and from the growth and advancement of our clinical pipeline and an increase in non-cash stock-based compensation expense.

Research and development expenses by program are summarized in the table below:

(in thousands)	Nine months ended September 30, 2022	Nine months ended September 30, 2021
PRT543	$ 5,912	$ 10,477
PRT811	3,875	8,928
PRT1419 (Oral and IV)	5,872	5,813
PRT2527	2,312	2,410
Discovery programs	17,068	10,788
Internal costs, including personnel related	31,981	23,184
	$ 67,020	$ 61,600

General and Administrative Expenses

General and administrative expenses increased by $4.0 million to $23.1 million for the nine months ended September 30, 2022 from $19.1 million for the nine months ended September 30, 2021. Included in the general and administrative expenses for the nine months ended September 30, 2022, was $10.4 million of non-cash expense related to stock-based compensation expense, including employee stock options, as compared to $7.9 million for the same period in 2021. The increase in general and administrative expense was primarily due to an increase in non-cash stock-based compensation expense and an increase in personnel related expenses due to a higher employee headcount.

Other Income, net

Other income, net increased by $1.5 million to $3.4 million for the nine months ended September 30, 2022 from $1.9 million for the nine months ended September 30, 2021, primarily due to the receipt and recognition of research and development tax credits from the State of Delaware during 2022, as well as interest earned on the investment of our cash proceeds.

Liquidity and Capital Resources

Overview

Since our inception, we have not recognized any revenue and have incurred operating losses and negative cash flows from our operations. We have not yet commercialized any product and we do not expect to generate revenue from sales of any products for several years, if at all. Since our inception, we have funded our operations through the sale of convertible preferred stock and common stock. As of September 30, 2022, we had $224.0 million in cash, cash equivalents and marketable securities and had an accumulated deficit of $305.9 million. We expect our existing cash, cash equivalents and marketable securities to enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2024. We have based these estimates on assumptions that may prove to be imprecise, and we could utilize our available capital resources sooner than we expect.

Funding Requirements

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

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the scope, timing, progress and results of discovery, preclinical development, laboratory testing and clinical trials for our product candidates;
- the costs of manufacturing our product candidates for clinical trials and in preparation for marketing approval and commercialization;
- the extent to which we enter into collaborations or other arrangements with additional third parties in order to further develop our product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the costs and fees associated with the discovery, acquisition or in-license of additional product candidates or technologies;
- expenses needed to attract and retain skilled personnel;
- costs associated with being a public company;
- the costs required to scale up our clinical, regulatory and manufacturing capabilities;
- the costs of future commercialization activities, if any, including establishing sales, marketing, manufacturing and distribution capabilities, for any of our product candidates for which we receive marketing approval; and
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval.

We will need additional funds to meet operational needs and capital requirements for clinical trials, other research and development expenditures, and business development activities. We currently have no credit facility or committed sources of capital. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical studies.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of common stockholders. 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 acquisitions or 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. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our research, 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.

Cash Flows

The following table shows a summary of our cash flows for the periods indicated:

	Nine months ended September 30,	
(in thousands)	**2022**	**2021**
Cash used in operating activities	$ (60,802)	$ (57,829)
Cash provided by (used in) investing activities	80,336	(261,999)
Cash provided by financing activities	660	162,943
Net increase in cash and cash equivalents	$ 20,194	$ (156,885)

Operating Activities

During the nine months ended September 30, 2022, we used $60.8 million of cash in operating activities. Cash used in operating activities reflected our net loss of $86.8 million offset by a $1.7 million net decrease in our operating assets and liabilities and noncash charges of $24.3 million, which consisted of $19.3 million in stock-based compensation, $2.7 million in amortization of premiums and discounts on marketable securities, $1.3 million noncash lease expense, and $1.0 million in depreciation. The primary use of cash was to fund our operations related to the development of our product candidates.

During the nine months ended September 30, 2021, we used $57.8 million of cash in operating activities. Cash used in operating activities reflected our net loss of $78.9 million, offset by a $4.0 million net decrease in our operating assets and liabilities and noncash charges of $17.1 million, which consisted of $15.2 million in stock-based compensation, $0.6 million in depreciation, $0.9 million noncash lease expense, and $0.4 million in amortization of premiums and discounts on marketable securities. The primary use of cash was to fund our operations related to the development of our product candidates.

Investing Activities

During the nine months ended September 30, 2022, net cash provided by investing activities of $80.3 million consisted primarily of $168.9 million in proceeds from maturities of marketable securities partially offset by $86.0 million used for purchases of marketable securities. During the nine months ended September 30, 2021 net cash used in investing activities of $262.0 million consisted of $260.0 million of cash to purchase marketable securities and $2.0 million of cash for the purchase of property and equipment.

Financing Activities

During the nine months ended September 30, 2022, financing activities provided $0.7 million from the exercise of stock options and purchases of stock under the Employee Stock Purchase Plan. During the nine months ended September 30, 2021, financing activities provided $162.9 million, which reflected the receipt of net cash of $161.4 million from the sale of common stock as well as the receipt of $1.5 million from the exercise of stock options.

Critical Accounting Policies

During the three months ended September 30, 2022, there were no material changes to our critical accounting policies and estimates from those described under the heading “Management’s Discussion and Analysis of Financial Condition and Results of Operations-Critical Accounting Policies and Estimates” in our Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 17, 2022.

JOBS Act Accounting Election

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies.

We have elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until the earliest of (1) the last day of our first fiscal year (a) in which we have total annual gross revenues of at least $1.235 billion, or (b) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the prior June 30th, (2) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period and (3) December 31, 2025.

Recent Accounting Pronouncements

See Note 3 to our interim financial statements included elsewhere in this Quarterly Report on Form 10-Q for a description of recent accounting pronouncements applicable to our financial statements.

Emerging Growth Company and Smaller Reporting Company Status

In April 2012, the JOBS Act was enacted. Section 107 of the JOBS Act provides that an “emerging growth company” can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, 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 elected to avail ourselves of this exemption from complying with new or revised accounting standards and, therefore, will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

Subject to certain conditions, as an emerging growth company, we may rely on certain other exemptions and reduced reporting requirements, including without limitation, exemption to the requirements for providing an auditor’s attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act. We will remain an emerging growth company until the earlier to occur of (a) the last day of the fiscal year (i) following the fifth anniversary of the completion of our IPO, (ii) in which we have total annual gross revenues of at least $1.235 billion or (iii) in which we are deemed to be a “large accelerated filer” under the rules of the SEC, which means the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the prior June 30th, or (b) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

We are also a “smaller reporting company,” meaning that the market value of our stock held by non-affiliates is less than $700.0 million and our annual revenue is less than $100.0 million during the most recently completed fiscal year. We may continue to be a smaller reporting company after if either (i) the market value of our stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

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

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedure

As of September 30, 2022, management, with the participation of our Principal Executive Officer and Principal Financial and Accounting Officer, performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC’s rules and forms, and that such information is accumulated and communicated to our management, including the Principal Executive Officer and the Principal Financial and Accounting Officer, to allow timely decisions regarding required disclosures. Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Principal Executive Officer and Principal Financial and Accounting Officer concluded that, as of September 30, 2022, the design and operation of our disclosure controls and procedures were effective at a reasonable assurance level.

Changes in Internal Control over Financial Reporting

Management determined that, as of September 30, 2022, there were no changes in our internal control over financial reporting that occurred during the fiscal quarter then ended that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 1. Legal Proceedings.

From time to time, we may be involved in legal proceedings arising in the ordinary course of our business. In addition, we may receive letters alleging infringement of patents or other intellectual property rights. We are not presently a party to any legal proceedings that, in the opinion of management, would have a material adverse effect on our business, operating results, cash flows or financial conditions should such litigation be resolved unfavorably. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm, and other factors.

Item 1A. Risk Factors

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before making your decision to invest in shares of our common stock, you should carefully consider the risks and uncertainties described below, together with the other information contained in this Quarterly Report on Form 10-Q, including our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations". The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that affect us. We cannot assure you that any of the events discussed below will not occur. These events could have a material and adverse impact on our business, financial condition, results of operations and prospects. If that were to happen, the trading price of our common stock could decline, and you could lose all or part of your investment.

Summary of Risk Factors

Our business is subject to several risks and uncertainties, including those immediately following this summary. Some of these risks are:

- 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 incurred significant operating losses since our inception and have not generated any revenue. We expect to incur continued losses for the foreseeable future and may never achieve or maintain profitability. Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.
- We will require substantial additional funding to pursue our business objectives. If we are unable to raise capital when needed or on terms acceptable to us, we could be forced to delay, reduce or eliminate our research or drug development programs, any future commercialization efforts or other operations.
- We are highly dependent on the success of our product candidates, PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789 which are in early clinical development. We have not completed successful late-stage pivotal clinical trials or obtained regulatory approval for any product candidate. We may never obtain approval for any of our product candidates or achieve or sustain profitability.
- We may incur additional costs or experience delays in completing, or ultimately be unable to complete the development and/or commercialization of PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 or our other product candidates.
- We may be adversely affected by the effects of inflation.
- If we experience delays or difficulties in enrolling patients in our ongoing or planned clinical trials, our receipt of necessary regulatory approval could be delayed or prevented.
- The ongoing COVID-19 pandemic could adversely impact our business, including our clinical trials and clinical trial operations.
- Adverse side effects or other safety risks associated with PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 or our other product candidates could delay or preclude approval, cause us to suspend or discontinue clinical trials or abandon further development, limit the commercial profile of an approved product, or result in significant negative consequences following marketing approval, if any.
- 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.
- Health care policy changes, including U.S. health care reform legislation, may have a material adverse effect on our business.
- We rely, and intend to continue to rely, on third parties to conduct our clinical trials and perform some of our research and preclinical studies. If these third parties do not satisfactorily carry out their contractual duties, fail to comply with applicable regulatory requirements or do not meet expected deadlines, our development programs may be delayed or subject to increased costs or we may be unable to obtain regulatory approval, each of which may have an adverse effect on our business, financial condition, results of operations and prospects.
- Manufacturing pharmaceutical products is complex and subject to product loss for a variety of reasons. We rely on third-party suppliers, including single source suppliers, to manufacture preclinical and clinical supplies of our product candidates and we intend to rely on third parties to produce commercial supplies of any approved product candidate. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products

or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

- We may enter into collaborations with third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.
- The incidence and prevalence for target patient populations of our product candidates have not been established with precision. If the market opportunities for our product candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue potential and ability to achieve profitability will be adversely affected.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.
- Our future success depends on our ability to retain key employees and to attract, retain and motivate qualified personnel and manage our human capital.
- We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.
- Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation and/or adverse publicity and could negatively affect our operating results and business.
- We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.
- If we are unable to obtain and maintain sufficient patent protection for our product candidates, or if the scope of the patent protection is not sufficiently broad, third parties, including our competitors, could develop and commercialize products similar or identical to ours, and our ability to commercialize our product candidates successfully may be adversely affected.
- We may become involved in lawsuits or administrative disputes to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.
- We may not be able to effectively protect or enforce our intellectual property and proprietary rights throughout the world.
- If we are sued for infringing, misappropriating or otherwise violating intellectual property or proprietary rights of third parties, such litigation or disputes could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.
- Rights to improvements to our product candidates may be held by third parties.
- An active and liquid trading market for our common stock may never be sustained. As a result, you may not be able to resell your shares of common stock at or above the purchase price.
- The market price of our common stock is likely to be highly volatile, which could result in substantial losses for purchasers of our common stock.
- Our principal stockholders and management own a significant percentage of our stock and are able to exert significant control over matters subject to stockholder approval.
- We are an "emerging growth company" and a "smaller reporting company" and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies or smaller reporting companies will make our common stock less attractive to investors.
- We will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

Risks Related to Our Financial Position and Need for Capital

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 incurred significant operating losses since our inception and have not generated any revenue. We expect to incur continued losses for the foreseeable future and may never achieve or maintain profitability.

Investment in drug development is a highly speculative undertaking and involves a substantial degree of risk. We commenced operations in 2016 and are a clinical-stage biopharmaceutical company with a limited operating history. We have not yet commercialized any product and we do not expect to generate revenue from sales of any products for several years, if at all. Consequently, there have been limited operations upon which we or you can evaluate our business. Predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing cancer therapies. For the nine months ended September 30, 2022 and 2021, we reported a net loss of $86.8 million and $78.9 million, respectively. As of September 30, 2022, we had an accumulated deficit of $305.9 million. We expect to continue to incur significant research and development and other expenses related to our ongoing operations.

Since our inception, we have focused substantially all of our efforts and financial resources on the research, preclinical and clinical development of our product candidates, PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789 and our research efforts on other potential product candidates targeting PRMT5, MCL1, CDK9, and BRM, otherwise known as SMARCA2. As of September 30, 2022, our cash, cash equivalents, and marketable securities were $224.0 million.

We expect to incur increasing levels of operating losses for the foreseeable future, particularly as we advance PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789 through clinical development. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect our research and development expenses to significantly increase in connection with our additional planned clinical trials for our lead product candidates, including the ongoing Phase 1 clinical trials and the expansion cohorts of PRT543 and PRT811, the ongoing Phase 1 clinical trials for both the oral formulation and IV formulation of PRT1419, the ongoing Phase 1 clinical trial for PRT2527, the Phase 1 clinical trial for PRT3645 and PRT3789, and development and subsequent INDs of other future product candidates we may choose to pursue. In addition, if we obtain marketing approval for any of our product candidates, we will incur significant sales, marketing and outsourced manufacturing expenses in connection with the commercialization. We will also continue to incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis. We expect our financial condition and operating results to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue and we do not know when, or if, we will generate any revenue. We do not expect to generate significant revenue unless and until we obtain marketing approval for, and begin to sell, PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 or another product candidate. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- complete successful Phase 1 portions of PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789 clinical trials;
- initiate and successfully complete all safety, pharmacokinetic and other studies required to obtain U.S. and foreign marketing approval for PRT543 as a treatment for patients with hematological malignancies and advanced solid tumors, PRT811 as a treatment for patients with glioblastoma and advanced solid tumors and PRT1419 as a treatment for patients with certain solid tumors and hematological malignancies;
- initiate and complete successful later-stage clinical trials that meet their clinical endpoints;
- obtain favorable results from our clinical trials and apply for and obtain marketing approval for PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789;
- establish licenses, collaborations, or strategic partnerships that may increase the value of our programs;
- successfully manufacture or contract with others to manufacture PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 and our other product candidates;

- commercialize PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789 if approved, respectively, by building a sales force or entering into collaborations with third parties;
- submit INDs for a kinase inhibitor and SMARCA2 protein degrader that are made effective by the FDA;
- obtain, maintain, protect and defend our intellectual property portfolio; and
- achieve market acceptance of PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 and our other successful product candidates with the medical community and with third-party payors.

To become and remain profitable, we must succeed in designing, developing, and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials for our product candidates, designing additional product candidates, establishing arrangements with third parties for the manufacture of clinical supplies of our product candidates, obtaining marketing approval for our product candidates and manufacturing, marketing and selling any products for which we may obtain marketing approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

In cases where we are successful in obtaining regulatory approval to market one or more of our product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to obtain coverage and reimbursement, and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the treatment population is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we will incur or when, or if, we will be able to achieve profitability. If we decide to or are required by the FDA or regulatory authorities in other jurisdictions to perform studies or clinical trials in addition to those currently expected, or if there are any delays in establishing appropriate manufacturing arrangements for, in initiating or completing our current and planned clinical trials for, or in the development of, any of our product candidates, our expenses could increase materially and profitability could be further delayed.

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, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will require substantial additional funding to pursue our business objectives. If we are unable to raise capital when needed or on terms acceptable to us, we could be forced to delay, reduce or eliminate our research or drug development programs, any future commercialization efforts or other operations.

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance our product candidates, PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789, and other pipeline product candidates through clinical development, and seek to design additional product candidates from our discovery programs. We expect increased expenses as we continue our research and development, expand operations and build our new facility, initiate additional clinical trials, and seek marketing approval for our lead programs and our other product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. Adequate additional financing may not be available to us on favorable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. If we are unable to raise capital when needed or on favorable terms, we could be forced to delay, reduce or eliminate our research and development programs, our commercialization plans or other operations.

We believe that our existing cash, cash equivalents, and marketable securities will enable us to fund our operating expenses, and capital expenditure requirements into the fourth quarter of 2024. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Changes beyond our control may occur that would cause us to use our available capital before that time, including changes in and progress of our drug development activities and changes in regulation. Our future capital requirements will depend on many factors, including:

- the progress, timing and results of preclinical studies and clinical trials for our current or any future product candidates;
- the extent to which we develop, in-license or acquire other pipeline product candidates or technologies;
- the number and development requirements of other product candidates that we may pursue, and other indications for our current product candidates that we may pursue;
- the costs, timing and outcome of obtaining regulatory approvals of our current or future product candidates and any companion diagnostics we may pursue;
- the scope and costs of making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our current or future product candidates;
- the costs involved in growing our organization to the size needed to allow for the research, development and potential commercialization of our current or future product candidates;
- the cost associated with commercializing any approved product candidates, including establishing sales, marketing and distribution capabilities;
- the cost associated with completing any post-marketing studies or trials required by the FDA or other regulatory authorities;
- the revenue, if any, received from commercial sales of PRT543, PRT811, PRT1419, PRT2527, PRT3645, or PRT3789 if any are approved, or our other pipeline product candidates that receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims that we may become subject to, including any litigation costs and the outcome of such litigation;
- the costs associated with potential product liability claims, including the costs associated with obtaining insurance against such claims and with defending against such claims; and
- to the extent we pursue strategic collaborations, including collaborations to commercialize PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 or any of our other pipeline product candidates, our ability to establish and maintain collaborations on favorable terms, if at all, as well as the timing and amount of any milestone or royalty payments we are required to make or are eligible to receive under such collaborations, if any.

We will require additional capital to complete our planned clinical development programs for our current product candidates to obtain regulatory approval. Our ability to raise additional funds will depend on financial, economic and market conditions and other factors, over which we may have no or limited control. If adequate funds are not available on commercially acceptable terms when needed, we may be forced to delay, reduce or terminate the development or commercialization of all or part of our research programs or product candidates or we may be unable to take advantage of future business opportunities. Furthermore, any additional capital-raising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our current and future product candidates, if approved.

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

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest 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 acquisitions or 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. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our research, product development or future commercialization efforts or grant rights to third parties to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We may be adversely affected by the effects of inflation.

Inflation has the potential to adversely affect our liquidity, business, financial condition and results of operations by increasing our overall cost structure. The existence of inflation in the economy has resulted in, and may continue to result in, higher interest rates and capital costs, supply shortages, increased costs of labor, components, manufacturing and shipping, as well as weakening exchange rates and other similar effects. As a result of inflation, we have experienced and may continue to experience cost increases. Although we may take measures to mitigate the effects of inflation, if these measures are not effective, our business, financial condition, results of operations and liquidity could be materially adversely affected. Even if such measures are effective, there could be a difference between the timing of when these beneficial actions impact our results of operations and when the cost of inflation is incurred.

Risks Related to Design and Development of our Product Candidates

We are highly dependent on the success of our product candidates, PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789, which are in early clinical development. We have not completed successful late-stage pivotal clinical trials or obtained regulatory approval for any product candidate. We may never obtain approval for any of our product candidates or achieve or sustain profitability.

Our future success is highly dependent on our ability to obtain regulatory approval for, and then successfully commercialize, our product candidates, PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789. We are early in our development efforts and our lead product candidates, PRT543, PRT811, PRT1419 and PRT2527, are each currently in a Phase 1 clinical trial. Our other product candidates are in earlier stages of development. We currently have no products that are approved for sale in any jurisdiction. There can be no assurance that PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 or our other product candidates in development will achieve success in their clinical trials or obtain regulatory approval.

Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789, or other product candidates in development. The success of our product candidates, including PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789 will depend on several factors, including the following:

- successful completion of preclinical studies and clinical trials;
- acceptance of INDs by the FDA or other similar clinical trial applications from foreign regulatory authorities for our future clinical trials for our pipeline product candidates;
- timely and successful enrollment of patients in, and completion of, clinical trials with favorable results;
- demonstration of safety, efficacy and acceptable risk-benefit profiles of our product candidates to the satisfaction of the FDA and foreign regulatory agencies;
- our ability, or that of our collaborators, to develop and obtain clearance or approval of companion diagnostics, on a timely basis, or at all;
- receipt and related terms of marketing approvals from applicable regulatory authorities, including the completion of any required post-marketing studies or trials;
- raising additional funds necessary to complete clinical development of and commercialize our product candidates;
- obtaining and maintaining patent, trade secret and other intellectual property protection and regulatory exclusivity for our product candidates;
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our product candidates;
- developing and implementing marketing and reimbursement strategies;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;

- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining third-party payor coverage and adequate reimbursement;
- protecting and enforcing our rights in our intellectual property portfolio; and
- maintaining a continued acceptable safety profile of the products following approval.

Many of these factors are beyond our control, and it is possible that none of our product candidates will ever obtain regulatory approval even if we expend substantial time and resources seeking such approval. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. For example, our business could be harmed if results of our ongoing and future clinical trials of PRT543, PRT811, PRT1419, PRT2527, PRT3645, or PRT3789 vary adversely from our expectations.

Drug development involves a lengthy and expensive process, and clinical testing is uncertain as to the outcome.

We currently have three product candidates in Phase 1 clinical development and additional product candidates in preclinical development, and the risk of failure for each is high. We are unable to predict when or if our product candidates will prove effective or safe in humans or will obtain marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to the outcome.

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 or of clinical trials of the same product candidates in other indications, and interim or preliminary results of a clinical trial do not necessarily predict final results. Later-stage clinical trials could differ in significant ways from early-stage clinical trials, including changes to inclusion and exclusion criteria, efficacy endpoints, dosing regimen and statistical design. In particular, the small number of patients in our current Phase 1 clinical trials may make the results of these trials less predictive of the outcome of later clinical trials. In addition, although we have observed encouraging clinical activity in the dose escalation portion of the Phase 1 portion of our ongoing PRT543 and PRT811 clinical trials, the primary objectives were to determine the safety, tolerability and maximum tolerated dose of PRT543 and PRT811, respectively, and to determine a recommended Phase 2 dose for the expansion portion of our Phase 1 clinical trials, and not to demonstrate efficacy. The assessments of clinical activity from this portion of the clinical trials, some of which were not pre-specified, may not be predictive of the results in dose expansion cohorts, specific tumor types or further clinical trials of PRT543 and PRT811. In addition, while we may believe certain results in patients, such as stable disease, suggest encouraging clinical activity, stable disease is not considered a response for regulatory purposes. Stable disease, or SD, is defined as failure to meet the definition of objective clinical response or progressive disease. Furthermore, safety events may be observed in later trials that alter the anticipated risk-benefit profiles of PRT543 and PRT811.

We may incur additional costs or experience delays in completing, or ultimately be unable to complete the development and/or commercialization of PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 or our other product candidates.

