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 June 30, 2019

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: 001-38653

Principia Biopharma Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**26-3487603**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
220 East Grand Avenue South San Francisco, California	**94080**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (650) 416-7700

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 ☒

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	**PRNB**	**The Nasdaq Global Select Market**

As of July 31, 2019, the registrant had 23,970,822 shares of common stock, $0.0001 par value per share, outstanding.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report contains forward-looking statements that involve risks, uncertainties and assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. The statements contained in this Quarterly Report that are not purely historical are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Forward-looking statements are often identified by the use of words such as, but not limited to, "anticipate," "believe," "can," "continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "project," "seek," "should," "target," "will," "would" and similar expressions or variations intended to identify forward-looking statements. These statements are based on the beliefs and assumptions of our management, which are in turn based on information currently available to management. Such forward-looking statements are subject to risks, uncertainties and other important factors that could cause actual results and the timing of certain events to differ materially from future results expressed or implied by such forward-looking statements. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this Quarterly Report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section entitled "*Risk Factors*" included under Part II, Item 1A below. Furthermore, such forward-looking statements speak only as of the date of this report. Except as required by law, we undertake no obligation to update any forward-looking statements to reflect events or circumstances after the date of such statements.

PART I—FINANCIAL INFORMATION

Item 1. Financial Statements (Unaudited)

PRINCIPIA BIOPHARMA INC.
Condensed Consolidated Balance Sheets
(Unaudited)
(In thousands, except share and per share amounts)

	June 30, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 41,073	$ 34,489
Short-term marketable securities	128,492	142,436
Restricted cash	—	82
Prepaid expenses and other current assets	2,157	3,765
Total current assets	171,722	180,772
Property and equipment, net	10,598	1,666
Long-term restricted cash	567	567
Long-term marketable securities	8,972	3,712
Other long-term assets	480	8,804
Total assets	$ 192,339	$ 195,521
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 4,052	$ 4,439
Deferred rent, current portion	1,132	344
Deferred revenue	—	5,616
Accrued research and development liabilities	4,823	1,520
Accrued other liabilities	591	649
Accrued compensation	2,850	4,312
Total current liabilities	13,448	16,880
Long-term deferred rent	8,213	8,781
Commitments and contingencies (Note 7)		
Stockholders' equity (deficit)		
Common stock, $0.0001 par value, 500,000,000 authorized at June 30, 2019 and December 31, 2018; 23,966,418 and 23,865,451 shares issued and outstanding at June 30, 2019 and December 31, 2018, respectively	2	2
Additional paid-in-capital	309,088	302,393
Accumulated other comprehensive income (loss)	111	(128)
Accumulated deficit	(138,523)	(132,407)
Total stockholders' equity	170,678	169,860
Total liabilities and stockholders’ equity	$ 192,339	$ 195,521

See accompanying notes.

PRINCIPIA BIOPHARMA INC.
Condensed Consolidated Statements of Operations
(Unaudited)
(In thousands, except share and per share amounts)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Revenue	$ 30,000	$ 12,987	$ 35,160	$ 24,436
Operating expenses:				
Research and development	18,718	8,894	34,241	17,655
General and administrative	5,233	2,222	9,740	4,378
Total operating expenses	23,951	11,116	43,981	22,033
Income (loss) from operations	6,049	1,871	(8,821)	2,403
Other income (expense), net	(42)	(186)	(41)	(523)
Interest income	1,108	112	2,290	227
Net income (loss)	$ 7,115	$ 1,797	$ (6,572)	$ 2,107
Net income (loss) attributable to common stockholders	$ 7,115	$ —	$ (6,572)	$ —
Net income (loss) per share attributable to common stockholders				
Basic	$ 0.30	$ —	$ (0.28)	$ —
Diluted	$ 0.28	$ —	$ (0.28)	$ —
Weighted-average shares used to calculate net income (loss) per share attributable to common stockholders				
Basic	23,927,172	681,616	23,896,788	656,129
Diluted	25,792,101	1,412,928	23,896,788	1,508,584

See accompanying notes.

PRINCIPIA BIOPHARMA INC.
Condensed Consolidated Statements of Comprehensive Income (Loss)
(Unaudited)
(In thousands)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Net income (loss)	$ 7,115	$ 1,797	$ (6,572)	$ 2,107
Other comprehensive income (loss):				
Net unrealized gain on available-for-sale securities	90	—	239	—
Comprehensive income (loss)	$ 7,205	$ 1,797	$ (6,333)	$ 2,107

See accompanying notes.

PRINCIPIA BIOPHARMA INC.
Condensed Consolidated Statements of Changes in Convertible Preferred Stock and Stockholders' Equity (Deficit)
(Unaudited)
(In thousands, except share amounts)

	Convertible Preferred Stock		Common Stock		Additional	Accumulated Other		Total Stockholders'
	Number of Shares	Amount	Number of Shares	$0.0001 Par Value	Paid-In Capital	Comprehensive Income (Loss)	Accumulated Deficit	Equity (Deficit)
Balance at December 31, 2018	—	$ —	23,865,451	$ 2	$ 302,393	$ (128)	$ (132,407)	$ 169,860
Stock-based compensation expense	—	—	—	—	2,205	—	—	2,205
Exercise of stock options and vesting of early exercise shares	—	—	1,230	—	7	—	—	7
Unrealized gain on available-for-sale securities	—	—	—	—	—	149	—	149
Cumulative-effect adjustment from adoption of ASC 606 accounting standard on revenue recognition	—	—	—	—	—	—	456	456
Net loss	—	—	—	—	—	—	(13,687)	(13,687)
Balance at March 31, 2019	—	$ —	23,866,681	$ 2	$ 304,605	$ 21	$ (145,638)	$ 158,990
Stock-based compensation expense	—	—	—	—	3,476	—	—	3,476
Exercise of stock options and vesting of early exercise shares	—	—	20,057	—	135	—	—	135
Issuance of common stock upon exercise of warrants	—	—	20,860	—	—	—	—	—
Issuance of shares under the Employee Stock Purchase Plan	—	—	58,820	—	872	—	—	872
Unrealized gain on available-for-sale securities	—	—	—	—	—	90	—	90
Net income	—	—	—	—	—	—	7,115	7,115
Balance at June 30, 2019	—	$ —	23,966,418	$ 2	$ 309,088	$ 111	$ (138,523)	$ 170,678

	Convertible Preferred Stock		