Before we can initiate clinical trials of a product candidate in any indication, we must submit the results of preclinical studies to the FDA or to comparable foreign authorities, respectively, along with other information, including information about the product candidate's chemistry, manufacturing and controls and our proposed clinical trial protocol, as part of an IND or comparable foreign regulatory filings.

The FDA may require us to conduct additional preclinical studies for any product candidate before it allows us to initiate subsequent clinical trials under any IND, which may lead to additional delays and increase the costs of our preclinical development programs.

Any delays in the commencement or completion of our ongoing, planned or future clinical trials could significantly affect our product development costs. We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to obtain marketing approval or commercialize our product candidates, including:

- regulators, institutional review boards, or IRBs, or ethics committees, or ECs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- the FDA may disagree as to the design or implementation of our clinical trials or with our recommended Phase 2 doses for any of our pipeline programs;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective CROs and prospective trial sites;
- clinical trials for our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials, delay or halt clinical trials or abandon product development programs;
- lack of adequate funding to continue the clinical trial;
- the number of patients required for clinical trials for our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or may be lower than we anticipate due to challenges in recruiting and enrolling suitable patients that meet the study criteria, participants may drop out of these clinical trials at a higher rate than we anticipate or the duration of these clinical trials may be longer than we anticipate;
- competition for clinical trial participants from investigational and approved therapies may make it more difficult to enroll patients in our clinical trials;
- we may experience difficulties in maintaining contact with patients after treatment, resulting in incomplete data;
- we or third-party collaborators may fail to obtain regulatory approval of companion diagnostic tests, if required, on a timely basis, or at all;
- our third-party contractors may fail to meet their contractual obligations to us in a timely manner, or at all, or may fail to comply with regulatory requirements;
- we may have to suspend or terminate clinical trials for our product candidates for various reasons, including a finding by us or by a Data Monitoring Committee for a trial that the participants are being exposed to unacceptable health risks;
- our product candidates may have undesirable or unexpected side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs/ECs to suspend or terminate the trials;
- the cost of clinical trials for our product candidates may be greater than we anticipate;
- changes to clinical trial protocol;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials for our product candidates may be insufficient or inadequate and result in delays or suspension of our clinical trials; and
- the impact of the ongoing COVID-19 pandemic, which may slow potential enrollment, reduce the number of eligible patients for clinical trials, or reduce the number of patients that remain in our trials.

Delays, including delays caused by the above factors, can be costly and could negatively affect our ability to complete a clinical trial or obtain timely marketing approvals. We do not know whether any of our planned preclinical studies or clinical trials will begin on a timely basis or at all, will need to be restructured or will be completed on schedule, or at all. For example, the FDA may place a partial or full clinical hold on any of our clinical trials for a variety of reasons, including safety concerns and noncompliance with regulatory requirements. If we are not able to complete successful clinical trials, we will not be able to obtain regulatory approval and will not be able to commercialize our product candidates.

Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

If we experience delays or difficulties in enrolling patients in our ongoing or planned clinical trials, our receipt of necessary regulatory approval could be delayed or prevented.

We may not be able to initiate or continue our ongoing or planned clinical trials for our product candidates if we are unable to identify and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or comparable foreign regulatory authorities. In addition, some of our competitors currently have ongoing clinical trials for product candidates that would treat the same patients as our clinical product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. This is acutely relevant for our development of PRT543 for the treatment of patients with myeloid malignancies and other solid tumors, including adenoid cystic carcinoma, indications for which investigational drugs by our competitors are competing for clinical trial participants. Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;
- our ability to recruit clinical trial investigators of appropriate competencies and experience;
- the incidence and prevalence of our target indications;
- clinicians' and patients' awareness of, and perceptions as to the potential advantages and risks of our product candidates in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- competing studies or trials with similar eligibility criteria;
- invasive procedures required to enroll patients and to obtain evidence of the product candidate's performance during the clinical trial;
- availability and efficacy of approved medications for the disease under investigation;
- eligibility criteria defined in the protocol for the trial in question;
- the size and nature of the patient population required for analysis of the trial's primary endpoints;
- efforts to facilitate timely enrollment in clinical trials;
- whether we are subject to a partial or full clinical hold on any of our clinical trials;
- reluctance of physicians to encourage patient participation in clinical trials;
- the ability to monitor patients adequately during and after treatment;
- our ability to obtain and maintain patient consents; and
- proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll and maintain a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials, including due to the ongoing COVID-19 pandemic, may result in increased development costs, which would cause the value of our company to decline and limit our ability to obtain additional financing.

The ongoing COVID-19 pandemic could adversely impact our business, including our clinical trials and clinical trial operations.

The ongoing COVID-19 pandemic in the United States and in other countries in which we have planned or have active clinical trial sites and where our third-party manufacturers operate, could cause significant disruptions that could severely impact our business and clinical trials, including:

- delays or difficulties in screening, enrolling and maintaining patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;

- inability or unwillingness of subjects to travel to the clinical trial sites;
- delays, difficulties, or incompleteness in data collection and analysis and other related activities;
- decreased implementation of protocol required clinical trial activities and quality of source data verification at clinical trial sites;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials and our other research and development activities, including because of sickness of employees or their families or mitigation measures such as lock-downs and social distancing;
- delays due to production shortages resulting from any events affecting raw material supply or manufacturing capabilities domestically and abroad;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials;
- interruption in global and domestic shipping that may affect the transport of clinical trial materials, such as investigational drug products used in our clinical trials;
- changes in local regulations as part of a response to the ongoing COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, delays, or to discontinue the clinical trials altogether;
- 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;
- refusal of regulatory authorities such as FDA or European Medicines Agency, or EMA, to accept data from clinical trials in affected geographies; and
- adverse impacts on global economic conditions which could have an adverse effect on our business and financial condition, including impairing our ability to raise capital when needed.

Such disruptions could impede, delay, limit or prevent completion of our ongoing clinical trials and preclinical studies or commencement of new clinical trials and ultimately lead to the delay or denial of regulatory approval of our product candidates, which would seriously harm our operations and financial condition and increase our costs and expenses. We are in close contact with our CROs, CMOs and clinical sites as we seek to mitigate the impact of the ongoing COVID-19 pandemic on our studies and current timelines. Measures we have taken in response to the ongoing COVID-19 pandemic include, where feasible, conducting remote clinical trial site activations and data monitoring, and limiting on-site patient visits by adjusting patient assessments and protocol. However, despite these efforts, we have experienced limited delays in trial site initiations, patient participation and patient enrollment in some of our clinical trials and we may continue to experience some delays in our clinical trials and preclinical studies and delays in data collection and analysis. These delays so far have had a limited impact, but this may change as the ongoing COVID-19 pandemic and the response to such ongoing COVID-19 pandemic continues to evolve, and could have an adverse impact on our timelines and our business. The ongoing COVID-19 pandemic could also affect the business of the FDA, EMA or other health authorities, which could result in delays in meetings related to planned or completed clinical trials and ultimately of reviews and approvals of our product candidates. The ongoing global COVID-19 pandemic continues to rapidly evolve. The extent to which the ongoing COVID-19 pandemic may impact our business and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing 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.

Adverse side effects or other safety risks associated with PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 or our other product candidates could delay or preclude approval, cause us to suspend or discontinue clinical trials or abandon further development, limit the commercial profile of an approved product, or result in significant negative consequences following marketing approval, if any.

As is the case with pharmaceuticals generally, we have observed side effects and adverse events associated with our clinical product candidate, PRT543. These side effects included diarrhea, nausea and fatigue, but none of these side effects were considered related to PRT543. At the highest dose level of our clinical product candidate, PRT543, there were occurrences of grade 4 thrombocytopenia that were deemed related to PRT543, but the toxicity was reversible after a one to two week drug holiday and the affected patients remained on the study and were restarted at a lower dose. We have also observed side effects and adverse effects associated with PRT811. These side effects included nausea, constipation, vomiting and hyponatremia, but none of these side effects were considered related to PRT811.

Results of our ongoing and planned clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates could result in the delay, suspension or termination of clinical trials by us or regulatory authorities for a number of reasons. Furthermore, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of subjects and limited duration of exposure, rare and severe side effects of our product candidates or those of our competitors may only be uncovered with a significantly larger number of patients exposed to the drug.

Additionally, due to the high mortality rates of the cancers for which we are initially pursuing development and the pretreated nature of many patients in our ongoing clinical trials of PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789, a material percentage of patients in these clinical trials may die during a trial, which could impact development of PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789, respectively. If we elect or are required to delay, suspend or terminate any clinical trial, the commercial prospects of our product candidates will be harmed and our ability to generate product revenues from this product candidate will be delayed or eliminated. Serious adverse events observed in clinical trials could hinder or prevent market acceptance of our product candidates. Any of these occurrences may harm our business, prospects, financial condition and results of operations significantly.

Moreover, if our product candidates are associated with undesirable side effects in clinical trials or have characteristics that are unexpected, we may elect to abandon or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which may limit the commercial expectations for our product candidates, if approved. We may also be required to modify our study plans based on findings in our clinical trials. Such side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial. Many drugs that initially showed promise in early stage testing have later been found to cause side effects that prevented further development. In addition, regulatory authorities may draw different conclusions, require additional testing to confirm these determinations, require more restrictive labeling, or deny regulatory approval of the product candidate.

It is possible that, as we test our product candidates in larger, longer and more extensive clinical trials, including with different dosing regimens, or as the use of our product candidates becomes more widespread following any regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. If such side effects become known later in development or upon approval, if any, such findings may harm our business, financial condition, results of operations and prospects significantly.

In addition, if any of our product candidates receive marketing approval, and we or others later identify undesirable side effects caused by treatment with such drug, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approval of the drug;
- we may be required to recall a product or change the way the drug is administered to patients;
- regulatory authorities may require additional warnings in the labeling, such as a contraindication or a boxed warning, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we may be required to implement a Risk Evaluation and Mitigation Strategy, or REMS, or create a medication guide outlining the risks of such side effects for distribution to patients;
- additional restrictions may be imposed on the marketing or promotion of the particular product or the manufacturing processes for the product or any component thereof;
- we could be sued and held liable for harm caused to patients;
- we may be subject to regulatory investigations and government enforcement actions;
- the drug could become less competitive; and

- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our product candidates, if approved, and could significantly harm our business, financial condition, results of operations and prospects.

Preliminary, interim and topline data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary, interim or topline data from our clinical trials, such as the preliminary data analysis for the Phase 1 dose expansion portions of our PRT543 and PRT811 trials. These updates are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. Additionally, interim data from clinical trials that we may complete 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. Therefore, positive interim results in any ongoing clinical trial may not be predictive of such results in the completed study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Adverse changes between preliminary or interim data and final data could significantly harm our business and prospects. Further, additional disclosure of interim data by us or by our competitors in the future could result in volatility in the price of our common stock. See the description of risks under the heading “Risks Related to our Common Stock” for more disclosure related to the risk of volatility in our stock price.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, product candidate or our business. If the preliminary or topline data that we report differ from late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 or any other product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

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.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We may not be successful in our efforts to design additional potential product candidates.

A key element of our strategy is to identify molecular targets and intervention points leading to treatment failure, and then apply our expertise of cancer biology and medicinal chemistry, as well as our in-depth understanding of the current landscape of oncology treatments, to design solutions that can be precisely tailored in a target class agnostic fashion. The therapeutic design and development activities that we are conducting may not be successful in developing product candidates that are safe and effective in treating cancer or other diseases. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- the target selection methodology used may not be successful in identifying potential product candidates;
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will obtain marketing approval or achieve market acceptance; or
- potential product candidates may not be effective in treating their targeted diseases.

Research programs to identify and design new product candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. If we are unable to identify and design suitable product candidates for preclinical and clinical development, we will not be able to obtain revenues from the sale of products in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

Risks Related to Government Regulation

The development and commercialization of pharmaceutical products are subject to extensive regulation, and we may not obtain regulatory approvals for PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 or any other product candidates, on a timely basis or at all.

The clinical development, manufacturing, labeling, packaging, storage, recordkeeping, advertising, promotion, export, import, marketing, distribution, adverse event reporting, including the submission of safety and other post-marketing information and reports, and other possible activities relating to PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789 currently our only product candidates in planned or ongoing clinical trials, as well as any other product candidate that we may develop in the future, are subject to extensive regulation. Marketing approval of drugs in the United States requires the submission of an NDA to the FDA, and we are not permitted to market any product candidate in the United States until we obtain approval from the FDA of the NDA for that product. An NDA must be supported by extensive clinical and preclinical data, as well as extensive information regarding pharmacology, chemistry, manufacturing and controls. Our product candidates must be approved by comparable regulatory authorities in other jurisdictions prior to commercialization.

FDA approval of an NDA is not guaranteed, and the review and approval process is an expensive and uncertain process that may take several years. Of the large number of drugs in development in the United States, only a small percentage will successfully complete the FDA regulatory approval process and will be commercialized. Accordingly, there can be no assurance that any of our product candidates will receive regulatory approval in the United States, or other jurisdictions.

The FDA also has substantial discretion in the approval process. The number and types of preclinical studies and clinical trials that will be required for NDA approval varies depending on the product candidate, the disease or the condition that the product candidate is designed to treat and the regulations applicable to any particular product candidate. For example, if successful, we believe that the expansion portions of the Phase 1 clinical trials of PRT543 or PRT811 may be sufficient to support FDA approval of an NDA for PRT543 or PRT811, respectively, but the FDA may disagree with the sufficiency of our data and require additional clinical trials. Additionally, depending upon the results of the expansion portions of the Phase 1 clinical trials of PRT543 or PRT811, we may choose to seek Subpart H accelerated approval for PRT543 or PRT811, respectively, which would require completion of a confirmatory trial to validate the clinical benefit of the drug. Despite the time and expense associated with preclinical studies and clinical trials, failure can occur at any stage. The results of preclinical and early clinical trials of PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 or any other product candidate may not be predictive of the results of our later-stage clinical trials.

Clinical trial failure may result from a multitude of factors including flaws in trial design, dose selection, placebo effect, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits, and failure in clinical trials can occur at any stage. Companies in the pharmaceutical industry frequently suffer setbacks in the advancement of clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Based upon negative or inconclusive results, we may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. In addition, data obtained from clinical trials are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may further delay, limit or prevent marketing approval.

The FDA could delay, limit or deny approval of a product candidate for many reasons, including because the FDA:

- may not deem our product candidate to be safe and effective;
- determines that the product candidate does not have an acceptable benefit-risk profile;
- determines in the case of an NDA seeking accelerated approval that the NDA does not provide evidence that the product candidate represents a meaningful advantage over available therapies;
- determines that the objective response rate, or ORR, and duration of response are not clinically meaningful;
- may not agree that the data collected from preclinical studies and clinical trials are acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval, and may impose requirements for additional preclinical studies or clinical trials;
- may determine that adverse events experienced by participants in our clinical trials represent an unacceptable level of risk;
- may determine that population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- may not accept clinical data from trials, which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States;
- may disagree regarding the formulation, labeling and/or the specifications;
- may not approve the manufacturing processes associated with our product candidate or may determine that a manufacturing facility does not have an acceptable compliance status;
- may change approval policies or adopt new regulations; or
- may not file a submission due to, among other reasons, the content or formatting of the submission.

In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials, and the review process. For example, the Oncology Center of Excellence, or OCE, within the FDA has recently advanced Project Optimus, which is an initiative to reform the dose optimization and dose selection paradigm in oncology drug development to emphasize selection of an optimal dose, which is a dose or doses that maximizes not only the efficacy of a drug but the safety and tolerability as well. This shift from the prior approach, which generally determined the maximum tolerated dose, may require sponsors to spend additional time and resources to further explore a product candidate’s dose-response relationship to facilitate optimum dose selection in a target population. Other recent OCE initiatives have included Project FrontRunner, a new initiative with a goal of developing a framework for identifying candidate drugs for initial clinical development in the earlier advanced setting rather than for treatment of patients who have received numerous prior lines of therapies or have exhausted available treatment options. We are considering these policy changes as they relate to our programs. We have not obtained FDA approval for any product. This lack of experience may impede our ability to obtain FDA approval in a timely manner, if at all, for our clinical product candidates.

We have not obtained FDA approval for any product. This lack of experience may impede our ability to obtain FDA approval in a timely manner, if at all, for our clinical product candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of PRT543, PRT811, PRT1419, PRT2527, PRT3645, or PRT3789 our commercial prospects will be harmed and our ability to generate revenues will be materially impaired which would adversely affect our business, prospects, financial condition and results of operations.

The accelerated approval pathway for our product candidates may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our product candidates will receive marketing approval.

Under the FDA’s accelerated approval program, the FDA may approve a drug for a serious or life- threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. We may seek accelerated approval for one or more of our product candidates on the basis of ORR with an acceptable duration of response, a surrogate endpoint that we believe is reasonably likely to predict clinical benefit.

For drugs granted accelerated approval, post-marketing confirmatory trials are required to describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. These confirmatory trials must be completed with due diligence and, in some cases, the FDA may require that the trial be designed, initiated, and/or fully enrolled prior to approval. If any of our competitors were to receive full approval on the basis of a confirmatory trial for an indication for which we are seeking accelerated approval before we receive accelerated approval, the indication we are seeking may no longer qualify as a condition for which there is an unmet medical need and accelerated approval of our product candidate would be more difficult or may not occur. Moreover, the FDA may withdraw approval of our product candidate approved under the accelerated approval pathway if, for example:

- the trial or trials required to verify the predicted clinical benefit of our product candidate fail to verify such benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug;
- other evidence demonstrates that our product candidate is not shown to be safe or effective under the conditions of use;
- we fail to conduct any required post-approval trial of our product candidate with due diligence; or
- we disseminate false or misleading promotional materials relating to the relevant product candidate.

Recently, the accelerated approval pathway has come under scrutiny within the FDA and by Congress. The FDA has put increased focus on ensuring that confirmatory studies are conducted with diligence and, ultimately, that such studies confirm the benefit. For example, FDA has convened its Oncologic Drugs Advisory Committee to review what the FDA has called dangling or delinquent accelerated approvals where confirmatory studies have not been completed or where results did not confirm benefit. In addition, the OCE has recently announced Project Confirm, which is an initiative to promote the transparency of outcomes related to accelerated approvals for oncology indications and provide a framework to foster discussion, research and innovation in approval and post-marketing processes, with the goal to enhance the balance of access and verification of benefit for therapies available to patients with cancer and hematologic malignancies. Furthermore, Congress is considering various proposals to potentially make changes to the accelerated approval pathway, including proposals to increase the likelihood of withdrawal of approval in such circumstances.

Our failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in those jurisdictions, and any approval we are granted for our product candidates in the United States would not assure approval of product candidates in foreign jurisdictions.

In order to market and sell our products in any jurisdiction outside the United States, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to submit for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

We may not be able to obtain or maintain orphan drug designation or exclusivity for our product candidates.

Regulatory authorities in some jurisdictions, including the United States, may designate drugs for relatively small patient populations as “orphan drugs.” Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or if the disease or condition affects more than 200,000 individuals in the United States and there is no reasonable expectation that the cost of developing the drug for the type of disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation entitles a party to financial incentives, such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Additionally, if a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years, except in certain circumstances, such as a showing of clinical superiority (i.e., another product is safer, more effective or makes a major contribution to patient care) over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. Competitors, however, may receive approval of different products for the same indication for which the orphan product has exclusivity, or obtain approval for the same product but for a different indication than that for which the orphan product has exclusivity.

We may apply for an orphan drug designation in the United States or other geographies for our product candidates in the future. However, obtaining an orphan drug designation can be difficult, and we may not be successful in doing so. Even if we obtain orphan drug designation for our product candidates in specific indications, we may not be the first to obtain regulatory approval of these product candidates for the orphan- designated indication, due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for orphan designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan drug designation does not ensure that we will receive marketing exclusivity in a particular market, and we cannot assure you that any future application for orphan drug designation in any other geography or with respect to any other product candidate will be granted. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process.

A Breakthrough Therapy Designation by the FDA for any of our current or future product candidates may not lead to a faster development or regulatory review or approval process, and it would not increase the likelihood that the product candidate will receive marketing approval.

We may seek a Breakthrough Therapy Designation for one or more of our current or future product candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the submission of the NDA.

Designation as a breakthrough therapy is at the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a drug may not result in a faster development process, review, or approval compared to drugs considered for approval under conventional FDA procedures and it would not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the product candidate no longer meets the conditions for qualification or that the time period for FDA review or approval will not be shortened.

If we are unable to successfully develop, validate, obtain regulatory approval of and commercialize companion diagnostic tests for any product candidates that require such tests, or experience significant delays in doing so, we may not realize the full commercial potential of these product candidates.

A companion diagnostic is a medical device, often an *in vitro* device, which provides information that is essential for the safe and effective use of a corresponding therapeutic drug product. A companion diagnostic can be used to identify patients who are most likely to benefit from the therapeutic product. In the future, we may evaluate opportunities to develop, either by ourselves or with collaborators, companion diagnostic tests for our product candidates for certain indications.

A companion diagnostic is generally developed in conjunction with the clinical program for an associated therapeutic product. To date, the FDA has required premarket approval of the vast majority of companion diagnostics for cancer therapies. Generally, when a companion diagnostic is essential to the safe and effective use of a drug product, the FDA requires that the companion diagnostic be approved before or concurrent with approval of the therapeutic product and before a product can be commercialized. The approval of a companion diagnostic as part of the therapeutic product's labeling limits the use of the therapeutic product to only those patients who express the specific genetic alteration that the companion diagnostic was developed to detect.

Development of a companion diagnostic could include additional meetings with regulatory authorities, such as a pre-submission meeting and the requirement to submit an investigational device exemption application. In the case of a companion diagnostic that is designated as "significant risk device," approval of an investigational device exemption by the FDA and IRB is required before such diagnostic is used in conjunction with the clinical trials for a corresponding product candidate.

To be successful in developing, validating, obtaining approval of and commercializing a companion diagnostic, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. We have no prior experience with medical device or diagnostic test development. If we choose to develop and seek FDA approval for companion diagnostic tests on our own, we will require additional personnel. We may rely on third parties for the design, development, testing, validation and manufacture of companion diagnostic tests for our therapeutic product candidates that require such tests, the application for and receipt of any required regulatory approvals, and the commercial supply of these companion diagnostics. If these parties are unable to successfully develop companion diagnostics for these therapeutic product candidates, or experience delays in doing so, we may be unable to enroll enough patients for our current and planned clinical trials, the development of these therapeutic product candidates may be adversely affected, these therapeutic product candidates may not obtain marketing approval, and we may not realize the full commercial potential of any of these therapeutics that obtain marketing approval. For any product candidate for which a companion diagnostic is necessary to select patients who may benefit from use of the product candidate, any failure to successfully develop a companion diagnostic may cause or contribute to delayed enrollment of our clinical trials, and may prevent us from initiating a pivotal trial. In addition, the commercial success of any of our product candidates that require a companion diagnostic will be tied to and dependent upon the receipt of required regulatory approvals and the continued ability of such third parties to make the companion diagnostic commercially available to us on reasonable terms in the relevant geographies. Any failure to do so could materially harm our business, results of operations and financial condition.

If we decide to pursue a Fast Track Designation by the FDA, it may not lead to a faster development or regulatory review or approval process.

We may seek Fast Track Designation for one or more of our product candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the product sponsor may apply for FDA Fast Track Designation. The FDA has broad discretion whether to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program.

Even if we obtain marketing approval for our product candidates, the terms of approvals, ongoing regulation of our products or other post-approval restrictions may limit how we manufacture and market our products and compliance with such requirements may involve substantial resources, which could materially impair our ability to generate revenue.

Any product candidates for which we receive accelerated approval from the FDA are required to undergo one or more confirmatory clinical trials. If such a product candidate fails to meet its safety and efficacy endpoints in such confirmatory clinical trials, the regulatory authority may withdraw its conditional approval. There is no assurance that any such product will successfully advance through its confirmatory clinical trial(s). Therefore, even if a product candidate receives accelerated approval from the FDA, such approval may be withdrawn at a later date.

Even if marketing approval of a product candidate is granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation, which may include the requirement to implement a REMS or to conduct costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product.

We must also comply with requirements concerning advertising and promotion for any of our product candidates for which we obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product’s approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers’ facilities are required to ensure that quality control and manufacturing procedures conform to current good manufacturing practices, or cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We and our CMOs could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we obtain marketing approval for one or more of our product candidates, we and our CMOs will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for our products withdrawn by regulatory authorities and our ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. As a result, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

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

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include, but are not limited to, restrictions governing promotion of an approved product, submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding drug distribution and the distribution of samples to physicians and recordkeeping.

The FDA and other federal and state agencies, including the Department of Justice, closely regulate compliance with all requirements governing prescription drug products, including requirements pertaining to marketing and promotion of drugs in accordance with the provisions of the approved labeling and manufacturing of products in accordance with cGMP requirements. For example, the FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. Violations of such requirements may lead to investigations alleging violations of the Federal Food, Drug, and Cosmetic Act, or FDCA, and other statutes, including the False Claims Act and other federal and state healthcare fraud and abuse laws as well as state consumer protection laws. Our failure to comply with all regulatory requirements, and later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, may yield various results, including:

- litigation involving patients taking our products;
- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance by us or any future collaborator with regulatory requirements, including safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population can also result in significant financial penalties.

Our current and future relationships with customers and third-party payors may be subject to applicable anti-kickback, fraud and abuse, transparency, health privacy, and other healthcare laws and regulations, which could expose us to significant penalties, including criminal, civil, and administrative penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, including physicians, and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare providers, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, as well as, market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations that may be applicable to our business include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the False Claims Act, which can be enforced by civil whistleblower or qui tam actions on behalf of the government, and criminal false claims laws and the civil monetary penalties law, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented false or fraudulent claims for payment by a federal government program, or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, prohibits, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, regardless of the payor (*e.g.*, public or private), and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious or fraudulent statements 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 their implementing regulations, impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates and their subcontractors that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security, and transmission of such individually identifiable health information;

- the federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively referred to as the ACA, requires certain manufacturers of drugs, devices, biologics and medical supplies to annually report to the Centers for Medicare & Medicaid Services, or CMS, information related to payments and other transfers of value provided to, and ownership and investment interests held by, physicians, defined to include doctors, dentists, optometrists, podiatrists and chiropractors, and their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report such information regarding payments and transfers of value provided, as well as ownership and investment interests held, during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified nurse anesthetists and certified nurse-midwives; and

- analogous state laws and regulations such as state anti-kickback and false claims laws and analogous non-U.S. fraud and abuse laws and regulations, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance regulations promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures, or drug pricing, including price increases. State and local laws require the registration of pharmaceutical sales representatives. State and non-U.S. laws that also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional integrity reporting and oversight obligations, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to significant criminal, civil and administrative sanctions, including exclusions from government funded healthcare programs, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

Health care policy changes, including U.S. health care reform legislation, may have a material adverse effect on our business.

In response to perceived increases in health care costs in recent years, there have been and continue to be proposals by the federal government, state governments, regulators, and third-party payors to control these costs and, more generally, to reform the U.S. health care system. Certain of these proposals could limit the prices we are able to charge for our products or the amounts of reimbursement available for our products and could limit the acceptance and availability of our products. Further, while the United States has begun shifting to pay-for-performance rather than fee-for-service models and has been embracing many shared-risk arrangements, CMS and OIG specifically excluded medical device manufacturers from utilizing the new, more flexible Stark Law exceptions and Anti-Kickback Statute safe harbors under the Final Rules, part of the U.S. Department of Health and Human Services' Regulatory Sprint to Coordinated Care, which were published on December 2, 2020 in the Federal Register and were largely effective January 19, 2021. The exclusion of manufacturers from utilizing these exceptions and safe harbors will not allow us to avail ourselves of immunity from liability under the laws, potentially inviting greater scrutiny over our shared risk arrangements.

Additionally, on November 16, 2020 the OIG published a Special Fraud Alert addressing manufacturer Speaker Programs signaling both a more narrow government view of AKS compliance with respect to such programs as well as the potential for increased enforcement in this space by government oversight agencies such as the OIG and DOJ. In response to this Special Fraud Alert, PhRMA issued its Statement on Revisions to the PhRMA Code on Interactions with Health Care Professionals on August 6, 2021 asserting, among other things, that pharmaceutical companies should not pay for or provide alcohol in connection with speaker programs. The updated PhRMA Code updates also clarified that repeat attendance at a speaker program on the same or substantially the same topic where a meal is provided to the attendee is generally not appropriate. The updated PhRMA Code was made effective as of January 1, 2022. AdvaMed has not made corollary revisions to its Code of Ethics to date. We continue to assess industry response to the Special Fraud Alert and have and may continue to make modifications to certain aspects of our speaker programs, which may have a detrimental impact on our ability to educate healthcare providers about our products and to promote use of our products, which may lead to decreased product sales and negatively impact our business, financial condition and results of operations.

Comprehensive healthcare legislation, signed into law in the United States in March 2010, titled the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, collectively, the ACA, imposes certain stringent compliance, recordkeeping, and reporting requirements on companies in various sectors of the life sciences industry, and enhanced penalties for non-compliance. Despite the ACA going into effect over a decade ago, there have been numerous legal and Congressional challenges to the law's provisions and the effect of certain provisions have made compliance costly. More recently, in June 2021, a case challenging the constitutionality of the ACA's individual mandate (*California v. Texas*) was overturned at the Supreme Court.

We cannot predict what additional new legislation, agency priorities, and rulemakings may be on the horizon as the United States continues to reassess how it pays for healthcare. As a result, we cannot quantify or predict what impact any changes might have on our business and results of operations. However, any changes that lower reimbursement for our products could materially and adversely affect our business, financial condition and results of operations.

Other legal, regulatory and commercial policy influences are subjecting our industry to significant changes, and we cannot predict whether new regulations or policies will emerge from U.S. federal or state governments, foreign governments, or third-party payors. Government and commercial payors may, in the future, consider healthcare policies and proposals intended to curb rising healthcare costs, including those that could significantly affect reimbursement for healthcare products such as our systems. These policies have included, and may in the future include: basing reimbursement policies and rates on clinical outcomes, the comparative effectiveness, and costs, of different treatment technologies and modalities; imposing price controls and taxes on medical device providers; and other measures. These policies recently culminated in the enactment of the Inflation Reduction Act, or IRA, in August 2022, which will, among other things, allow the U.S. Department of Health and Human Services, or HHS, to negotiate the selling price of certain drugs and biologics that CMS reimburses under Medicare Part B and Part D, although this will only apply to high-expenditure single-source drugs that have been approved for at least 7 years (11 years for biologics). The negotiated prices, which will first become effective in 2026, will be capped at a statutory ceiling price beginning in October 2023, penalize drug manufacturers that increase prices of Medicare Part B and Part D drugs at a rate greater than the rate of inflation. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. These provisions will take effect progressively starting in 2023, although they may be subject to legal challenges. Future significant changes in the healthcare systems in the United States or elsewhere could also have a negative impact on the demand for our current and future products. These include changes that may reduce reimbursement rates for our products and changes that may be proposed or implemented by the current or future laws or regulations.

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

In some countries, particularly the countries of the European Union, or the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states, and parallel trade, such as arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries. In addition, the recent withdrawal of the United Kingdom from its membership in the EU, often referred to as “Brexit”, could lead to legal and regulatory uncertainty in the United Kingdom and may lead to the United Kingdom and EU adopting divergent laws and regulations, including those related to the pricing of prescription pharmaceuticals, as the United Kingdom determines which EU laws to replicate or replace. If the United Kingdom were to significantly alter its regulations affecting the pricing of prescription pharmaceuticals, we could face significant new costs. As a result, Brexit could impair our ability to transact business in the EU and the United Kingdom.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain product candidates and products outside of the United States and require us to develop and implement costly compliance programs.

If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of such third party in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the company, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing or selling certain product candidates and products outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The Securities and Exchange Commission, or the SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA’s accounting provisions.

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

We and our third-party contractors are subject to numerous foreign, federal, state and local environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources, including any available insurance.

In addition, our leasing and operation of real property may subject us to liability pursuant to certain of these laws or regulations. Under existing U.S. environmental laws and regulations, current or previous owners or operators of real property and entities that disposed or arranged for the disposal of hazardous substances may be held strictly, jointly and severally liable for the cost of investigating or remediating contamination caused by hazardous substance releases, even if they did not know of and were not responsible for the releases.

We could incur significant costs and liabilities which may adversely affect our financial condition and operating results for failure to comply with such laws and regulations, including, among other things, civil or criminal fines and penalties, property damage and personal injury claims, costs associated with upgrades to our facilities or changes to our operating procedures, or injunctions limiting or altering our operations.

Although we maintain liability insurance to cover us for costs and expenses we may incur due to injuries to our employees, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations, which are becoming increasingly more stringent, may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We are subject to certain U.S. and certain foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations. We can face serious consequences for violations.

U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations prohibit, among other things, companies and their employees, agents, CROs, CMOs, legal counsel, accountants, consultants, contractors and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of these laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We also expect our non-U.S. activities to increase over time. We expect to rely on third parties for research, preclinical studies and clinical trials and/or to obtain necessary permits, licenses, patent registrations and other marketing approvals. We can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

Risks Related to Our Reliance on Third Parties

We rely, and intend to continue to rely, on third parties to conduct our clinical trials and perform some of our research and preclinical studies. If these third parties do not satisfactorily carry out their contractual duties, fail to comply with applicable regulatory requirements or do not meet expected deadlines, our development programs may be delayed or subject to increased costs or we may be unable to obtain regulatory approval, each of which may have an adverse effect on our business, financial condition, results of operations and prospects.

We do not have the ability to independently conduct all aspects of our preclinical testing or clinical trials ourselves. As a result, we are dependent on third parties to conduct our ongoing and planned clinical trials of PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789 and any preclinical studies and clinical trials of any other product candidates. The timing of the initiation and completion of these trials will therefore be partially controlled by such third parties and may result in delays to our development programs. Specifically, we expect CROs, clinical investigators and consultants to play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, these CROs and other third parties are not our employees, and we will not be able to control all aspects of their activities. Nevertheless, we are responsible for ensuring that each clinical trial is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with good clinical practices, or GCP, requirements, which are regulations and guidelines enforced by the FDA for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical trial investigators and clinical trial sites. If we or any of our CROs or clinical trial sites fail to comply with applicable GCP requirements, the data generated in our clinical trials may be deemed unreliable, and the FDA may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that our clinical trials comply with GCPs. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure or the failure of third parties on whom we rely on to comply with these regulations may require us to stop and/or repeat clinical trials, which would delay the marketing approval process.

There is no guarantee that any such CROs, clinical trial investigators or other third parties on which we rely will devote adequate time and resources to our development activities or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, otherwise perform in a substandard manner, or terminate their engagements with us, the timelines for our development programs may be extended or delayed or our development activities may be suspended or terminated. If our clinical trial site terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in such clinical trial unless we are able to transfer those subjects to another qualified clinical trial site, which may be difficult or impossible.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors for whom they may also be conducting clinical trials or other pharmaceutical product development activities that could harm our competitive position. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 or any other product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our products.

Manufacturing pharmaceutical products is complex and subject to product loss for a variety of reasons. We rely on third-party suppliers, including single source suppliers, to manufacture preclinical and clinical supplies of our product candidates and we intend to rely on third parties to produce commercial supplies of any approved product candidate. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, product development purposes, to support regulatory application submissions, as well as for commercial manufacture if any of our product candidates obtain marketing approval. In addition, we expect to contract with analytical laboratories for release and stability testing of our product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. In addition, the ongoing COVID-19 pandemic may result in disruptions to the operations or an extended shutdown of certain businesses, which could include certain of our contract manufacturers.

We may be unable to establish any agreements with third-party manufacturers or do so on favorable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory, compliance and quality assurance;
- reliance on the third party for product development, analytical testing, and data generation to support regulatory applications;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier, the issuance of an FDA Form 483 notice or warning letter, or other enforcement action by FDA or other regulatory authority;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- carrier disruptions or increased costs that are beyond our control; and
- failure to deliver our drugs under specified storage conditions and in a timely manner.

We have only limited supply arrangements in place with respect to our product candidates, and these arrangements do not extend to commercial supply. We acquire many key materials on a purchase order basis. As a result, we do not have long-term committed arrangements with respect to our product candidates and other materials. We will need to establish one or more agreements with third parties to develop and scale up the drug manufacturing process, conduct drug testing, and generate data to support a regulatory submission. If we obtain marketing approval for any of our product candidates, we will need to establish an agreement for commercial manufacture with a third party.

In addition, we are dependent on a sole supplier for certain components of our manufacturing process. Even if we are able to replace any raw materials or other materials with an alternative, such alternatives may cost more, result in lower yields or not be as suitable for our purposes. In addition, some of the materials that we use to manufacture our product candidates are complex materials, which may be more difficult to substitute. Therefore, any disruptions arising from our sole suppliers could result in delays and additional regulatory submissions.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If the FDA determines that our CMOs are not in compliance with FDA laws and regulations, including those governing cGMPs, the FDA may deny a new drug application, or NDA, approval until the deficiencies are corrected or we replace the manufacturer in our application with a manufacturer that is in compliance. Moreover, our failure, or the failure of our third-party manufacturers and suppliers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. In addition, approved products and the facilities at which they are manufactured are required to maintain ongoing compliance with extensive FDA requirements and the requirements of other similar agencies, including ensuring that quality control and manufacturing procedures conform to cGMP requirements. As such, our CMOs are subject to continual review and periodic inspections to assess compliance with cGMPs. Furthermore, although we do not have day-to-day control over the operations of our CMOs, we are responsible for ensuring compliance with applicable laws and regulations, including cGMPs.

In addition, our third-party manufacturers and suppliers are subject to numerous environmental, health and safety laws and regulations, including those governing the handling, use, storage, treatment and disposal of waste products, and failure to comply with such laws and regulations could result in significant costs associated with civil or criminal fines and penalties for such third parties. Based on the severity of regulatory actions that may be brought against these third parties in the future, our clinical or commercial supply of drug and packaging and other services could be interrupted or limited, which could harm our business.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. As a result, we may not obtain access to these facilities on a priority basis or at all. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

As we prepare for later-stage clinical trials and potential commercialization, we will need to take steps to increase the scale of production of our product candidates. We have not yet scaled up the manufacturing process for any of our product candidates. Third party manufacturers may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up or commercial activities. For example, if microbial, viral or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance. If our current CMOs for preclinical and clinical testing cannot perform as agreed, we may be required to replace such CMOs. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement manufacturer or be able to reach agreement with any alternative manufacturer. Further, our third-party manufacturers may experience manufacturing or shipping difficulties due to resource constraints or as a result of natural disasters, labor disputes, unstable political environments, including the ongoing conflict in Ukraine, or public health epidemics such as the ongoing COVID-19 pandemic. If our current third-party manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that obtain marketing approval on a timely and competitive basis.

We may enter into collaborations with third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We may seek third-party collaborators for the development and commercialization of some of our product candidates on a select basis. We have not entered into any collaborations to date. Our likely collaborators for any future collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for a future collaboration will depend, among other things, upon our assessment of the future collaborator’s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator’s evaluation of a number of factors.

If we do enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our future collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our future collaborators’ abilities and efforts to successfully perform the functions assigned to them in these arrangements. Collaborations with future collaborators involving our product candidates would pose numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;
- collaborators may de-emphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators’ strategic focus, including as a result of a sale or disposition of a business unit or development function, or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to multiple products may not commit sufficient resources to the marketing and distribution of our product relative to other products;
- collaborators may not properly obtain, maintain, defend or enforce our intellectual property rights or may use our proprietary information and intellectual property in such a way as to invite litigation or other intellectual property related proceedings that could jeopardize or invalidate our proprietary information and intellectual property or expose us to potential litigation or other intellectual property related proceedings;

- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates;
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all; and
- if a 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.

If we establish one or more collaborations, all of the risks relating to product development, regulatory approval and commercialization described herein would also apply to the activities of any such future collaborators.

Risks Related to Commercialization of our Product Candidates

The incidence and prevalence for target patient populations of our product candidates have not been established with precision. If the market opportunities for our product candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue potential and ability to achieve profitability will be adversely affected.

The total addressable market opportunity for PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 and any other product candidates we may develop will ultimately depend upon, among other things, the diagnosis criteria included in the final labeling for each such product candidate if our product candidates are approved for sale for these indications, acceptance by the medical community, patient access, drug and any related companion diagnostic pricing and their reimbursement. We may initially seek regulatory approval of some of our product candidates as therapies for relapsed or refractory patients. The number of patients in our targeted commercial markets and elsewhere may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our drugs, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current cancer treatments, such as existing targeted therapies, chemotherapy, and radiation therapy, are well established in the medical community, and doctors may continue to rely on these treatments. If our product candidates 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 our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- the acceptance of our product candidates as front-line treatment for various indications;
- the prevalence and severity of any side effects, in particular compared to alternative treatments;
- limitations or warnings contained in the labeling approved for our product candidates by the FDA;
- the size of the target patient population;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the strength of marketing and distribution support;
- publicity for our product candidates and competing products and treatments;

- the existence of distribution and/or use restrictions, such as through a REMS;
- the availability of third-party payor coverage and adequate reimbursement;
- the timing of any marketing approval in relation to other product approvals;
- support from patient advocacy groups; and
- any restrictions on the use of our products together with other medications.

We currently have no marketing and sales organization and have no experience as a company in commercializing products and we may have to invest significant resources to develop these capabilities. If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our products, we may not be able to generate revenue.

We currently have no sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish sales, marketing and distribution capabilities, either ourselves or through collaboration or other arrangements with third parties.

There are risks involved with establishing our own sales and marketing capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. 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. These efforts are expected to 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 products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- our inability to raise financing necessary to build our commercialization infrastructure;
- the inability of sales personnel to obtain access to physicians or educate an adequate number of physicians as to the benefits of our products;
- unfavorable third-party payor coverage and reimbursement in any geography;
- 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.

If we enter into arrangements with third parties to perform sales and marketing services, our product revenues and our profitability, if any, are likely to be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to market and sell our product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of these third parties 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 any of our product candidates for which we receive marketing approval.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of pharmaceutical products is highly competitive. We face competition with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and existing or emerging biotechnology companies, academic research institutions and governmental agencies and public and private research institutions worldwide. There are a number of pharmaceutical and biotechnology companies that currently are pursuing the development of precision oncology therapies optimized to effectively target the key driver mechanisms in cancers with high unmet need, including Arvinas Inc., Aurigene, Black Diamond Therapeutics, Inc., Boehringer Ingelheim, C4 Therapeutics, Constellation Pharmaceuticals, Inc., Eli Lilly and Company, F. Hoffman-La Roche, Foghorn Therapeutics Inc., Fochon Pharmaceuticals, G1 Therapeutics Inc., Genentech, Kronos Bio, Inc., Kura Oncology, Inc., Kymera Therapeutics Inc., Mirati Therapeutics Inc., Nuvation Bio Inc. Repare Therapeutics Inc., Revolution Medicines, Inc., Relay Therapeutics, Inc., Springworks Therapeutics, Inc., Syndax Pharmaceuticals, Inc., and Zentalis Pharmaceuticals, Inc. In addition, we may face competition from companies developing product candidates that are based on targeting pathways of adaptive resistance, including Amgen Inc., AbbVie Inc., AstraZeneca plc, GlaxoSmithKline plc, Ideaya Biosciences, Johnson & Johnson Services, Inc., Pfizer Inc., Tango Therapeutics, Inc., Vincerx Pharma, Inc., Novartis AG, and Gilead Sciences, Inc.

Specifically, with respect to our PRMT5 programs, PRT543 and PRT811, several companies are developing PRMT5 inhibitors with clinical trials ongoing, including Amgen (AMG193), GlaxoSmithKline (GSK3326595), Ideaya Biosciences (IDE397), Johnson & Johnson (JNJ-64619178), Pfizer (PF-06939999), and Tango Therapeutics (TNG908). For our MCL1 program, PRT1419, other companies are developing MCL1 inhibitors with monotherapy and/or combination trials ongoing, including Amgen (AMG176), AstraZeneca (AZD5991), Novartis (MIK665), and Gilead (GS-9716). For our CDK9 program, PRT2527, both AstraZeneca (AZD4573), Vincerx (VIP512), and Kronos (KB-0742) have CDK9 programs in Phase 1 clinical trials. For our CDK4/6 program, PRT3645, Novartis (ribociclib), Lilly (abemaciclib), Pfizer (palbociclib), G1 Therapeutics (G1T38), and Fochon Pharmaceuticals (FCN-437) have clinical trials ongoing. For our SMARCA2 (BRM) degrader program, other companies, including Amgen, Aurigene, C4 Therapeutics, F. Hoffmann-La Roche, Foghorn Therapeutics, Inc., Kymera Therapeutics, Arvinas, Genentech, Boehringer Ingelheim, and Lilly have publicly disclosed their pre-clinical research efforts.

Many of the companies against which we are competing or against which we may compete in the future, either alone or through collaborations, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific, management and sales and marketing personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Furthermore, we also face competition more broadly across the oncology market for cost-effective and reimbursable cancer treatments. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our product candidates, if any are approved, may compete with these existing drugs and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our product candidates may not be competitive with them. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or specific branded products. As a result, obtaining market acceptance of, and gaining significant share of the market for, any of our product candidates that we successfully introduce to the market may pose challenges. In addition, many companies are developing new oncology therapeutics, and we cannot predict what the standard of care will be as our product candidates progress through clinical development.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient to administer, are less expensive or with a more favorable labeling than our current or future product candidates. Our competitors also may obtain FDA, foreign regulatory authority, or other marketing or regulatory approval for their products more rapidly than any approval we may obtain for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost- effectiveness of our product candidate to other available therapies. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues, if any, we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if such product candidates obtain marketing approval.

Our ability to commercialize any product candidates successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors, including government healthcare programs, private health insurers and other organizations. Third-party payors decide which medications they will pay for and establish reimbursement levels. In the United States, the principal decisions about reimbursement for new medicines are typically made by the CMS, which decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors often, but not always, follow CMS's decisions regarding coverage and reimbursement.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. 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 drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining coverage and adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

Additionally, we may develop, either by ourselves or with collaborators, companion diagnostic tests for our product candidates for certain indications. We, or our collaborators, if any, will be required to obtain coverage and reimbursement for these tests separate and apart from the coverage and reimbursement we seek for our product candidates, once approved. While we have not yet developed any companion diagnostic test for our product candidates, if we do, there is significant uncertainty regarding our ability to obtain coverage and adequate reimbursement for the same reasons applicable to our product candidates.

There may also be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, but also have their own methods and approval process apart from Medicare determinations. Our inability to promptly obtain coverage and adequate reimbursement rates from third-party payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercialize any products that we may develop. If we cannot successfully defend ourselves against any claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- initiation of investigations by regulators;
- withdrawal of clinical trial participants;
- significant time and costs to defend the related litigation;

- diversion of management and scientific resources from our business operations;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Our current product liability insurance coverage for the United States and certain other jurisdictions may not be adequate to cover all liabilities that we may incur. We likely will need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. A successful product liability claim or series of claims brought against us could decrease our cash and adversely affect our business and financial condition.

Risks Related to Employee Matters and Our Operations

Our future success depends on our ability to retain key employees and to attract, retain and motivate qualified personnel and manage our human capital.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract, motivate and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on the development and management expertise of Kris Vaddi, Ph.D., our founder and Chief Executive Officer, as well as the other principal members of our management, scientific and clinical team. We currently do not maintain key person insurance on these individuals. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time.

Our industry has experienced a high rate of turnover in recent years. Our ability to compete in the highly competitive pharmaceuticals industry depends upon our ability to attract, retain and motivate highly skilled and experienced personnel with scientific, clinical, regulatory, manufacturing and management skills and experience. We conduct our operations in the greater Delaware area, a region that is home to other pharmaceutical companies as well as many academic and research institutions and in addition, the ongoing COVID-19 pandemic has increased companies' willingness to hire remote workers, resulting in fierce competition for qualified personnel. We may not be able to attract or retain qualified personnel in the future due to the intense competition for a limited number of qualified personnel among pharmaceutical companies. Many of the other pharmaceutical companies against which we compete have greater financial and other resources, different risk profiles and a longer history in the industry than we do. Our competitors may provide higher compensation, more diverse opportunities and/or better opportunities for career advancement. Any or all of these competing factors may limit our ability to continue to attract and retain high quality personnel, which could negatively affect our ability to successfully develop and commercialize our product candidates and to grow our business and operations as currently contemplated.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of September 30, 2022, we had 120 full-time employees. We expect significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical development, clinical operations, manufacturing, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth and with developing sales, marketing and distribution infrastructure, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources.

Further, we currently rely, and for the foreseeable future will continue to rely, in substantial part on certain third-party contract organizations, advisors and consultants to provide certain services, including assuming substantial responsibilities for the conduct of our clinical trials and the manufacture of PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789 or any future product candidates. We cannot assure you that the services of such third-party contract organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by our vendors or consultants is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain marketing approval of PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 or any future product candidates or otherwise advance our business. We cannot assure you that we will be able to properly manage our existing vendors or consultants or find other competent outside vendors and consultants on economically reasonable terms, or at all.

If we are not able to effectively manage growth and expand our organization, we may not be able to successfully implement the tasks necessary to further develop and commercialize PRT543, PRT811, PRT1419, PRT2527, PRT3645, or PRT3789 our other pipeline product candidates or any future product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our employees, clinical trial investigators, CROs, CMOs, consultants, vendors and any potential commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, clinical trial investigators, CROs, CMOs, consultants, vendors and any potential commercial partners. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (i) FDA regulations or those of comparable foreign regulatory authorities, including those laws that require the reporting of true, complete and accurate information, (ii) manufacturing standards, (iii) federal and state health and data privacy, security, fraud and abuse, government price reporting, transparency reporting requirements, and other healthcare laws and regulations in the United States and abroad, (iv) sexual harassment and other workplace misconduct, or (v) laws that require the true, complete and accurate reporting of financial information or data. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation.

We have adopted a code of conduct applicable to all of our employees, as well as a disclosure program and other applicable policies and procedures, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these 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, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional integrity reporting and oversight obligations, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Our internal information technology systems, or those of our third-party CROs, CMOs, or other vendors, contractors or consultants, may fail or suffer security breaches, cyber-attacks, loss or leakage of data and other disruptions, which could result in a material disruption of our development programs, compromise sensitive information related to our business or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business.

We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we collect, store and transmit confidential information (including but not limited to intellectual property, proprietary business information and personal information). It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We also have outsourced elements of our operations to third parties, and as a result we manage a number of third-party CROs, CMOs, vendors, and other contractors and consultants who have access to our confidential information. Our internal information technology systems and infrastructure are also vulnerable to damage from natural disasters, terrorism, war, telecommunication and electrical failures. System failures or outages, including any potential disruptions due to significantly increased global demand on certain cloud-based systems during the ongoing COVID-19 pandemic, could compromise our ability to perform these functions in a timely manner, which could harm our ability to conduct business or delay our financial reporting. Such failures could materially adversely affect our operating results and financial condition.

Despite the implementation of security measures, given their size and complexity and the increasing amounts of confidential information that they maintain, our internal information technology systems and those of our third-party CROs, CMOs, vendors and other contractors and consultants are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, accidents by our employees or third party service providers, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, third-party CROs, CMOs, vendors, contractors, consultants, business partners and/or other third parties, or from cyber-attacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure, or that of our third-party CROs, CMOs, vendors and other contractors and consultants, or lead to data leakage. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. The ongoing COVID-19 pandemic is generally increasing the attack surface available for exploitation, as more companies and individuals work online and work remotely, and as such, the risk of a cybersecurity incident potentially occurring, and our investment in risk mitigations against such an incident, is increasing. For example, there has been an increase in phishing and spam emails as well as social engineering attempts from "hackers" hoping to use the ongoing COVID-19 pandemic to their advantage. We may not be able to anticipate all types of security threats, nor may we be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or those of our third-party CROs, CMOs, vendors and other contractors and consultants, or inappropriate disclosure of confidential or proprietary information, we could incur liability and reputational damage and the further development and commercialization of PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 or any future product candidates could be delayed. Any breach, loss or compromise of clinical trial participant personal data may also subject us to civil fines and penalties, including under HIPAA, and other relevant state and federal privacy laws in the United States. The costs related to significant security breaches or disruptions could be material and exceed the limits of the cybersecurity insurance we maintain against such risks. If the information technology systems of our third-party CROs, CMOs, vendors and other contractors and consultants become subject to disruptions or security breaches, we may have insufficient recourse against such third parties and we may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature from occurring.

While we have not experienced any such system failure, accident or security breach to date, and believe that our data protection efforts and our investment in information technology reduce the likelihood of such incidents in the future, we cannot assure you that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages, breaches in our systems, or those of our third-party CROs, CMOs, vendors and other contractors and consultants, or other cyber incidents that could have a material adverse effect upon our reputation, business, operations or financial condition. For example, if such an event were to occur and cause interruptions in our operations, or those of our third-party CROs, CMOs, vendors and other contractors and consultants, it could result in a material disruption of our programs and the development of our product candidates could be delayed. In addition, the loss of clinical trial data for PRT543, PRT811, PRT1419, PRT2527, PRT3645, PRT3789 or any other product candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, significant disruptions of our internal information technology systems or those of our third-party CROs, CMOs, vendors and other contractors and consultants, or security breaches could result in the loss, misappropriation and/or unauthorized access, use, or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information and personal information), which could result in financial, legal, business and reputational harm to us. For example, any such event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business.

Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation and/or adverse publicity and could negatively affect our operating results and business.

We and any potential collaborators may be subject to federal, state and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws and federal and state consumer protection laws (*e.g.*, Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA, as amended by HITECH. Depending on the facts and circumstances, we could be subject to criminal penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

International data protection laws, including Regulation 2016/679, known as the General Data Protection Regulation, or GDPR, may also apply to health-related and other personal information obtained outside of the United States. The GDPR went into effect on May 25, 2018. The GDPR introduced new data protection requirements in the EU, as well as potential fines for noncompliant companies of up to the greater of €20 million or 4% of annual global revenue. The regulation imposes numerous new requirements for the collection, use and disclosure of personal information, including more stringent requirements relating to consent and the information that must be shared with data subjects about how their personal information is used, the obligation to notify regulators and affected individuals of personal data breaches, extensive new internal privacy governance obligations and obligations to honor expanded rights of individuals in relation to their personal information (*e.g*., the right to access, correct and delete their data). In addition, the GDPR includes restrictions on cross-border data transfer. The GDPR will increase our responsibility and liability in relation to personal data that we process, and we may be required to put in place additional mechanisms to ensure compliance with the new EU data protection rules. In addition, the GDPR prohibits the transfer of personal data to countries outside of the European Economic Area, or EEA, such as the United States, which are not considered by the European Commission to provide an adequate level of data protection. Switzerland has adopted similar restrictions. Although there are legal mechanisms to allow for the transfer of personal data from the EEA and Switzerland to the United States, they are subject to pending legal challenges that, if successful, could invalidate these mechanisms, restrict our ability to process personal data of Europeans outside of Europe and adversely impact our business. For example, in July 2020, the European Courts of Justice invalidated the EU-U.S. Privacy Shield, which enabled the transfer of personal data from EU to the U.S. for companies that had self-certified to the Privacy Shield. On August 10, 2020, the U.S. Department of Commerce and the European Commission announced new discussions to evaluate the potential for an enhanced EU-U.S. Privacy Shield framework to comply with the July 16 judgment of the Court of Justice. While the Court of Justice upheld the use of other data transfer mechanisms, such as the Binding Corporate Rules, the decision has led to some uncertainty regarding the use of such mechanisms for data transfers to the United States, and the court made clear that reliance on Binding Corporate Rules alone may not necessarily be sufficient in all circumstances. Use of the data transfer mechanisms must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals. The European Data Protection Board issued additional guidance regarding the Court of Justice's decision on November 11, 2020 which imposes higher burdens on the use of data transfer mechanisms, such as the Binding Corporate Rules, for cross-border data transfers. To comply with this guidance, we may need to implement additional safeguards to further enhance the security of data transferred out of the European Economic Area, which could increase our compliance costs, expose us to further regulatory scrutiny and liability, and adversely affect our business. To the extent that we were to rely on Privacy Shield, we will not be able to do so in the future, which could increase our costs and our ability to efficiently process personal data from the EU.

Further, Brexit has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, while the Data Protection Act of 2018, that "implements" and complements the GDPR achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is still unclear whether transfer of data from the EEA to the United Kingdom will remain lawful under GDPR. Beginning in 2021, the United Kingdom became a "third country" under the GDPR. We may, however, incur liabilities, expenses, costs, and other operational losses under GDPR and applicable EU Member States and the United Kingdom privacy laws in connection with any measures we take to comply with them.

In addition, the state of California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the CCPA) and places increased privacy and security obligations on entities handling certain personal data of consumers or households. The CCPA requires covered companies to provide new disclosure to consumers about such companies' data collection, use and sharing practices, provide such consumers new ways to opt-out of certain sales or transfers of personal information, and provide consumers with additional causes of action. The CCPA went into effect on January 1, 2020 and became enforceable by the California Attorney General on July 1, 2020, along with related regulations which came into force on August 14, 2020 and may impact our business activities and exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information. Additionally, although not effective until January 1, 2023, the California Privacy Rights Act, or the CPRA, which expands upon the CCPA, was passed in the election on November 3, 2020. The CCPA gives (and the CPRA will give) California residents expanded privacy rights, including the right to request correction, access, and deletion of their personal information, the right to opt out of certain personal information sharing, and the right to receive detailed information about how their personal information is processed. The CCPA and CPRA provide for unlimited civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA and CPRA may increase our compliance costs and potential liability, particularly in the event of a data breach. Additionally, the CCPA has prompted a number of proposals in the U.S. for new federal and state-level privacy legislation that, if passed, could increase our potential liability, increase our compliance costs, and adversely affect our business. Other states are also seeking to regulate consumer privacy stringently, and both Virginia and Colorado signed comprehensive privacy legislation in 2021.

These laws (the Virginia Consumer Data Protection Act and the Colorado Privacy Act) are set to come into force in 2023 and a number of other state legislatures are actively considering passing similar consumer privacy laws, including those in New York and Washington.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with U.S. and international data protection laws and regulations could result in government enforcement actions (which could include civil, criminal, and administrative penalties), private litigation and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time consuming to defend and could result in adverse publicity that could harm our business.

We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our company is located in Delaware. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemic, including the ongoing COVID-19 pandemic, power shortage, telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize our facilities, or the manufacturing facilities of our third-party CMOs, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. For example, our operations are concentrated primarily on the east coast of the United States, and any adverse weather event or natural disaster, such as a hurricane or heavy snowstorm, could have a material adverse effect on a substantial portion of our operations. Extreme weather conditions or other natural disasters could further disrupt our operations, and have a material and adverse effect on our business, financial condition, results of operations and prospects. In addition, the long-term effects of climate change on general economic conditions and the pharmaceutical industry in particular are unclear, and may heighten or intensify existing risk of natural disasters. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our research facilities or the manufacturing facilities of our third-party CMOs, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our third-party CMOs, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Changes in tax laws or regulations that are applied adversely to us may have a material adverse effect on our business, cash flow, financial condition or results of operations.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, the Tax Cuts and Jobs Act, enacted many significant changes to the U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Cuts and Jobs Act may affect us, and certain aspects of the Tax Cuts and Jobs Act could be repealed or modified in future legislation. For example, the CARES Act modified certain provisions of the Tax Cuts and Jobs Act. In addition, it is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act, the CARES Act, or any newly enacted federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses under the Tax Cuts and Jobs Act, the CARES Act or future reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense.

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

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. Unused losses incurred in taxable years beginning on or prior to December 31, 2017, will carry forward to offset future taxable income, if any, until such unused losses expire. Under the Tax Cuts and Jobs Act, as modified by the CARES Act, unused U.S. federal net operating losses generated in tax years beginning after December 31, 2017, will not expire and may be carried forward indefinitely but the deductibility of such federal net operating losses (particularly those generated in taxable years beginning after December 31, 2020) in taxable years beginning after December 31, 2020, is limited to 80% of current year taxable income. It is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act or the CARES Act. In addition, both our current and our future unused losses and other tax attributes may be subject to limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the Code) if we undergo, or have undergone, an "ownership change," generally defined as a greater than 50 percentage point change (by value) in our equity ownership by certain stockholders over a three-year period. We have not completed a Section 382 study to assess whether an ownership change has occurred or whether there have been multiple ownership changes since our formation due to the complexity and cost associated with such a study and the fact that there may be additional ownership changes in the future. As a result, our net operating loss carryforwards generated in taxable years beginning on or before December 31, 2017, may expire prior to being used, and the deductibility of our net operating loss carryforwards generated in taxable years beginning after December 31, 2017 in taxable years beginning after December 31, 2020, may be limited, and, if we undergo an ownership change (or if we previously underwent such an ownership change), our ability to use all of our pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset our post-change income or taxes may be limited. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of net operating losses is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, even if we attain profitability, we may be unable to use all or a material portion of our net operating losses and other tax attributes, which could adversely affect our future cash flows.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as acquisitions of companies, businesses or assets and out-licensing or in-licensing of products, product candidates or technologies. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near term or long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention in order to develop acquired products, product candidates or technologies;
- incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions;
- higher than expected acquisition and integration costs;
- write-downs of assets or goodwill or impairment charges;
- increased amortization expenses;
- difficulty and cost in combining the operations, systems and personnel of any acquired businesses with our operations, systems and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

Our portfolio of investments may be subject to market, interest and credit risk that may reduce its value.

The value of our investments may decline due to increases in interest rates, downgrades of the bonds and other securities included in our commercial money market account portfolio and instability in the global financial markets that reduces the liquidity of securities included in our portfolio. In addition, a possible recession, rising inflation, and the ongoing COVID-19 pandemic has and may continue to adversely affect the financial markets in some or all countries worldwide. Each of these events may cause us to record charges to reduce the carrying value of our investment portfolio or sell investments for less than our acquisition cost. Although we attempt to mitigate these risks through diversification of our investments and continuous monitoring of our portfolio's overall risk profile, the value of our investments may nevertheless decline.

Risks Related to Intellectual Property

If we are unable to obtain and maintain sufficient patent protection for our product candidates, or if the scope of the patent protection is not sufficiently broad, third parties, including our competitors, could develop and commercialize products similar or identical to ours, and our ability to commercialize our product candidates successfully may be adversely affected.

Our success depends in large part on our ability to protect our proprietary technologies that we believe are important to our business, including pursuing, obtaining and maintaining patent protection in the United States and other countries intended to cover the compositions of matter of our product candidates, for example, PRT543, PRT811, PRT1419, PRT2527, PRT3645, and PRT3789 their methods of use, related technologies and other inventions that are important to our business. In addition to patent protection, we also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. If we do not adequately pursue, obtain, maintain, protect or enforce our intellectual property, third parties, including our competitors, may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability.

To protect our proprietary position, we have currently filed patent applications in the United States related to our product candidates that we consider important to our business, including patent applications relating to compositions of matter covering our compounds, the processes for manufacturing such compounds and use of such compounds in therapies. We have also filed patent applications in foreign jurisdictions relating to PRT543, PRT811, PRT1419, PRT2527, PRT3645 and PRT3789.

The patent application and approval process is expensive, time-consuming and complex. We may not be able to file, prosecute and maintain all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions. We also cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdictions. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, depending on the terms of any future license agreements to which we may become a party, we may not have the right to control the preparation, filing, and prosecution of patent applications, or to maintain the patents, covering technology licensed from third parties. Therefore, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Furthermore, the patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. The standards applied by the United States Patent and Trademark Office, or the USPTO, and foreign patent offices in granting patents are not always applied uniformly or predictably. In addition, the determination of patent rights with respect to biological and pharmaceutical products commonly involves complex legal and factual questions, which have in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Thus, we cannot offer any assurances about which, if any, patents will issue, the breadth of any such patents, whether any issued patents will be found invalid and unenforceable or will be threatened by third parties or whether any issued patents will effectively prevent others from commercializing competing technologies and product candidates. While we have filed patent applications covering aspects of our current product candidates, we currently have four issued U.S. patents covering PRT543 that is expected to expire no earlier than August 9, 2038; three issued U.S. patents covering PRT811 that are expected to expire no earlier than March 14, 2039; and one issued U.S. patent covering PRT1419 that is expected to expire no earlier than November 8, 2039. We do not yet have issued patents on all of our product candidates.

Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until at least one patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file or invent (prior to March 16, 2013) any patent application related to our product candidates. In addition, we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, collaborators, CROs, CMOs, hospitals, independent treatment centers, consultants, independent contractors, suppliers, advisors and other third parties; however, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Furthermore, if third parties have filed patent applications related to our product candidates or technology, we may not be able to obtain our own patent rights to those product candidates or technology.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, our patents or pending patent applications may be challenged in the courts or patent offices in the United States and abroad. For example, we may be subject to a third-party pre-issuance submission of prior art to the USPTO or become involved in post-grant review procedures, oppositions, derivations, revocation, reexaminations, inter partes review or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party rights. Moreover, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge priority of invention or other features of patentability. Such challenges may result in loss of exclusivity or in our patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products or limit the duration of the patent protection of our technology and products. Such challenges also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, our patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Moreover, some of our patents and patent applications may in the future be co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Our pending and future patent applications may not result in patents being issued that protect our product candidates, in whole or in part, or which effectively prevent others from commercializing competitive products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued and its scope can be reinterpreted after issuance. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors and other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors and other third parties may also seek approval to market their own products similar to or otherwise competitive with our products. Alternatively, our competitors or other third parties may seek to market generic versions or "follow-on" versions of any approved products by submitting abbreviated new drug applications, or ANDAs, or new drug applications under Section 505(b)(2) of the FDCA, respectively, to the FDA during which they may claim that patents owned by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Furthermore, future patents may be subject to a reservation of rights by one or more third parties. For example, to the extent the research resulting in future patent rights or technologies is funded in the future in part by the U.S. government, the government could have certain rights in any resulting patents and technology, including a non-exclusive license authorizing the government to use the invention or to have others use the invention on its behalf for non-commercial purposes. If the U.S. government then decides to exercise these rights, it is not required to engage us as its contractor in connection with doing so. These rights may also permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The government may also exercise its march-in rights if it determines that action is necessary because we failed to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such government-funded inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of aforementioned proprietary rights could harm our competitive position, business, financial condition, results of operations, and prospects.

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the pharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or the Leahy-Smith Act, signed into law in September 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. For example, the Leahy-Smith Act allows third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, inter partes review, and derivation proceedings. In addition, the Leahy-Smith Act has transformed the U.S. patent system from a "first-to-invent" system to a "first-to-file" system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. The first-to-file provisions, however, only became effective on March 16, 2013. It is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our or our future collaboration partners' patent applications and the enforcement or defense of our or our future collaboration partners' issued patents, all of which could harm our business, results of operations, financial condition and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We may become involved in lawsuits or administrative disputes to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate or otherwise violate our patents, trademarks, copyrights, trade secrets or other intellectual property. To counter infringement, misappropriation or other violations, we may be required to file infringement, misappropriation or other violation claims, which can be expensive and time consuming and divert the time and attention of our management and business and scientific personnel. In addition, many of our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can.

Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe, misappropriate or otherwise violate their patents or their other intellectual property, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In patent litigation in the United States, counterclaims challenging the validity, enforceability or scope of asserted patents are commonplace. Similarly, third parties may initiate legal proceedings against us seeking a declaration that certain of our intellectual property is non-infringed, invalid or unenforceable. The outcome of any such proceeding is generally unpredictable.

In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. If a defendant were to prevail on a legal assertion of invalidity or unenforceability of our patents covering one of our product candidates, we could lose at least a part, and perhaps all, of the patent protection covering such a product candidate. Competing drugs may also be sold in other countries in which our patent coverage might not exist or be as strong. If we lose a foreign patent lawsuit, alleging our infringement of a competitor's patents, we could be prevented from marketing our drugs in one or more foreign countries. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. 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 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 shares of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

Furthermore, third parties may also raise invalidity or unenforceability claims before administrative bodies in the United States or foreign authorities, even outside the context of litigation. Such mechanisms include re-examination, inter partes review, post-grant review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions (*e.g.*, opposition proceedings). Such proceedings could result in revocation, cancellation or amendment to our patents in such a way that they no longer cover and protect our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or written description. Grounds for an unenforceability assertion could be an allegation that someone connected with the prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution of the patent. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our licensors, our patent counsel and the patent examiner were unaware during prosecution. Moreover, it is possible that prior art may exist that we are aware of but do not believe is relevant to our current or future patents, but that could nevertheless be determined to render our patents invalid. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our product candidates. Any such loss of patent protection could have a material adverse impact on our business, financial condition, results of operations and prospects.

We may not be able to effectively protect or enforce our intellectual property and proprietary rights throughout the world.

Filing, prosecuting and defending patents with respect to our product candidates in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. The requirements for patentability may differ in certain countries, particularly in developing countries. In addition, any future intellectual property license agreements may not always include worldwide rights. Consequently, competitors and other third parties may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection, but where patent enforcement is not as strong as that in the United States and where our ability to enforce our patents to stop infringing activities may be inadequate. These products may compete with our products in such territories and in jurisdictions where we do not have any patent rights or where any future patent claims or other intellectual property or proprietary rights may not be effective or sufficient to prevent them from competing with us, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Moreover, our ability to protect and enforce our intellectual property and proprietary rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, the laws of some countries outside of the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending intellectual property and proprietary rights in certain foreign jurisdictions. The legal systems of some countries, including, for example, India, China and other developing countries, do not view favorably the enforcement of patents and other intellectual property or proprietary rights, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement, misappropriation or other violation of our patents or other intellectual property or proprietary rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business, could put our patents, trademarks or other intellectual property and proprietary rights 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. Furthermore, while we intend to protect our intellectual property and proprietary rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property and proprietary rights in such countries may be inadequate.

If we are sued for infringing, misappropriating or otherwise violating intellectual property or proprietary rights of third parties, such litigation or disputes could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and other proprietary rights of third parties. If any third-party patents, patent applications or other proprietary rights are found to cover our product candidates or any related companion diagnostics or their compositions, methods of use or manufacturing, we may be required to pay damages, which could be substantial, and we would not be free to manufacture or market our product candidates or to do so without obtaining a license, which may not be available on commercially reasonable terms, or at all.

We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property or proprietary rights with respect to our product candidates and technologies we use in our business. Our competitors or other third parties may assert infringement claims against us, alleging that our product candidates are covered by their patents. We cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our product candidates. If a patent holder believes our product candidate infringes its patent rights, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property or proprietary rights with respect to our product candidates, including interference proceedings before the USPTO. Third parties may assert infringement, misappropriation or other claims against us based on existing or future intellectual property or proprietary rights. The outcome of intellectual property litigation and other disputes is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of using or manufacturing products. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods of use, manufacturing or other applicable activities either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be successful in doing so. However, proving invalidity or unenforceability is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, or enforceability. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and business and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe, misappropriate or otherwise violate a third party's intellectual property or proprietary rights and we are unsuccessful in demonstrating that such intellectual property or proprietary rights are invalid or unenforceable, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain such a license, it could be granted on non-exclusive terms, thereby giving our competitors and other third parties access to the same technologies licensed to us. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed such third-party patent rights. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

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

Some of our employees and consultants are currently or have been previously employed at universities or at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. These employees and consultants may have executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such other current or previous employment. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of third parties. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property or personnel or sustain damages. Such intellectual property could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our management. Any of the foregoing would have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, while it is our policy to require our employees, consultants and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. In addition, such agreements may not be self-executing such that the intellectual property subject to such agreements may not be assigned to us without additional assignments being executed, and we may fail to obtain such assignments. In addition, such agreements may be breached. In addition, we have multiple sponsored research agreements relating to our lead product candidates with various academic institutions. Some of these academic institutions may not have intellectual property assignments or similar agreements with their employees and consultants, which may result in claims by or against us related to ownership of any intellectual property. Accordingly, we may be forced to bring claims against third parties, or defend claims that they may bring against us to determine the ownership of what we regard as our intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

Rights to improvements to our product candidates may be held by third parties.

In the course of testing our product candidates, we have entered into agreements with third parties to conduct clinical testing, which provide that improvements to our product candidates may be owned solely by a party or jointly between the parties. If we determine that rights to such improvements owned solely by a third party are necessary to commercialize our product candidates or maintain our competitive advantage, we may need to obtain a license from such third party in order to use the improvements and continue developing, manufacturing or marketing the product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain such a license, it could be granted on non-exclusive terms, thereby giving our competitors and other third parties access to the same technologies licensed to us. Failure to obtain a license on commercially reasonable terms or at all, or to obtain an exclusive license, could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. If we determine that rights to improvements jointly owned between us and a third party are necessary to commercialize our product candidates or maintain our competitive advantage, we may need to obtain an exclusive license from such third party. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such improvements, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our intellectual property in order to enforce such intellectual property against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

The term of our patents may be inadequate to protect our competitive position on our products.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Depending upon the timing, duration and other factors relating to any FDA marketing approval we receive for any of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or the Hatch- Waxman Amendments. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Hatch-Waxman Amendments permit a patent term extension of up to five years beyond the normal expiration of the patent, limited to the approved indication (or any additional indications approved during the period of extension), as compensation for patent term lost to the regulatory review process during which the sponsor was unable to commercially market its new product. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to an approved drug is eligible for the extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended, and the application for the extension must be submitted prior to the expiration of the patent. However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available for our patents, may refuse to grant extensions to our patents, or may grant more limited extensions than we request. We may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors and other third parties may be able to obtain approval of competing products following our patent expiration and take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. Any of the foregoing would have a material adverse effect on our business, financial condition, results of operations and prospects.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by governmental patent offices, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on any issued patent are due to be paid to the USPTO and patent offices in foreign countries in several stages over the lifetime of the patent. The USPTO and patent offices in foreign countries require compliance with a number of procedural, documentary, fee payment and other requirements during the patent application process. In the future, we may rely on licensing partners to pay these fees due to U.S. and non-U.S. patent agencies and to comply with these other requirements with respect to any future licensed patents and patent applications. While an inadvertent lapse can 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 a patent or patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors and other third parties might be able to enter the market with similar or identical products of technology, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

We rely on proprietary know-how and trade secret protection and confidentiality agreements to protect proprietary know-how or trade secrets that are not patentable or that we elect not to patent. We seek to protect our trade secrets and proprietary know-how in part by entering into non-disclosure and confidentiality agreements with parties who have access to such knowledge, such as our employees, consultants, independent contractors, advisors, CMOs, CROs, hospitals, independent treatment centers, suppliers, collaborators and other third parties. We also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary know-how. Additionally, our confidentiality agreements and other contractual protections may not be adequate to protect our intellectual property from unauthorized disclosure, third-party infringement or misappropriation. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts in the United States and certain foreign jurisdictions are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our business, financial condition, results of operations and prospects our business and competitive position could be materially harmed.

Intellectual property rights do not necessarily address all potential threats.

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. For example:

- others may be able to make products similar to any product candidates we may develop or utilize similarly related technologies that are not covered by the claims of the patents that we may license or may own in the future;
- we, or any future license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or may own in the future;
- we, or any future license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing, misappropriating or otherwise violating any of our owned or licensed intellectual property rights;
- it is possible that our pending patent applications or those that we may own in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;

- our competitors or other third parties 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 harm our business; and

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

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

Risks Related to Our Common Stock

An active and liquid trading market for our common stock may never be sustained. As a result, you may not be able to resell your shares of common stock at or above the purchase price.

An active trading market for our common stock may never be sustained. The market value of our common stock may decrease from the purchase price. As a result of these and other factors, you may be unable to resell your shares of our common stock at or above the purchase price. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. The lack of an active market may also reduce the fair market value of your shares. Furthermore, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic collaborations or acquire companies or products by using our shares of common stock as consideration.

Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expense related to the planned and ongoing development of our product candidates or future development programs, including scale-up CMC expenses;

- results of clinical trials, or the addition or termination of future preclinical or clinical trials or funding support by us, or future collaborators or licensing partners;

- our execution of any collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under existing or future arrangements or the termination or modification of any such existing or future arrangements;

- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved;

- additions and departures of key personnel;

- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;

- if any of our product candidates receives regulatory approval, the terms of such approval and market acceptance and demand for such product candidates;

- regulatory developments affecting our product candidates or those of our competitors; and

- changes in political, economic and general macroeconomic conditions, including but not limited to the ongoing war in Ukraine, supply chain disruptions, rising interest rates, rising inflation rates, a potential recession or the ongoing COVID-19 pandemic.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our common stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

The market price of our common stock is likely to be highly volatile, which could result in substantial losses for purchasers of our common stock.

The market price of our common stock has been highly volatile since our initial public offering, or IPO. From September 30, 2021 to September 30, 2022, the closing price of common stock on the Nasdaq Global Select Market has ranged from $4.00 to $31.74 per share. The market price of our common stock is likely to continue to be highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid. The market price for our common stock may be influenced by many factors, including the other risks described in this section of this Quarterly Report on Form 10-Q and the following:

- enrollment or results of clinical trials of our product candidates, or those of our competitors or our future collaborators, or changes in the development status of our product candidates;
- regulatory or legal developments in the United States and other countries, especially changes in laws or regulations applicable to our product candidates;
- the success of competitive products or technologies;
- introductions and announcements of new products by us, our future commercialization partners, or our competitors, and the timing of these introductions or announcements;
- actions taken by regulatory agencies with respect to our products, clinical studies, manufacturing process or sales and marketing terms;
- actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us;
- the success of our efforts to acquire or in-license additional technologies, products or product candidates;
- developments concerning any future collaborations, including but not limited to those with development and commercialization partners;
- market conditions in the pharmaceutical and biotechnology sectors;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our product candidates and products;
- our ability or inability to raise additional capital and the terms on which we raise it;
- the recruitment or departure of key personnel;
- changes in the structure of healthcare payment systems;
- actual or anticipated changes in earnings estimates or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- announcement and expectation of additional financing efforts;
- speculation in the press or investment community;
- share price and fluctuations of trading volume of our common stock;
- sales of our common stock by us, insiders or our stockholders;
- the concentrated ownership of our common stock;
- changes in accounting principles;
- terrorist acts, acts of war or periods of widespread civil unrest (including the current conflict in Ukraine);

- natural disasters and other calamities; and
- general economic, industry and market conditions, or other events or factors, many of which are beyond our control, including but not limited to a potential recession, rising interest rates, rising inflation, and the ongoing COVID-19 pandemic.

In addition, the stock market in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme price and volume fluctuations that have been often unrelated or disproportionate to the operating performance of the issuer. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this “Risk Factors” section, could have a dramatic and adverse impact on the market price of our common stock.

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

As of September 30, 2022, our executive officers, directors, beneficial owners of 5% or more of our capital stock and their respective affiliates beneficially owned a substantial portion of our common stock. The voting power of this group may increase to the extent they convert shares of non-voting common stock they hold into common stock.

This group of stockholders have the ability to control us through this ownership position and are able to determine all matters requiring stockholder approval. For example, these stockholders are able to control elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

The dual class structure of our common stock may limit your ability to influence corporate matters and may limit your visibility with respect to certain transactions.

The dual class structure of our common stock may limit your ability to influence corporate matters. Holders of our common stock are entitled to one vote per share, while holders of our non-voting common stock are not entitled to any votes. Nonetheless, each share of our non-voting common stock may be converted at any time into one share of our common stock at the option of its holder by providing written notice to us, subject to the limitations provided for in our restated certificate of incorporation. Consequently, if holders of our non-voting common stock exercise their option to make this conversion, this will have the effect of increasing the relative voting power of those prior holders of our non-voting common stock, and correspondingly decreasing the voting power of the holders of our common stock, which may limit your ability to influence corporate matters. For example, at September 30, 2022, the common stock will have 100% of the voting power, but if the holders of non-voting common stock were to convert all of their shares into common stock, the prior common stock would have 76.2% of the voting power, and the former non-voting common stock would represent 23.8% of the voting power. Additionally, stockholders who hold, in the aggregate, more than 10% of our common stock and non-voting common stock, but 10% or less of our common stock, and are not otherwise an insider of the company, may not be required to report changes in their ownership due to transactions in our non-voting common stock pursuant to Section 16(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and may not be subject to the short-swing profit provisions of Section 16(b) of the Exchange Act.

We are an “emerging growth company” and a “smaller reporting company” and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies or smaller reporting companies will make our common stock less attractive to investors.

We are an “emerging growth company” as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including (i) not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, (ii) reduced disclosure obligations regarding executive compensation in our Annual Reports on Form 10-K as well as our periodic reports and proxy statements and (iii) exemptions from the requirements of holding nonbinding advisory stockholder votes on executive compensation and stockholder approval of any golden parachute payments not approved previously. In addition, as an emerging growth company, we are only required to provide two years of audited financial statements in our Annual Reports on Form 10-K.

We could be an emerging growth company until December 31, 2025, although circumstances could cause us to lose that status earlier, including if we are deemed to be a "large accelerated filer," which occurs when the market value of our common stock that is held by non-affiliates equals or exceeds $700 million as of the prior June 30, or if we have total annual gross revenue of $1.235 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31, or if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, in which case we would no longer be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, if our revenues remain less than $100.0 million, and reduced disclosure obligations regarding executive compensation in our Annual Reports on Form 10-K as well as our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may 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 share price may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to take advantage of the benefits of this extended transition period. Our financial statements may therefore not be comparable to those of companies that comply with such new or revised accounting standards. Until the date that we are no longer an "emerging growth company" or affirmatively and irrevocably opt out of the exemption provided by Section 7(a)(2)(B) of the Securities Act, upon issuance of a new or revised accounting standard that applies to our financial statements and that has a different effective date for public and private companies, we will disclose the date on which adoption is required for non-emerging growth companies and the date on which we will adopt the recently issued accounting standard.

We are also a "smaller reporting company," meaning that the market value of our stock held by non-affiliates is less than $700.0 million as of the prior June 30 and our annual revenue is less than $100.0 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 million as of the prior June 30. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Anti-takeover provisions in our charter documents and under Delaware law could prevent or delay an acquisition of us, which may be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Our restated certificate of incorporation and our restated bylaws contain provisions that could delay or prevent a change in control of our company. These provisions could also make it difficult for stockholders to elect directors who are not nominated by current members of our board of directors or take other corporate actions, including effecting changes in our management. These provisions:

- establish a classified board of directors so that not all members of our board are elected at one time;
- permit only the board of directors to establish the number of directors and fill vacancies on the board;
- provide that directors may only be removed "for cause" and only with the approval of two-thirds of our stockholders;
- require super-majority voting to amend some provisions in our restated certificate of incorporation and restated bylaws;
- authorize the issuance of "blank check" preferred stock that our board could use to implement a stockholder rights plan;
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting; and

- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings.

In addition, Section 203 of the Delaware General Corporation Law, or DGCL, may discourage, delay or prevent a change in control of our company. Section 203 imposes certain restrictions on mergers, business combinations and other transactions between us and holders of 15% or more of our common stock.

The exclusive forum provision in our organizational documents may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims.

Our restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for: any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the DGCL, our restated certificate of incorporation, or our restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. This exclusive forum provision does not apply to suits brought to enforce a duty or liability created by the Exchange Act. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum provision.

This 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 any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims. Alternatively, if a court were to find the choice of forum provisions contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, results of operations and financial condition.

Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all claims brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. Our restated bylaws provide that the federal district courts of the United States of America will, to the fullest extent permitted by law, be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or a Federal Forum Provision. Our decision to adopt a Federal Forum Provision followed a decision by the Supreme Court of the State of Delaware holding that such provisions are facially valid under Delaware law. While there can be no assurance that federal or state courts will follow the holding of the Delaware Supreme Court or determine that the Federal Forum Provision should be enforced in a particular case, application of the Federal Forum Provision means that suits brought by our stockholders to enforce any duty or liability created by the Securities Act must be brought in federal court and cannot be brought in state court.

Section 27 of the Exchange Act creates exclusive federal jurisdiction over all claims brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. In addition, neither the exclusive forum provision nor the Federal Forum Provision applies to suits brought to enforce any duty or liability created by the Exchange Act. Accordingly, actions by our stockholders to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder must be brought in federal court.

Our stockholders will not be deemed to have waived our compliance with the federal securities laws and the regulations promulgated thereunder.

Any person or entity purchasing or otherwise acquiring or holding any interest in any of our securities shall be deemed to have notice of and consented to our exclusive forum provisions, including the Federal Forum Provision. These provisions may limit a stockholders' ability to bring a claim in a judicial forum of their choosing for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers, and other employees.

We will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an emerging growth company, we will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, we expect these rules and regulations to substantially increase our legal and financial compliance costs and to make some activities more time consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain sufficient coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers. The increased costs may require us to reduce costs in other areas of our business or increase the prices of our products once commercialized. Moreover, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

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

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

General Risk Factors

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If no or few securities or industry analysts commence coverage of us, the trading price for our common stock could be impacted negatively. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our preclinical studies and clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of such analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause a decline in our stock price or trading volume.

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 Exchange Act, the Sarbanes-Oxley Act and the rules and the listing requirements of the Nasdaq Global Select Market. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting.

We perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting in our Annual Report on Form 10-K filing for that year, as required by Section 404(a) of the Sarbanes-Oxley Act. This requires that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts.

Our internal control over financial reporting will not prevent or detect all errors 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 are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the SEC, or other regulatory authorities.

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock may be volatile. The stock market in general, and Nasdaq and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

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

Unregistered Sales of Equity Securities

None.

Use of Proceeds

In the third quarter of 2020, we completed our IPO and sold 9,573,750 shares of common stock at an IPO price of $19.00 per share. The offer and sale of all of the shares in the IPO were registered under the Securities Act pursuant to registration statements on Form S-1 (File No. 333-248628), which was declared effective by the SEC on September 24, 2020, as supplemented by a registration statement on Form S-1 filed pursuant to Rule 462(b) (File No. 333-248628). We received net proceeds from the IPO of approximately $166.6 million, after deducting underwriting discounts and commissions of approximately $12.7 million and offering expenses of approximately $2.5 million. Morgan Stanley, Goldman Sachs & Co. LLC and BofA Securities acted as joint book-running managers of the offering and as representatives of the underwriters. None of the expenses associated with the IPO were paid to directors, officers, persons owning 10% or more of any class of equity securities, or to their associates, or to our affiliates.

There has been no material change in the planned use of proceeds from our IPO as described in the prospectus filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act on September 25, 2020.

Item 3. Defaults Upon Senior Securities.

None.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

None.

Item 6. Exhibits.

Furnish the exhibits required by Item 601 of Regulation S-K (§ 229.601 of this chapter).

Exhibit Number	Description	Form	File No.	Exhibit No.	Exhibit Filing Date	Filed/Furnished Herewith
10.1††	Second Amendment to Single-Tenant Triple Net Lease, dated August 8, 2022, by and between Prelude Therapeutics Incorporated and CRISP Partners LLC					X
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
101.INS	Inline XBRL Instance Document					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document.					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.					X
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)					X

†† Certain of the exhibits and schedules to these exhibits have been omitted in accordance with Regulation S-K Item 601(a)(5). The registrant agrees to furnish a copy of all omitted exhibits and schedules to the SEC upon its request.

**The certifications furnished in Exhibits 32.1 and 32.2 hereto are deemed to accompany this Form 10-Q and are not deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liability of that section, nor shall they be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act.*

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.

		Prelude Therapeutics Incorporated
Date: November 14, 2022	By:	/s/ Krishna Vaddi
		Krishna Vaddi, PhD
		Chief Executive Officer
		(Principal Executive Officer)
Date: November 14, 2022	By:	/s/ Laurent Chardonnet
		Laurent Chardonnet
		Chief Financial Officer
		(Principal Accounting Officer)

EXHIBIT 10.1

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [***], HAS BEEN OMITTED BECAUSE IT IS NOT MATERIAL AND WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICY DISCLOSED.

SECOND AMENDMENT TO SINGLE-TENANT TRIPLE NET LEASE

This **SECOND AMENDMENT TO SINGLE-TENANT TRIPLE NET LEASE** (this “Second Amendment”), is made on this 8th day of August, 2022, by and between **CRISP PARTNERS LLC**, a Delaware limited liability company (“Landlord”), and **PRELUDE THERAPEUTICS INCORPORATED**, a Delaware corporation (“Tenant”).

BACKGROUND:

A. Landlord and Tenant are parties to that certain Single-Tenant Triple Net Lease dated September 13, 2021 (the “Original Lease”), as amended by that certain First Amendment to Single-Tenant Triple Net Lease dated November 15, 2021 (the “First Amendment” and, together with the Original Lease, collectively, the “Lease”), covering that certain premises (the “Premises”) consisting of approximately 80,874 rentable square feet, known as Building 709 and located in Landlord’s building (the “Building”) at Chestnut Run Plaza, 984 Centre Road, Wilmington, Delaware, as more fully described in the Lease.

B. Subject to the provisions of this Second Amendment, Landlord and Tenant desire to modify the Lease in certain respects. Accordingly, Landlord and Tenant desire to amend the Lease.

NOW, THEREFORE, the parties hereto, in consideration of the mutual promises and covenants contained herein, and in the Lease, and intending to be legally bound, hereby agree that the Lease is amended as follows:

1. All capitalized terms used herein and not otherwise defined herein shall have the meanings ascribed to them in the Lease.

2. **Premises.** Section 1.2 of the Original Lease, entitled “Premises”, is hereby deleted in its entirety and replaced with the following:

> “1.2. “**Premises**” shall mean all of the interior space within the Building walls and below the Building ceiling, containing approximately 101,000 gross square feet and approximately 80,874 rentable square feet and shown on **Exhibit B** attached hereto.”

3. **Base Rent.** Section 1.03 of the Original Lease, entitled “Base Rent”, is hereby deleted in its entirety and replaced with the following:

“1.3 “**Base Rent”**:

Months of Term	RSF	Base Rent Per RSF	Monthly Base Rent
*Commencement Date - Last day of the 7th full calendar month of the Term	--	--	--
First day of the 8th full calendar month of the Term - Last day of the 12th full calendar month of the Term	60,000	$35.42	$177,100.00
First day of the 13th full calendar month of the Term - Last day of the 18th full calendar month of the Term	70,000	$35.42	$206,616.67
First day of the 19th full calendar month of the Term - Last day of the 30th full calendar month of the Term	80,874	$36.31	$244,711.25
First day of the 31st full calendar month of the Term - Last day of the 42nd full calendar month of the Term	80,874	$37.22	$250,844.19
First day of the 43rd full calendar month of the Term - Last day of the 54th full calendar month of the Term	80,874	$38.15	$257,111.93
First day of the 55th full calendar month of the Term - Last day of the 66th full calendar month of the Term	80,874	$39.10	$263,514.45
First day of the 67th full calendar month of the Term - Last day of the 78th full calendar month of the Term	80,874	$40.08	$270,119.16
First day of the 79th full calendar month of the Term - Last day of the 90th full calendar month of the Term	80,874	$41.08	$276,858.66
First day of the 91st full calendar month of the Term - Last day of the 102nd calendar month of the Term	80,874	$42.11	$283,800.35

First day of the 103rd full calendar month of the Term - Last day of the 114th full calendar month of the Term	80,874	$43.16	$290,876.82
First day of the 115th full calendar month of the Term - Last day of the 126th full calendar month of the Term	80,874	$44.24	$298,155.48
First day of the 127th full calendar month of the Term - Last day of the 138th full calendar month of the Term	80,874	$45.35	$305,636.33
First day of the 139th full calendar month of the Term - Last day of the 150th full calendar month of the Term	80,874	$46.48	$313,251.96
First day of the 151st full calendar month of the Term - Last day of the 162nd full calendar month of the Term	80,874	$47.64	$321,069.78

*This reflects an abatement of Base Rent in the amount of $177,100.00 per month, for a total of $1,239,700.00 for the first seven full calendar months of the Term."

4. **Estimated Expenses.** Section 1.4 of the Original Lease, entitled "Estimated Expenses", is hereby deleted in its entirety and replaced with the following:

"1.4 **"Estimated Expenses":** As of the date hereof, Estimated Expenses for the calendar year in which the Term commences are $562,883.04, payable in monthly installments of $46,906.92, subject to adjustment and reconciliation as provided for in this Lease. Notwithstanding the foregoing, monthly installments of Real Property Taxes and Operating Expenses shall be abated for the first six (6) full calendar months of the Term, provided, however, that Tenant shall be obligated to pay for the cost of janitorial, electricity, gas, telecommunications, water, sewer, data and any other utility or service contracted directly by Tenant. For the avoidance of doubt, Tenant's obligations to pay Estimated Expenses in accordance with the terms and conditions of this Lease shall be calculated using the entire rentable square feet of the Building in the amount of 80,874 (regardless that Base Rent for the first 18 full calendar months of the Term may be calculated using a lesser amount for rentable square feet)."

5. Term. Section 1.6 of the Original Lease, entitled "Term", is hereby deleted in its entirety and replaced with the following:

1.6. **"Term":** The period commencing on the Commencement Date (as defined below) and, unless terminated earlier in accordance with this Lease, ending on the date (the "Expiration Date") that is the last day of the 162nd full calendar month after the

Commencement Date. The "Commencement Date" shall mean the date that is the earlier of (i) the Landlord Work Substantial Completion Date (defined in Exhibit G), or (ii) the date Tenant takes possession of the Premises for the conduct of Tenant's business (provided that for the avoidance of doubt, Tenant entering the Premises for the performance of Tenant Fixturing (as defined in Exhibit G) shall not be deemed to trigger the Commencement Date). Landlord and Tenant shall confirm the Commencement Date and the Expiration Date by executing a "Confirmation of Lease Terms Certificate" in the form attached hereto as Exhibit F, provided, however, that (i) the enforceability of this Lease, and (ii) the determination of the Commencement Date, in each case, shall not be affected should either party fail or refuse to execute such certificate.

6. **Brokers.** Landlord and Tenant hereby expressly acknowledge and agree that the "separate agreement" referred to in the second sentence of Section 26.11 of the Original Lease specifically concerns the Leasing Commission Agreement dated September 10, 2021, as modified by that certain Addendum to Leasing Commission Agreement dated September 10, 2021, and as such, Landlord agrees only to pay the Broker(s) the commission due the Broker(s) pursuant to the express terms and conditions of the commission agreements referred to in this sentence. For the avoidance of doubt, Landlord and Tenant hereby expressly acknowledge and agree that the commission due to the Broker(s) is to be calculated using the original Base Rent schedule contained in Section 1.3 of the Original Lease (prior to such Section being amended by this Second Amendment) and not the amended Base Rent schedule contained in Section 2 of this Second Amendment.

7. **Possession.** Section 3 of the Original Lease, entitled "Possession", is hereby deleted in its entirety and replaced with the following:

"3. **Possession**. Landlord shall not be liable for any loss or damage to Tenant resulting from any delay in delivering possession of the Premises due to circumstances outside of Landlord's reasonable control. Notwithstanding the foregoing, if the Landlord Work Substantial Completion Date and delivery of possession of the Premises to Tenant is not achieved on or before May 1, 2023, as such date shall be extended for Excusable Delays (as defined below) (such date, as extended, the "First Penalty Date"), then Tenant shall receive a credit, which credit shall be applied against Base Rent next due and owing under the Lease, of one day's Base Rent for each day after the First Penalty Date until the earlier of (a) the date that the Landlord Work Substantial Completion Date is achieved and possession of the Premises is delivered to Tenant, or (b) the Second Penalty Date (as defined below). Notwithstanding the foregoing, if the Landlord Work Substantial Completion Date and delivery of possession of the Premises to Tenant is not achieved on or before June 1, 2023, as such date shall be extended for Excusable Delays (such date, as extended, the "Second Penalty Date"), then Tenant shall receive a credit, which credit shall be applied against Base Rent next due and owing under the Lease, of two days' Base Rent for each day after the Second Penalty Date until the date that the Landlord Work Substantial Completion Date is achieved and possession of the Premises is delivered to Tenant. Tenant shall have the right, at Tenant's own risk, expense and responsibility, at all reasonable times prior to the Commencement Date (as reasonably determined by Landlord), to enter the Premises for the sole and exclusive purpose of reviewing the condition of the Premises, provided that (a) Tenant obtains Landlord's prior written consent, not to be unreasonably withheld, conditioned or delayed, (b) Tenant does not interfere with or delay the Landlord Work, (c) Tenant uses contractors and workers compatible with the contractors and workers engaged by Landlord to complete the Landlord Work. If Tenant enters the Premises prior to the Commencement Date, then Tenant shall abide by the terms and conditions of this Lease as if the term of this Lease had already commenced, except that: (i) Tenant shall have no maintenance and repair obligations (unless and to the extent something is damaged by the acts or omissions of Tenant or any Tenant Party) and no obligation to pay (a) Base Rent until the first day of the eighth full calendar month of the Term, and (b) Real Property Taxes and Operating Expenses until the Commencement Date, in each case, unless and to the extent Base Rent, Real Property Taxes and Operating Expenses are payable during any partial month, as set forth in Section 4 of this Lease; and (ii) Tenant shall be responsible for paying for all utilities supplied to the Premises, including, without limitation, electric, gas, water and sewer, as set forth in Section 6 of this Lease; provided, however, Tenant shall not be responsible for paying for any utilities supplied to the Premises solely in connection with Landlord's construction activities at the Premises."

8. **Contingency.** Section 26.21 of the Original Lease, entitled "Contingency", is hereby deleted in its entirety.

9. **Project Amenities.** Section 26.23 of the Original Lease, entitled "Project Amenities", is hereby amended by deleting the reference to "February 15, 2023" and substituting "August 15, 2023" therefor. Accordingly, the Project Amenities Penalty Date is August 15, 2023.

10. **Work Letter.** The Work Letter attached as Exhibit G to the Original Lease, and Exhibit "G-1", Exhibit "G-2" and Exhibit "G-3" attached thereto, are all hereby deleted their entireties and replaced with Exhibit "G-Revised", Exhibit "G-1 Revised" and Exhibit "G-2 Revised" attached to this Second Amendment.

11. Except as expressly modified herein, the Lease shall remain in full force and effect in accordance with its terms. In the event of any conflict between the terms contained in this Second Amendment and the Lease, the terms herein contained shall supersede and control the obligations and liabilities of the parties.

12. Tenant acknowledges and agrees that the Lease, as hereby amended, is in full force and effect and, to Tenant's knowledge, Tenant has no claims or offsets against Rent due or to become due under the Lease, as hereby amended.

13. This Second Amendment shall be binding upon and inure to the benefit of the parties and their respective successors and permitted assigns.

14. This Second Amendment may be executed in counterparts, each of which shall constitute an original, but which, taken together, shall be one original agreement. Any counterpart of this Second Amendment may be executed and delivered by electronic transmission (including, without limitation, e-mail) or by portable document format (pdf) and shall have the same force and effect as an original.

{SIGNATURES APPEAR ON THE FOLLOWING PAGE}

IN WITNESS WHEREOF, Landlord and Tenant have caused this Second Amendment to be duly executed, under seal, as of the day and year first above written.

LANDLORD:

CRISP PARTNERS LLC

By: /s/ Lawrence J. Stuardi
Name: Lawrence J. Stuardi
Title: Member

TENANT:

PRELUDE THERAPEUTICS INCORPORATED

By: /s/ Jane Huang
Name: Jane Huang
Title: President and CMO

<u>EXHIBIT "G- REVISED"</u>

<u>WORK LETTER</u>

This **Exhibit "G-REVISED"** (referred to herein and in the Lease as the "**Work Letter**") accompanies and forms a material part of that certain Single-Tenant Triple Net Lease between **CRISP PARTNERS LLC**, as Landlord, and **PRELUDE THERAPEUTICS INCORPORATED**, as Tenant (the "**Lease**"), and sets forth the respective obligations of Landlord and Tenant for the finalization of design and continuation and completion of the Base Building Work, the Tenant Improvements and the Tenant Fixturing (as those terms are defined herein). Any capitalized terms used herein and not otherwise defined herein shall have the meaning ascribed to such terms as set forth in the Lease.

1. **Intentionally Deleted**

2. **Construction Representatives**

(a) In order to streamline communication and decision-making, in addition to the terms and conditions set forth herein, Landlord and Tenant have each assigned a designated representative (with respect to Tenant, Tim Mueller, the "**Tenant's Construction Representative**" and, with respect to Landlord, Keith Metzger, the "**Landlord's Construction Representative**") who will facilitate and coordinate design and construction, and Landlord and Tenant may rely on all instructions, consents, agreements, changes and modifications made by such representatives as having been given or made by, and binding upon, Landlord or Tenant, as the case may be. In the event Tenant's Construction Representative is unavailable, Tenant has assigned a designated secondary representative, Aimee Crombie, to act on behalf of Tenant's Construction Representative. In the event Landlord's Construction Representative is unavailable, Landlord has assigned a designated secondary representative, Hank Merrill, to act on behalf of Landlord's Construction Representative.

3. **Base Building Work**

(a) <u>Description; Project Contractor</u>. The Building and Exterior Areas and all site work and other improvements to be constructed in connection therewith by or on behalf of Landlord, as more particularly described in the "**Base Building Plans and Specifications**" as more fully defined in and attached hereto as "**Exhibit "G-1 REVISED**" shall constitute and be referred to herein as the "**Base Building Work**". As used in the Lease and this Work Letter, the term "**Project Contractor**" shall mean Bancroft Construction, who will be engaged by Landlord to complete both the Base Building Work and the Tenant Improvements. Landlord, Tenant and the Project Contractor shall work as a team to ensure that both the Base Building Work and the Tenant Improvements shall be performed simultaneously to ensure that the Project is delivered in a timely manner and in accordance with the Base Building Plans and Specifications and the TI Plans and Specifications as further defined below.

(b) <u>Base Building Plans and Specifications</u>.

(i) Landlord with Tenant's acknowledgement engaged L2P (" **Project Architect**") and CDA Engineering, Inc. ("**Project Civil Engineer**") to prepare, in collaboration with each of Landlord's Construction Representative and Tenant's Construction Representative and through the collective input of Landlord and Tenant, the Base Building Plans and Specifications. As the Base Building Plans and Specifications progressed through the schematic design and design development stages, Landlord and Tenant, with budgetary input from Project Contractor, made various changes to the Base Building Plans and Specifications intended to reduce the overall cost of the Base Building Work (collectively, the "**Base Building Value Engineering Changes**"). The Base Building Value Engineering Changes have been incorporated into the Base Building Plans and Specifications listed in **Exhibit "G-1 REVISED"**. In the event Landlord, Tenant, Project Contractor, Project Architect or Project Civil Engineer recommends or requests in writing further Base Building Value Engineering Changes, any such changes, if approved (such approval not to be unreasonably withheld, conditioned or delayed) by Landlord and Tenant in writing, as the case may be, shall be incorporated into the Base Building Plans and Specifications.

(ii) For the avoidance of doubt, pursuant to the First Amendment to Single-Tenant Triple Net Lease dated November 15, 2021, by and between Landlord and Tenant, Landlord has entered into a BDA with DNREC, which BDA requires Landlord, at Landlord's sole cost and expense, to take certain measures to conduct a Brownfield Investigation and to implement any Remedial Action Work Plan and Final Plan of Remedial Action, as defined in the BDA, and as issued, approved, modified, or amended by DNREC, which plan is set forth on **Exhibit "G-4 REVISED"** attached hereto.

(iii) Any approval by Landlord of the Base Building Plans and Specifications, (or any iteration thereof) shall not be a representation or warranty of Landlord that the Base Building Work or such documents are adequate for Tenant's particular manner of use of the Premises.

(c) Permits. Landlord, at Landlord's cost, shall be responsible for obtaining from the applicable governmental authority(ies) having jurisdiction over the Premises (collectively, the "**Government Agency**") all building permits and other governmental licenses, permits and approvals necessary for the construction of the Base Building Work (collectively, "**Base Building Approvals**"). Tenant shall cooperate with Landlord, at no material cost to Tenant, in Landlord's efforts to obtain such permits and other approvals. Landlord shall notify Tenant's Construction Representative in writing (it being agreed that email notice shall suffice, which notice shall be sent to Tim Mueller at [***] until changed by Tenant upon notice to Landlord) of any and all changes or modifications to the Base Building Plans and Specifications required in order to obtain the Base Building Approvals, within three (3) business days following the date Landlord becomes aware of such required changes or modifications. If any such changes or modifications are materially inconsistent or incompatible with the Base Building Plans and Specifications or the Tenant Improvements, then Landlord's Construction Representative and Tenant's Construction Representative shall meet with such Governmental Agency as soon as practical after Tenant's Construction Representative's receipt of the notice of such changes or modifications required by any such Government Agency, to mutually determine, in good faith, what material changes or modifications are practical and acceptable to all parties (such determination not to be unreasonably withheld, conditioned, or delayed). Once deemed acceptable to all parties, the Base Building Plans and Specifications will be amended to comply with any conditions of the Base Building Approvals.

(d) Performance of the Base Building Work. Landlord shall engage Project Contractor to complete the Base Building Work in accordance with the Base Building Plans and Specifications.

(e) Costs of the Base Building Work. Except as otherwise expressly set forth herein, Landlord shall be solely responsible for all costs and expenses incurred in connection with designing and constructing the Base Building Work.

(f) Base Building Work Substantial Completion. Subject to Excusable Delays (as defined below), Landlord shall use commercially reasonable efforts to cause the Substantial Completion of the Base Building Work to occur on or before the Target Landlord Work Substantial Completion Date (as defined below). As used in this Section, the term "**Substantial Completion of the Base Building Work**" (or any variation or deviation thereof) shall mean the date that the Base Building Work has been substantially completed in accordance with the Base Building Plans and Specifications and all Applicable Laws, subject only to incomplete items which will not materially affect or impair Landlord's ability to complete the Tenant Improvements or preclude the issuance of a temporary or permanent certificate of occupancy upon the final completion of the Tenant Improvements. The date that Substantial Completion of the Base Building Work actually occurs is referred to as the "**Base Building Work Substantial Completion Date**." Notwithstanding anything contained herein, Tenant and Landlord mutually agree and understand that the Base Building Work and the Tenant Improvements and Tenant Fixturing may occur concurrently.

(g) Base Building Punch List. Upon Substantial Completion of the Base Building Work, Landlord, in consultation with Tenant, shall generate a punch list of all asserted incomplete work items in Landlord's construction of the Base Building Work (the "**Base Building Punch List**"). Landlord shall complete all items on the Base Building Punch List within 60 days after the date of the generation of the Base Building Punch List, unless due to Excusable Delays. Given that the Base Building Work, the Tenant Improvements, and Tenant Fixturing may occur concurrently, Tenant and Landlord mutually agree and understand that the Base Building Punch List and the Tenant Improvements Punch List may overlap.

4. **Tenant Improvements; Construction of Tenant Improvements by Project Contractor**

(a) Description. The interior finish work of the Premises as more particularly described in the TI Plans and Specifications (as defined below) shall constitute and be referred to herein as the "**Tenant Improvements**". Landlord and Tenant shall continue to use expeditious, diligent, good faith, commercially reasonable efforts to cause Project Architect, Project Civil Engineer to coordinate with Landlord's Construction Representative and Tenant's Construction Representative to align the Base Building Work and the Tenant Improvements.

(b) TI Plans and Specifications.

(i) Tenant engaged Project Architect and Landlord engaged Project Civil Engineer, on behalf of Tenant, to prepare, in collaboration with each of Landlord's Construction Representative and Tenant's Construction Representative, a complete set of plans and specifications for the Tenant Improvements as more particularly described in the "**TI Plans and Specifications**" more fully defined in and attached hereto as "**Exhibit "G-2 REVISED**", which have been developed through the collective input of Landlord and Tenant. As the TI Plans and Specifications progressed through the schematic design and design development stages, Landlord and Tenant, with budgetary input from Project Contractor, made various changes to the plans intended to reduce the overall cost of the Tenant Improvements (collectively, the "**TI Value Engineering Changes**"). The TI Value Engineering Changes have been incorporated into the TI Plans and Specifications listed in **Exhibit "G-2 REVISED"**. In the event Landlord, Tenant, Project Contractor, Project Architect or Project Civil Engineer recommends or requests in writing further TI Value Engineering Changes, any such changes, if approved (such approval not to be unreasonably withheld, conditioned or delayed) by Landlord and Tenant in writing, as the case may be, shall be incorporated into the TI Plans and Specifications.

(ii) Any approval by Landlord of the TI Plans and Specifications, (or any iteration thereof) shall not be a representation or warranty of Landlord that the Tenant Improvements or such documents are adequate for Tenant's particular manner of use of the Premises.

(c) Permits. Except as otherwise expressly set forth herein, Landlord shall be responsible for obtaining from the Governmental Agency, at Tenant's cost, all building permits and other governmental permits and approvals necessary for the construction of the Tenant Improvements (collectively, "**TI Approvals**"). Tenant shall cooperate with Landlord in Landlord's efforts to obtain such permits and other approvals. Landlord shall notify Tenant's Construction Representative in writing (it being agreed that email notice shall suffice, which notice shall be sent to Tim Mueller at [***] until changed by Tenant upon notice to Landlord) of any and all changes or modifications to the TI Plans and Specifications required in order to obtain the TI Approvals. If any such changes or modifications are materially inconsistent or incompatible with the Permitted Use of the Premises, then Landlord's Construction Representative and Tenant's Construction Representative shall meet with such Governmental Agency as soon as practical after Tenant's Construction Representative's receipt of the notice of such changes or modifications required by any such Government Agency, to mutually determine, in good faith, what material changes or modifications are practical and acceptable to all parties (such determination not to be unreasonably withheld, conditioned, or delayed). Once deemed acceptable to all parties, the TI Plans and Specifications will be amended to comply with any such agreed to changes or modifications.

(d) Construction of the Tenant Improvements. Landlord shall obtain, from Project Contractor, a GMP proposal for the completion of the Tenant Improvements, which proposal shall be issued on a fully open-book basis with Landlord and Tenant having access to all information during the bidding process. Following completion of the Project Contractor's subcontractor bidding process, submission of a GMP proposal, and acceptance by Landlord and Tenant of the GMP proposal from Project Contractor, Landlord shall enter into a contract with Project Contractor for the construction of the Tenant Improvements ("**Landlord's TI Construction Contract**"). Tenant shall be named in the Landlord's TI Construction Contract as a third-party beneficiary of Landlord's rights and remedies thereunder, and expressly granted the right to enforce all guarantees and warranties provided by Project Contractor, and its subcontractors and suppliers pursuant to the Landlord's TI Construction Contract.

(e) Costs of the Tenant Improvements: Allowance. Landlord agrees to complete the Tenant Improvements, at Tenant's sole cost and expense (but subject to the application of the Allowance (as defined below) as set forth below), equal to the aggregate of all costs, expenses, and fees incurred by or on behalf of Landlord in connection therewith (the "Tenant's Cost"), including without limitation, (i) architectural, engineering, and design costs, (ii) the cost charged to Landlord by Project Contractor and all subcontractors for performing the Tenant Improvements, (iii) the cost to Landlord of performing directly any portion of the Tenant Improvements and (iv) Landlord's project management manager, MRA Development Service, Inc., a fee for Landlord's supervision of the Tenant Improvements in an amount equal to $810,000.00, and (v) Jones Lang LaSalle Americas, Inc. a project management fee equal to $270,000.00. Tenant's Cost shall not include any other project or construction management fees from Landlord or Jones Lang LaSalle other than the two fees set forth above in this paragraph in subclauses (iv) and (v). Provided Tenant is not in default under the Lease, Landlord agrees to credit Tenant with an allowance (the "Allowance") equal to [***] (which is equal to [***] per rentable square foot of the Premises). Landlord's obligation to complete the Tenant Improvements is contingent upon Tenant paying Landlord the amount by which the Tenant's Cost exceeds the Allowance, estimated or otherwise, which excess amounts shall be paid by Tenant to Landlord as follows:

i. Tenant shall pay the initial [***] of the Tenant's Cost prior to any application by Landlord of the Allowance towards the Tenant's Cost. Tenant shall pay such amount within thirty (30) days following: (i) the completion of the portion(s) of the Tenant Improvements for which such amount is applied to; (ii) Tenant's receipt of an invoice or invoices, for such amount, or a portion thereof, as applicable; and (iii) Tenant's receipt of acknowledgment by Project Architect certifying that such portion of the Tenant Improvements have been substantially completed in accordance with the TI Plans and Specifications and all Applicable Laws;

ii. Thereafter, Tenant shall be responsible for paying Landlord [***] of each monthly invoice Landlord receives in connection with completion of the Tenant Improvements, until Landlord fully credits Tenant with the Allowance. Tenant shall pay such amount within thirty (30) days following: (i) the completion of the portion(s) of the Tenant Improvements for which such amount is applied to; (ii) Tenant's receipt of an invoice or invoices, for such amount, or a portion thereof, as applicable; and (iii) Tenant's receipt of acknowledgment by Project Architect certifying that such portion of the Tenant Improvements have been substantially completed in accordance with the TI Plans and Specifications and all Applicable Laws; and

iii. Thereafter, once the Allowance has been fully applied, Tenant shall be responsible for paying 100% of each monthly invoice Landlord receives in connection with completion of the Tenant Improvements. Tenant shall pay such amount within thirty (30) days following: (i) the completion of the portion(s) of the Tenant Improvements for which such amount is applied to; (ii) Tenant's receipt of an invoice or invoices, for such amount, or a portion thereof, as applicable and (iii) Tenant's receipt of acknowledgment by Project Architect certifying that such portion of the Tenant Improvements have been substantially completed in accordance with the TI Plans and Specifications and all Applicable Laws. In the event the estimated Tenant's Cost exceed the actual Tenant's Cost incurred, Landlord shall refund Tenant for any amount paid by Tenant pursuant to the payment structure set forth above, which exceeds the actual amount of the Tenant's Cost in excess of the Allowance.

Notwithstanding the foregoing, (i) Landlord's obligation to credit Tenant with the Allowance as set forth herein shall be delayed (but not terminated) during the pendency of any default by Tenant under this Lease, and (ii) Landlord shall reimburse Tenant as set forth herein if and when Tenant cures any such default. Upon completion of the Tenant Improvements and determination of the actual Tenant's Cost, which determination shall occur within a commercially reasonable time period following the completion of the Tenant Improvements, Landlord or Tenant shall, within 30 days following such completion, pay to the other (or, at Landlord's option, Landlord may credit Tenant) the amount of any overpayment or deficiency then due from one to the other in connection with the foregoing sentence. Landlord shall have no further obligations to pay for any costs incurred in connection with the Tenant Improvements, except as otherwise expressly set forth in the Lease.

(f) Standard of Performance. Landlord shall cause Project Contractor to construct and complete the Tenant Improvements in a good and workmanlike manner, in accordance with all Applicable Laws.

(g) Limitation on Landlord's Responsibility. Without limiting the foregoing provisions of this Section, Landlord and Tenant agree that Tenant shall be responsible to review the TI Plans and Specifications to ensure the proposed Tenant Improvements are adequate, appropriate, suitable and sufficient for Tenant's desired purposes and Tenant's specific manner of use of the Premises.

(h) Substantial Completion of the Tenant Improvements. Subject to Excusable Delays, Landlord shall use commercially reasonable efforts to cause the Substantial Completion of the Tenant Improvements (as defined below) to occur by April 27, 2023 (the "**Target Landlord Work Substantial Completion Date**"). As used in this Section 4, "**Substantial Completion of the Tenant Improvements**" (or any variation or derivation thereof) shall mean that Landlord has delivered to Tenant (a) physical possession of, and access to, the Premises, which shall comply with all Applicable Laws, (b) acknowledgment by Project Architect certifying that the Tenant Improvements have been substantially completed in accordance with the TI Plans and Specifications and all Applicable Laws, subject only to incomplete items which do not adversely affect in a material way or materially interfere with Tenant's use and occupancy of the Premises for the Permitted Use, which incomplete items shall be set forth on the Tenant Improvements Punch List (as defined below), and (c) a temporary or permanent certificate of occupancy for Tenant's use and occupancy of the Premises for the Permitted Use has been issued by the Governmental Agency (provided, however, in the event Landlord obtains a temporary certificate of occupancy, Landlord agrees to use commercially reasonable efforts to obtain a permanent certificate of occupancy as quickly as is reasonably possible and to maintain the temporary certificate of occupancy in effect until the permanent certificate of occupancy is obtained so that Tenant's occupancy of the Premises for the Permitted Use is not materially adversely affected). Tenant agrees to cooperate reasonably, at no material cost to Tenant, with Landlord in Landlord's efforts to obtain the certificate of occupancy and agrees, to the extent any ongoing or incomplete approved Tenant Fixturing (not the Tenant Improvements) could negatively impact Landlord's ability to obtain a certificate of occupancy for the Tenant Improvements, to suspend all such Tenant Fixturing and (to the extent safe, practicable and in accordance with Applicable Law) cause same not to appear to be in an "in process" condition on any day on which a physical inspection of the Premises is undertaken for issuance of such certificate of occupancy, provided Tenant receives reasonable advance notice thereof. The date that Substantial Completion of the Tenant Improvements actually occurs is referred to as the "**TI Substantial Completion Date**." The date on which both the Base Building Work Substantial Completion Date and the TI Substantial Completion Date are achieved and possession of the Premises is delivered to Tenant is referred to as the "**Landlord Work Substantial Completion Date**."

(i) Tenant Improvements Punch List. Upon Substantial Completion of the Tenant Improvements, Landlord, in consultation with Tenant, shall generate a punch list of all asserted defects or incomplete work items, if any, in Landlord's construction of the Tenant Improvements (the "**Tenant Improvements Punch List**"). Landlord shall complete all items on the Tenant Improvements Punch List within 60 days after the date of the generation of the Tenant Improvements Punch List, unless due to Excusable Delays.

(j) Inclusion of Plans. The Base Building Plans and Specifications, and the TI Plans and Specifications, as listed on **Exhibit "G-1 REVISED"** and **Exhibit "G-2 REVISED"**, respectively, are hereby incorporated into and made a part of the Lease as if originally attached thereto at the time of execution of the Lease.

5. **Field Adjustments and Change Orders**

(a) Tenant acknowledges and agrees that, except as expressly set forth in the Base Building Plans and Specifications and the TI Plans and Specifications, the Landlord Work shall be constructed using standard methods, materials and finishes designated by Landlord for the Building, in consultation with Tenant. Landlord shall have the right, from time to time, to make reasonable and non-material changes/field adjustments (collectively, "**Non-Material Field Adjustments**") in and to the Base Building Plans and Specifications and the TI Plans and Specifications to the extent that the same shall be necessary in order to adjust to actual field conditions or to cause the work shown on the Base Building Plans and Specifications and the TI Plans and Specifications to comply with any applicable requirements of public authorities and/or requirements of insurance bodies. All Non-Material Field Adjustments (which may be made immediately but confirmed by written change order and notice to Tenant) shall be noted on the applicable plans or documents. Except for Non-Material Field Adjustments, Landlord shall not make any other changes/field adjustments in and to the Base Building Plans and Specifications and the TI Plans and Specifications, without first obtaining the written consent of Tenant, which consent shall not be unreasonably withheld, conditioned or delayed. Tenant's failure to respond to Landlord in writing within 2 business days after the date of Tenant's receipt of Landlord's written request for such consent shall be deemed a Tenant Delay.

(b) The Base Building Work and the Tenant Improvements are collectively referred to as the "**Landlord Work**". If Tenant shall request any changes to the Base Building Plans and Specifications and the TI Plans and Specifications that are approved by Landlord pursuant to the process set forth herein ("**Change Orders**"), Landlord shall have any necessary revisions to the Base Building Plans and Specifications and/or the TI Plans and Specifications, as the case may be, prepared, and Tenant shall reimburse Landlord for the cost of preparing such revisions. Tenant shall be responsible for any Tenant Delay caused by Tenant or any Tenant Party in the completion of the Landlord Work resulting from any Change Orders pursuant to Section 6(c)(i)(1) below. Landlord shall notify Tenant in writing of (A) the estimated increased cost to the

Landlord Work, if any, which will be chargeable to Tenant by reason of such Change Orders, which increased costs together with the costs of preparing revisions to the Base Building Plans and Specifications and the TI Plans and Specifications are collectively referred to herein as the "**Excess Costs**", and (B) Landlord's estimate of delay resulting from the Change Order. Tenant shall, within 2 business days after receiving Landlord's estimate of the Excess Costs and delay, notify Landlord in writing whether it desires to proceed with such Change Order, such notification to be accompanied by payment from Tenant of the Excess Costs. In the absence of such written authorization, Landlord shall continue work on the construction of the Landlord Work; provided, however, that Landlord may discontinue work on the construction of that portion of the Landlord Work which may be affected by the pending Change Order until it receives notice of Tenant's decision, if, in Landlord's commercially reasonable, good faith discretion, Landlord has determined that proceeding with such construction will interfere with the performance of work set forth in the pending Change Order, in which event any delay caused by the discontinuation of such work shall be deemed to be a delay caused by Tenant. Following approval of the revised Base Building Plans and Specifications and the TI Plans and Specifications and the payment by Tenant of the required portion of the Excess Costs, if any, Landlord shall cause the Landlord Work to be constructed substantially in accordance with the approved Change Orders.

6. **Delays**

(a) Excusable Delay. Construction Force Majeure (as hereinafter defined) and/or Tenant Delay (as hereinafter defined) are collectively referred as "**Excusable Delays**".

(b) Construction Force Majeure. For purposes hereof, "**Construction Force Majeure**" shall mean time actually lost by Landlord, Project Contractor or any subcontractors or suppliers due to governmental restrictions, limitations and delays (including, without limitation, delays in the issuance of any governmental permit, license and/or approval required to complete the Landlord Work through no fault of Landlord or its agents, employees or contractors), scarcity, unavailability or delay in obtaining fuel, materials, equipment or components (so long as any delays occur despite Landlord's commercially reasonable diligent efforts), war or other national emergency, accidents, floods, defective materials, fire damage or other casualties, adverse weather conditions which reasonably prevent Landlord from pursuing construction activities in a normal manner, soil conditions, or any other cause similar or dissimilar to the foregoing in any case beyond the reasonable control of Landlord or Landlord's contractors, subcontractors or suppliers.

(c) Tenant Delay.

(i) For purposes hereof, the terms "**Tenant Delay**" or "**Delay caused by Tenant**" shall mean:

1. delay in completion of construction of the Landlord Work caused by any act or failure to act by Tenant or any Tenant Party in violation of this Lease, including, without limitation, (A) delay (beyond the time frames set forth in this Work Letter) by Tenant in approval of any plans and specifications (or revisions or updates thereto) covering work to be performed by Landlord in connection with the Landlord Work, (B) the interference of Tenant with the Landlord Work, or (C) delays resulting from any Change Orders; and

2. delay in the issuance of a temporary or permanent certificate of occupancy or completion of construction of the Landlord Work as a result of any act or omission (with respect to any omission, only to the extent in violation of this Lease or Applicable Laws) of Tenant or any Tenant Party (including, without limitation, any delay by Tenant or any Tenant Party in performing Tenant Fixturing), which continues for 1 business day following Tenant's receipt of notice (it being agreed that email notice shall suffice, which notice shall be sent to Tim Mueller at [***] until changed by Tenant upon notice to Landlord) of such delay or Tenant otherwise becoming aware of such delay.

(ii) For purposes of determining Tenant Delay, the term Tenant shall include any Tenant Party. If the Landlord Work Substantial Completion Date is delayed by a Tenant Delay, then the Landlord Work Substantial Completion Date shall be deemed to have occurred on the date it would have occurred but for such Tenant Delay. Landlord shall notify Tenant in writing (it being agreed that email notice shall suffice, which notice shall be sent to Tim Mueller at [***] until changed by Tenant upon notice to Landlord) of the occurrence of a Tenant Delay event within 3 business days after Landlord actually becomes aware of the occurrence of such Tenant Delay event, provided that if Landlord fails to so notify Tenant within 7 business days after Landlord actually becomes aware of the occurrence of such Tenant Delay event, then, except if Tenant otherwise has become aware of such Tenant Delay (in which case the ensuing language shall not apply), then such Tenant Delay shall not be deemed to commence unless and until Tenant's receipt of such notice at the time that such Tenant Delay is continuing.

7. **Tenant Fixturing and Permits**

(a) Concurrently with Landlord's completion of the Base Building Work and the Tenant Improvements, Tenant shall, at Tenant's sole cost and expense, commence and thereafter diligently pursue to completion, the installation in and equipping of the Premises with new personal property necessary or proper for the operation of the Permitted Use and perform all other work in the Premises necessary or proper to prepare the Premises for the conduct and operation of the Permitted Use therein (collectively, the "**Tenant Fixturing**"). All Tenant Fixturing shall be performed in a good and workmanlike manner and in accordance with all Applicable Laws and in accordance with the terms of the Lease. Tenant shall, at Tenant's sole cost and expense, obtain all permits and other governmental permits and approvals necessary for the Tenant Fixturing. Landlord shall reasonably cooperate with Tenant, at no material cost to Landlord, in Tenant's efforts to obtain such permits and other approvals. In addition, Tenant, at its sole cost and expense, shall be solely responsible for obtaining, and delivering copies to Landlord, prior to occupancy of the Premises (or any part thereof), all governmental permits and approvals necessary for the Tenant Fixturing and for Tenant to conduct its business of the Permitted Use in the Premises.

8. **Limited Warranty**

(a) Landlord guarantees, for a period of one year following the Landlord Work Substantial Completion Date, (i) the Landlord Work against defective workmanship and/or materials or non-compliance with the Base Building Plans and Specifications and/or the TI Plans and Specifications, and (ii) that the Building and the Building Systems, including the roof, floors, walls, doors, dock doors and all other mechanical systems, are and shall be in good, operable condition. Landlord agrees, during said one-year period at its sole cost and expense, to (i) repair or replace any defective item occasioned by defective workmanship and/or materials or non-compliance with the Base Building Plans and Specifications and/or the TI Plans and Specifications, and (ii) make all necessary repairs to keep the Building and the Building Systems, including the roof, floors, walls, doors, dock doors and all other mechanical systems in good, operable condition. Landlord agrees, upon Tenant's reasonable prior request, to jointly inspect the Building with a representative of Tenant at any time during the one year guaranty period. Notwithstanding anything in this paragraph to the contrary, in no event shall Landlord be obligated to make repairs or replacements to items (i) if the costs of such repair or replacement would have been covered by warranty but is no longer covered by warranty due to the acts or omissions (with respect to omissions, only to the extent in violation of this Lease or Applicable Laws) of Tenant or any Tenant Party, or (ii) due to any act or omission (with respect to omissions, only to the extent in violation of this Lease or Applicable Laws) of Tenant or any Tenant Party (including, without limitation, Tenant's failure to properly maintain or service any portions of the Building or the Premises or any systems contained thereon that Tenant is required to maintain pursuant to the Lease).

EXHIBIT “G-1 REVISED”

BASE BUILDING PLANS AND SPECIFICATIONS

CORE AND SHELL SPECIFICATIONS
PREPARED BY L2P
DATED APRIL 26, 2022

DIVISION 1	GENERAL REQUIREMENTS
11000	SUMMARY
12300	ALTERNATES
12500	SUBSTITUTION PROCEDURES
13100	PROJECT MANAGEMENT AND COORDINATION
13233	PHOTO DOCUMENTATION
13300	SUBMITTAL PROCEDURES
13000	QUALITY REQUIREMENTS
14525	EXTERIOR ENCLOSURE TESTING SERVICES
14200	REFERENCES
16000	PRODUCT REQUIREMENTS
17300	EXECUTION
17700	CLOSEOUT PROCEDURES
17823	OPERATION AND MAINTENANCE DATA
17839	PROJECT RECORD DOCUMENTS
17900	DEMONSTRATION AND TRAINING
18316	EXTERIOR ENCLOSURE GENERAL REQUIREMENTS
DIVISION 2	
24119	SELECTIVE DEMOLITION
DIVISION 3	CONCRETE
	NOT USED
DIVISION 4	MASONRY
44200	EXTERIOR STONE CLADDING
42700	CAST STONE MASONRY
DIVISION 5	METALS
54000	COLD FORMED METAL FRAMING
55000	METAL FABRICATIONS
55100	METAL STAIRS
55200	METAL RAILINGS
57313	GLAZED DECORATIVE METAL RAILINGS
DIVISION 6	WOOD, PLASTICS, AND COMPOSITS

61053	MISCELLANEOUS ROUGH CARPENTRY
61600	SHEATHING
67413	FIBERGLASS REINFORCED GIRTS
DIVISION 7	THERMAL AND MOISTURE PROTECTION
71326	SELF-ADHERING SHEET WATERPROOFING
72100	THERMAL INSULATION
72129	SPRAYED CELLULOSE ACOUSTICAL INSULATION
72713	AIR AND WEATHER BARRIER
74213	ALUMINUM COMPOSITE WALL PANELS AND EXTRUDED TRIM
75423	TPO ROOFING
76200	SHEET METAL FLASHING AND TRIM
77200	ROOF ACCESSORIES
78123	INTUMESCENT FIREPROOFING
78413	PENETRATION FIRE STOPPING
79205	EXTERIOR JOINT SEALANTS
DIVISION 8	OPENINGS
81113	HOLLOW METAL DOORS AND FRAMES
83323	OVERHEAD COILING DOORS
84213	ALUMINUM-FRAMED ENTRANCES AND STOREFRONT
84413	GLAZED ALUMINUM CURTAIN WALL
87100	FINISH HARDWARE
88010	EXTERIOR GLAZING
89119	FIXED LOUVERS
DIVISION 9	FINISHES
092116_23	GYPSUM BOARD SHAFT WALL ASSEMBLIES
92216	NON-STRUCTURAL METAL FRAMING
92900	GYPSUM BOARD
DIVISION 10	EQUIPMENT
104416	FIRE EXTINGUISHERS
DIVISION 11	
111300	LOADING DOCK EQUIPMENT
DIVISION 14	CONVEYING EQUIPMENT
142010	ELEVATORS

CORE AND SHELL PLANS
PREPARED BY L2P
DATED APRIL 26, 2022

ARCHITECTURAL	
CS-000	COVER SHEET
A002	GENERAL NOTES / ABBREVIATIONS
A003	ACCESSIBLE MOUNTING HEIGHTS & CLEARANCES
A010	LIFE SAFETY PLAN - BASEMENT
A011	LIFE SAFETY PLAN - 1ST FLOOR
A012	LIFE SAFETY PLAN - 2ND FLOOR
AD111	SELECTIVE DEMOLITION PLAN - FIRST FLOOR - OVERALL
AD112	SELECTIVE DEMOLITION PLAN - SECOND FLOOR - OVERALL
AD150	DEMO ROOF PLAN
A110	BASEMENT PLAN
A111	PARTITION PLAN - FIRST FLOOR - OVERALL
A112	PARTITION PLAN - SECOND FLOOR - OVERALL
A114	PENTHOUSE AND ROOF PLAN
A115	OVERALL ROOF PLAN
A121	REFLECTED CEILING PLAN - FIRST FLOOR
A122	REFLECTED CEILING PLAN - SECOND FLOOR
A151	ENLARGED PLANS - SOUTH CANOPY
A201	EXTERIOR ELEVATIONS
A202	EXTERIOR ELEVATIONS
A410	WALL SECTIONS
A411	EXTERIOR ASSEMBLIES AND DETAILS
A420	SECTION DETAILS
A421	EXTERIOR DETAILS
A422	EXTERIOR DETAILS
A500	PARTITION TYPES & DETAILS
A510	DOOR & FRAME TYPES & DETAILS
A600	SOUTH STAIR AND PASSENGER ELEVATOR
A601	NORTH STAIR PLANS AND SECTION
A602	SERVICE ELEVATOR PLANS AND SECTIONS
A603	RAMP AND STAIR DETAILS - SOUTH ENTRY
CIVIL	
C-01	COVER SHEET
C-02	SITE DEMOLITION & EROSION & SEDIMENT CONTROL PLAN
C-03	LINES AND GRADES PLAN
C-04	SITE CONSTRUCTION DETAILS
C-05	SITE CONSTRUCTION DETAILS
STRUCTURAL	

S001	COVER SHEET
S002	GENERAL NOTES
S003	GENERAL NOTES
S004	PROJECT SCHEDULES
S101	FOUNDATION PLAN
S102	SECOND FLOOR FRAMING PLAN
S103	ROOF FRAMING PLAN
S104	ENLARGED PLANS
S105	ENLARGED PLANS
S106	ENLARGED PLANS
S107	ENLARGED PLANS
S108	ENLARGED PLANS
S501	TYPICAL FOUNDATION DETAILS
S502	FOUNDATION SECTIONS AND DETAILS
S503	FOUNDATION SECTIONS AND DETAILS
S504	FOUNDATION SECTIONS AND DETAILS
S505	FOUNDATION SECTIONS AND DETAILS
S506	FOUNDATION SECTIONS AND DETAILS
S511	TYPICAL FRAMING DETAILS
S512	FRAMING SECTIONS AND DETAILS
S513	FRAMING SECTIONS AND DETAILS
S514	FRAMING SECTIONS AND DETAILS

EXHIBIT "G-2 REVISED"

TI PLANS AND SPECIFICATIONS

TI SPECIFICATIONS
PREPARED BY L2P
DATED APRIL 26, 2022

DIVISION 01	GENERAL REQUIREMTS
SECTIONS OF DIVISION 01 ISSUED AS PART OF PROJECT CRISP CORE AND SHELL UNLESS NOTED OTHERWISE	
017823	OPERATION AND MAINTENANCE DATA
DIVISION 02	EXISTING CONDITIONS
DIVISION 03	CONCRETE
DIVISION 04	MASONRY
DIVISION 05	METALS
057000	DECORATIVE METAL
DIVISION 06	WOOD, PLASTICS, AND COMPOSITS
061000	MISCELLANEOUS ROUGH CARPENTRY
064100	ARCHITECTURAL CASEWORK
061426	FLUSH WOOD PANELING
064600	WOOD TRIM
DIVISION 07	THERMAL AND MOISTURE PROTECTION
078413	PENETRATION FIRE STOPPING
078446.1	FIRE RESISTIVE JOINT SYSTEMS
079200	INTERIOR JOINT SEALANTS
DIVISION 08	OPENINGS
081113	HOLLOW METAL DOORS AND FRAMES
081416	FLUSH WOOD DOORS
083100	ACCESS DOORS AND PANELS
087100	DOOR HARDWARE
088000	INTERIOR GLAZING

088300	MIRRORS
083400	SPECIAL FUNCTION DOORS
DIVISION 09	FINISHES
092123	GYPSUM BOARD SHAFT WALL ASSEMBLIES
092216	NON-STRUCTURAL METAL FRAMING
092713	GLASS FIBER REINFORCED GYPSUM ASSEMBLIES
092900	GYPSUM BOARD
093013	TILING
095113	ACOUSTICAL PANEL CEILINGS
095133	ACOUSTICAL METAL PAN CEILINGS
096513	RESILIENT BASE AND ACCESSORIES
096519	RESILIENT TILE FLOORING
096546	STATIC-CONTROL RESILIENT FLOORING
096813	TILE CARPETING
097200	WALL COVERINGS
099123	INTERIOR PAINTING AND COATING
099600	INTERIOR HIGH PERFORMANCE COATINGS
DIVISION 10	EQUIPMENT
102113	TOILET COMPARTMENTS
102600	WALL PROTECTION
102613	CORNER GUARDS
102800	TOILET ACCESSORIES
104413	FIRE EXTINGUISHER CABINETS
104416	FIRE EXTINGUISHERS
105613	METAL STORAGE SHELVING
DIVISION 11	
113100	RESIDENTIAL APPLIANCES
114313	LABORATORY FUME HOODS
DIVISION 12	FURNISHINGS
123553	LABORATORY CASEWORK
DIVISION 13	SPECIAL CONSTRUCTION
132600	ENVIRONMENTAL CONTROL ROOMS
DIVISION 14	CONVEYING EQUIPMENT
DIVISION 20	RESERVED

200000	COMMON MECHANICAL/ELECTRICAL REQUIREMENTS
DIVISION 21	FIRE SUPPRESSION
210500	COMMON WORK RESULTS FOR FIRE SUPPRESSION
210553	IDENTIFICATION FOR FIRE SUPPRESSION PIPING AND EQUIPMENT
211300	WATER BASED FIRE SUPPRESSION SYSTEMS
212200	CLEAN AGENT FIRE EXTINGUISHING SYSTEMS
DIVISION 22	PLUMBING
220500	COMMON WORK RESULTS FOR PLUMBING
220513	COMMON MOTOR REQUIREMENTS FOR PLUMBING EQUIPMENT
220514	COMMON CONTROL PANEL REQUIREMENTS
220516	EXPANSION FITTINGS AND LOOPS FOR PLUMBING PIPING
220517	SLEEVES AND SLEEVE SEALS FOR PLUMBING PIPING
220518	ESCUTCHEONS FOR PLUMBING PIPING
220519	METERS AND GAGES FOR PLUMBING PIPING
220529	HANGERS AND SUPPORTS FOR PLUMBING PIPING AND EQUIPMENT
220549	VIBRATION CONTROLS
220553	IDENTIFICATION FOR PLUMBING PIPING AND EQUIPMENT
220716	PLUMBING EQUIPMENT INSULATION
220719	PLUMBING PIPING INSULATION
220800	COMMISSIONING OF PLUMBING
221110	COMMON PLUMBING PIPING
221119	WATER PIPING SPECIALTIES
221123	WATER PUMPS
221124	WATER PACKAGED BOOSTER PUMPS
221319	SANITARY WASTE PIPING SPECIALTIES
221329	SANITARY SEWERAGE PUMPS
221413	FACILITY STORM DRAINAGE PIPING
221423	STORM DRAINAGE PIPING SPECIALTIES
223400	FUEL-FIRED, WATER HEATERS
224200	COMMERCIAL PLUMBING FIXTURES
224500	EMERGENCY PLUMBING FIXTURES
224700	WATER COOLERS
226113	PIPING FOR LABORATORY FACILITIES
226115	LABORATORY GAS MANIFOLDS
226219	VACUUM EQUIPMENT FOR LABORATORY FACILITIES

226701	PURIFIED WATER PIPING - THERMOPLASTICS
226703	HIGH PURITY GAS PIPING
226722	PROCESSED WATER SYSTEMS FOR LABORATORY AND HEALTHCARE FACILITIES
DIVISION 23	HEATING, VENTILATING, AND AIR CONDITIONING (HVAC)
230500	COMMON WORK RESULTS FOR HVAC
230513	COMMON MOTOR REQUIREMENTS FOR HVAC EQUIPMENT
230516	EXPANSION FITTINGS AND LOOPS FOR HVAC PIPING
230517	SLEEVES AND SLEEVE SEALS FOR HVAC PIPING
230518	ESCUTCHEONS FOR HVAC PIPING
230519	METERS AND GAGES FOR HVAC PIPING
230523	GENERAL-DUTY VALVES FOR HVAC PIPING
230529	HANGERS AND SUPPORTS FOR HVAC PIPING AND EQUIPMENT
230533	HEAT TRACING FOR HVAC PIPING
230548	VIBRATION AND SEISMIC CONTROLS FOR HVAC
230553	IDENTIFICATION FOR HVAC PIPING AND EQUIPMENT
230593	TESTING, ADJUSTING, AND BALANCING FOR HVAC
230700	HVAC INSULATION
230900	DIRECT DIGITAL CONTROL (DDC) SYSTEM FOR HVAC
230901	LABORATORY AIR FLOW CONTROL SYSTEM
232113	HYDRONIC PIPING
232116	HYDRONIC PIPING SPECIALTIES
232123	HYDRONIC PUMPS
232213	STEAM AND CONDENSATE HEATING PIPING
232216	STEAM AND CONDENSATE PIPING SPECIALTIES
232500	HVAC WATER TREATMENT
233113	AIR DISTRIBUTION SYSTEMS-METAL DUCTS
233413	AXIAL HVAC FANS
233416	CENTRIFUGAL HVAC FANS
233423	HVAC POWER VENTILATORS
233433	AIR CURTAINS
233600	AIR TERMINAL UNITS
234100	PARTICULATE AIR FILTRATION
235100	BREECHINGS, CHIMNEYS, AND STACKS
235216	CONDENSING BOILERS
235700	HEAT EXCHANGERS FOR HVAC
238126	SPLIT-SYSTEM AIR-CONDITIONERS
238216	AIR COILS
238239.13	CABINET UNIT HEATERS
238413	EVAPORATIVE STEAM HUMIDIFICATION SYSTEM
DIVISION 26	ELECTRICAL

260500	COMMON WORK RESULTS FOR ELECTRICAL
260513	MEDIUM-VOLTAGE CABLES
260519	LOW-VOLTAGE CONDUCTORS AND CABLES
260526	GROUNDING AND BONDING FOR ELECTRICAL SYSTEMS
260529	HANGERS AND SUPPORTS FOR ELECTRICAL SYSTEMS
260533	RACEWAY AND BOXES FOR ELECTRICAL SYSTEMS
260543	UNDERGROUND ELECTRICAL PATHWAYS
260553	IDENTIFICATION FOR ELECTRICAL SYSTEMS
260573	ELECTRICAL STUDIES AND SETTINGS
260923	LIGHTING CONTROL DEVICES
260943	DIGITAL ROOM CONTROLLER (DRC) BASED LIGHTING CONTROLS
261200	MEDIUM-VOLTAGE PAD-MOUNTED TRANSFORMERS
262200	LOW-VOLTAGE TRANSFORMERS
262300	LOW-VOLTAGE SWITCHGEAR
262413	SWITCHBOARDS
262416	PANELBOARDS
262726	WIRING DEVICES
262813	FUSES
262816	ENCLOSED SWITCHES AND CIRCUIT BREAKERS
262913	ENCLOSED MOTOR CONTROLLERS
262923	VARIABLE FREQUENCY CONTROLLERS
263150	UNINTERRUPTIBLE POWER SUPPLY
263213	ENGINE GENERATOR
263600	TRANSFER SWITCHES
264113	LIGHTNING PROTECTION
265100	INTERIOR LIGHTING
DIVISION 27	COMMUNICATIONS
271000	STRUCTURED CABLING
274100	AUDIOVISUAL SYSTEMS
DIVISION 28	ELECTRICAL SAFETY AND SECURITY
281000	ELECTRONIC SECURITY SYSTEMS
283105	FIRE ALARM CABLES AND PATHWAYS
283111	DIGITAL, ADDRESSABLE FIRE ALARM SYSTEM

TI PLANS
PREPARED BY L2P
DATED APRIL 26, 2022

CIVIL	
C-01	COVER SHEET
C-02	SITE DEMOLITION & EROSION & SEDIMENT CONTROL PLAN
C-03	LINES AND GRADES PLAN
C-04	SITE CONSTRUCTION DETAILS
C-05	SITE CONSTRUCTION DETAILS
ARCHITECTURAL	
CS	COVER SHEET
A001	DRAWING LIST
A002	GENERAL NOTES / ABBREVIATIONS
A003	ACCESSIBLE MOUNTING HEIGHTS & CLEARANCES
A011	CODE ANALYSIS & EGRESS PLAN - FIRST FLOOR
A012	CODE ANALYSIS & EGRESS PLANS - SECOND FLOOR
A013	CONTROL AREAS
A111	PARTITION PLAN - FIRST FLOOR - OVERALL
A111.1	PARTITION PLAN - FIRST FLOOR - WEST
A111.2	PARTITION PLAN - FIRST FLOOR - EAST
A112	PARTITION PLAN - SECOND FLOOR - OVERALL
A112.1	PARTITION PLAN - SECOND FLOOR - EAST
A121	REFLECTED CEILING PLAN - FIRST FLOOR – OVERALL
A121.1	REFLECTED CEILING PLAN - FIRST FLOOR - WEST
A121.2	REFLECTED CEILING PLAN - FIRST FLOOR EAST
A122	REFLECTED CEILING - SECOND FLOOR - OVERALL
A122.1	REFLECTED CEILING PLAN - SECOND FLOOR - EAST
A131.1	EQUIPMENT PLAN - FIRST FLOOR - WEST
A131.2	EQUIPMENT PLAN - FIRST FLOOR - EAST
A132	EQUIPMENT PLAN - SECOND FLOOR - EAST

A141.1	FINISH PLAN - FIRST FLOOR - WEST
A141.2	FINISH PLAN - FIRST FLOOR - EAST
A142	FINISH PLAN - SECOND FLOOR
A500	PARTITION TYPES & DETAILS
A510	DOOR & FRAME TYPES & DETAILS
A520	CEILING DETAILS
A700	ENLARGED LAB PLAN
A701	ENLARGED LAB PLAN
A702	ENLARGED LAB PLAN
A703	ENLARGED LAB PLAN
A704	ENLARGED LAB PLAN
A705	ENLARGED PLANS
A710	LAB CASEWORK ELEVATIONS
A711	LAB CASEWORK ELEVATIONS
A712	LAB CASEWORK ELEVATIONS
A713	LAB CASEWORK ELEVATIONS
A714	LAB CASEWORK ELEVATIONS
A715	LAB CASEWORK ELEVATIONS
A716	LAB CASEWORK ELEVATIONS
A717	LAB CASEWORK ELEVATIONS
A718	LAB CASEWORK ELEVATIONS
A731	FUME HOOD ELEVATIONS AND DETAILS
A732	LABORATORY DETAILS
A733	LABORATORY DETAILS
A750	ENLARGED PLAN AND VIEWS - TOILET ROOMS
A751	ENLARGED PLANS AND VIEWS - TOILET ROOMS
A752	ENLARGED PLAN AND VIEWS - TOILET ROOMS
A800	INTERIOR ELEVATIONS - FEATURES
A810	INTERIOR ELEVATIONS - GLASS & OFFICE FRONTS
A811	INTERIOR ELEVATIONS - GLASS AND OFFICE FRONTS
A812	INTERIOR ELEVATIONS - GLASS AND OFFICE FRONTS
A820	INTERIOR ELEVATIONS - MILLWORK - FIRST FLOOR
A822	INTERIOR ELEVATIONS - MILLWORK - SECOND FLOOR
A850	INTERIOR DETAILS - MILLWORK
A860	INTERIOR DETAILS - FINISHES
A900	SCHEDULES - DOORS & FRAMES
A920	SCHEDULES - FINISH SPECIFICATIONS
STRUCTURAL	
S001TF	COVER SHEET
S002TF	GENERAL NOTES
S003TF	SPECIAL INSPECTIONS & PROJECT SCHEDULES
S101TF	FOUNDATION PLAN

S102TF	FLOOR FRAMING PLAN
S103TF	ROOF FRAMING PLAN
S104TF	ENLARGED PLAN
S105TF	ENLARGED PLANS
S501TF	TYPICAL FOUNDATION DETAILS
S511TF	TYPICAL FRAMING DETAILS
S512TF	FRAMING SECTIONS & DETAILS
MECHANICAL	
H-001	HVAC COVER SHEET
H-210	HVAC BASEMENT PLAN - DUCTWORK & PIPING
H-211.1	HVAC FIRST FLOOR - WEST - DUCTWORK
H-211.2	HVAC FIRST FLOOR - EAST - DUCTWORK
H-212.2	HVAC SECOND FLOOR - EAST - DUCTWORK
H-213	HVAC OVERALL SITE EQUIPMENT PLAN
H-213.1	HVAC ROOF - WEST - DUCTWORK & PIPING
H-213.2	HVAC ROOF - EAST - DUCTWORK & PIPING
H-311.1	HVAC FIRST FLOOR - WEST - PIPING
H-311.2	HVAC FIRST FLOOR - EAST - PIPING
H-312.2	HVAC SECOND FLOOR - EAST - PIPING
H-401	HVAC BUILDING AIRFLOW DIAGRAMS
H-402	HVAC BUILDING AIRFLOW DIAGRAMS
H-403	HVAC HYDRONIC FLOW DIAGRAMS
H-404	HVAC HEAT RECOVERY FLOW DIAGRAM
H-501	HVAC DETAILS 1
H-502	HVAC DETAILS 2
H-503	HVAC DETAILS 3
H-504	HVAC DETAILS 4
H-601	HVAC SCHEDULES 1
H-602	HVAC SCHEDULES 2
H-603	HVAC SCHEDULES 3
H-701	HVAC CONTROLS 1
H-702	HVAC CONTROLS 2
H-703	HVAC CONTROLS 3
H-704	HVAC CONTROLS 4
H-801	HVAC 1/4" SCALE PLAN - BIOLOGY 1 DUCTWORK
H-802	HVAC 1/4" SCALE PLAN - BIOLOGY 2 DUCTWORK
H-803	HVAC 1/4" SCALE PLAN - CHEMISTRY 1 DUCTWORK
H-804	HVAC 1/4" SCALE PLAN - CHEMISTRY 2 DUCTWORK
H-805	HVAC 1/4" SCALE PLAN - LOADING/STORAGE DUCTWORK
H-901	HVAC BIOLOGY LABORATORY AIR FLOW DIAGRAM 1
H-902	HVAC BIOLOGY LABORATORY AIR FLOW DIAGRAM 2

H-903	HVAC CHEMISTRY LABORATORY AIR FLOW DIAGRAM 1
H-904	HVAC CHEMISTRY LABORATORY AIR FLOW DIAGRAM 2
H-905	HVAC CHEMISTRY LABORATORY AIR FLOW DIAGRAM 3
PLUMBING	
P-001	PLUMBING LEGEND AND GENERAL NOTES
P-100	PLUMBING SITE PLAN
P-200	PLUMBING - UNDERGROUND - OVERALL
P-200.2	PLUMBING - BASEMENT PLAN - EAST
P-211	PLUMBING - FIRST FLOOR - OVERALL
P-211.1	PLUMBING - FIRST FLOOR - WEST
P-211.2	PLUMBING - FIRST FLOOR - EAST
P-212	PLUMBING - SECOND FLOOR - OVERALL
P-212.1	PLUMBING - SECOND FLOOR - WEST
P-212.2	PLUMBING - SECOND FLOOR - EAST
P-213	PLUMBING - ROOF PLAN - OVERALL
P-221	PLUMBING - FIRST FLOOR (GAS) - OVERALL
P-231	PLUMBING - FIRST FLOOR (PRESSURE) - OVERALL
P-301	PLUMBING PART PLANS (PRESSURE)
P-302	PLUMBING PART PLANS (PRESSURE)
P-303	PLUMBING PART PLANS
P-304	PLUMBING PART PLANS
P-501	PLUMBING DETAILS
P-502	PLUMBING DETAILS
P-503	PLUMBING DETAILS
P-504	PLUMBING DETAILS
P-505	PLUMBING DETAILS
P-506	PLUMBING DETAILS
P-601	PLUMBING SCHEDULES
P-602	PLUMBING SCHEDULES
P-701	PLUMBING RISER DIAGRAMS
P-702	PLUMBING RISER DIAGRAMS
P-703	PLUMBING RISER DIAGRAMS
P-704	PLUMBING RISER DIAGRAMS
P-705	PLUMBING RISER DIAGRAMS
P-706	PLUMBING RISER DIAGRAMS
P-707	PLUMBING RISER DIAGRAMS
P-708	PLUMBING RISER DIAGRAMS
P-709	PLUMBING RISER DIAGRAMS
P-710	PLUMBING RISER DIAGRAMS
P-711	PLUMBING RISER DIAGRAMS
P-712	PLUMBING RISER DIAGRAMS
P-713	PLUMBING RISER DIAGRAMS

P-714	PLUMBING RISER DIAGRAMS
P-715	PLUMBING RISER DIAGRAMS
P-716	PLUMBING RISER DIAGRAMS
P-717	PLUMBING RISER DIAGRAMS
P-718	PLUMBING RISER DIAGRAMS
P-800	PLUMBING ENLARGED BIOLOGY 1 (GAS)
P-801	PLUMBIGN ENLARGED BIOLOGY 2 (GAS)
P-802	PLUMBING ENLARGED CHEMISTRY 1 (GAS)
P-803	PLUMBING ENLARGED CHEMISTRY 2 (GAS)
P-900	ENLARGED BIOLOGY 1 (PRESSURE)
P-901	ENLARGED BIOLOGY 2 (PRESSURE)
P-902	ENLARGED CHEMISTRY 1 (PRESSURE)
P-903	ENLARGED CHEMISTRY 2 (PRESSURE)
FIRE PROTECTION	
FP-001	FIRE PROTECTION - SYMBOLS & ABBREVIATIONS
FP-002	FIRE PROTECTION - NOTES & DESIGN CRITERIA
FP-210	FIRE PROTECTION - BASEMENT
FP-211.1	FIRE PROTECTION - FIRST FLOOR - WEST
FP-211.2	FIRE PROTECTION - FIRST FLOOR - EAST
FP-212.2	FIRE PROTECTION - SECOND FLOOR - EAST
FP-701	FIRE PROTECTION - DETAILS
ELECTRICAL	
E-001	ELECTRICAL LEGEND SHEET 1
E-002	ELECTRICAL LEGEND SHEET 2
E-003	LIGHTING FIXTURE SCHEDULE
E-004	LIGHTING CONTROL SHEET
E-011	ELECTRICAL GENERAL DETAIL SHEET
E-100	ELECTRICAL SITE PLAN
E-101	ELECTRICAL SITE DETAILS
E-210	ELEC POWER - BASEMENT - EAST
E-211.1	ELEC POWER - FIRST FLOOR - WEST
E-211.2	ELEC POWER - FIRST FLOOR - EAST
E-212.2	ELEC POWER - SECOND FLOOR - EAST
E-213.1	ELEC POWER - ROOF PLAN - WEST
E-213.2	ELEC POWER - ROOF PLAN - EAST
E-310	ELEC LIGHTING - BASEMENT - EAST
E-311.1	ELEC LIGHTING - FIRST FLOOR - WEST
E-311.2	ELEC LIGHTING - FIRST FLOOR - EAST
E-312.1	ELEC LIGHTING - SECOND FLOOR - WEST
E-312.2	ELEC LIGHTING - SECOND FLOOR - EAST
E-401	POWER DISTRIBUTION SINGLE-LINE DIAGRAM
E-501	ELECTRICAL PART PLANS
E-701	ELECTRICAL GROUNDING PLAN
E-702	LIGHTNING PROTECTION SYSTEM ROOF PLAN

E-703	GROUNDING AND LIGHTNING PROTECTION DETAILS
E-800	ELEC POWER - ENLARGED BIOLOGY 1
E-801	ELEC POWER - ENLARGED BIOLOGY 2
E-802	ELEC POWER - ENLARGED CHEMISTRY 1
E-803	ELEC POWER - ENLARGED CHEMISTRY 2
E-901	ELECTRICAL PANEL SCHEDULES
E-902	ELECTRICAL PANEL SCHEDULES
E-903	ELECTRICAL PANEL SCHEDULES
E-904	ELECTRICAL PANEL SCHEDULES
E-905	ELECTRICAL PANEL SCHEDULES
E-906	ELECTRICAL PANEL SCHEDULES
E-907	ELECTRICAL PANEL SCHEDULES
FIRE ALARM	
FA-001	FIRE ALARM - SYMBOLS & ABBREVIATIONS
FA-002	FIRE ALARM - NOTES & DESIGN CRITERIA
FA-210	FIRE ALARM - BASEMENT
FA-211.1	FIRE ALARM - FIRST FLOOR - WEST
FA-211.2	FIRE ALARM - FIRST FLOOR - EAST
FA-212.2	FIRE ALARM - SECOND FLOOR - EAST
FA-701	FIRE ALARM – DETAILS
AV	
AV-001	TECH AV – LEGEND
AV-211	TECH AV - FIRST FLOOR - OVERALL
AV-211.1	TECH AV - FIRST FLOOR - WEST
AV-211.2	TECH AV - FIRST FLOOR - EAST
AV-212	TECH AV - SECOND FLOOR - OVERALL
AV-212.2	TECH AV - SECOND FLOOR - EAST
AV-221.1	TECH AV - FIRST FLOOR - WEST - ROUGH-IN
AV-221.2	TECH AV - FIRST FLOOR - EAST - ROUGH-IN
AV-222.2	TECH AV - SECOND FLOOR - EAST - ROUGH-IN
AV-501	TECH AV – DETAILS
AV-502	TECH AV – DETAILS
AV-503	TECH AV – DETAILS
AV-504	TECH AV – DETAILS
AV-700	TECH AV - EQUIPMENT LIST
SECURITY	
SE-001	SECURITY – LEGEND
SE-211	SECURITY - FIRST FLOOR - OVERALL
SE-211.1	SECURITY - FIRST FLOOR - WEST
SE-211.2	SECURITY - FIRST FLOOR - EAST
SE-212	SECURITY - SECOND FLOOR - OVERALL
SE-212.2	SECURITY - SECOND FLOOR - EAST

SE-213	SECURITY - ROOF PLAN - OVERALL
SE-501	SECURITY – DETAILS
SE-502	SECURITY - EQUIPMENT LIST
TELECOMMUNICATIONS	
TC-001	TELECOM – LEGEND
TC-211	TELECOM - FIRST FLOOR - OVERALL
TC-211.1	TELECOM - FIRST FLOOR - WEST
TC-211.2	TELECOM - FIRST FLOOR - EAST
TC-212	TELECOM - SECOND FLOOR - OVERALL
TC-212.2	TELECOM - SECOND FLOOR - EAST
TC-501	TELECOM – DETAILS
TC-502	TELECOM – DETAILS
TC-801	TELECOM - RISER DIAGRAM

EXHIBIT "G-4 REVISED"

REMEDIATION PLAN

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Krishna Vaddi, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Prelude Therapeutics Incorporated;

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 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 and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 14, 2022

By: /s/ Krishna Vaddi
Krishna Vaddi, PhD
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

**CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Laurent Chardonnet, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Prelude Therapeutics Incorporated;

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 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 and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 14, 2022

By: /s/ Laurent Chardonnet
Laurent Chardonnet
Chief Financial Officer
(Principal Accounting and Financial Officer)

Exhibit 32.1

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

I, Krishna Vaddi, Chief Executive Officer of Prelude Therapeutics Incorporated (the "Company"), do hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

(1) the Quarterly Report on Form 10-Q of the Company for the fiscal quarter ended September 30, 2022 (the "Report") 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: November 14, 2022	By:	/s/ Krishna Vaddi
		Krishna Vaddi, PhD *Chief Executive Officer* *(Principal Executive Officer)*

Exhibit 32.2

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

I, Laurent Chardonnet, Chief Financial Officer of Prelude Therapeutics Incorporated (the "Company"), do hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

(1) the Quarterly Report on Form 10-Q of the Company for the fiscal quarter ended September 30, 2022 (the "Report") 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 result of operations of the Company.

Date: November 14, 2022

By: /s/ Laurent Chardonnet
Laurent Chardonnet
Chief Financial Officer
(Principal Accounting and Finance Officer)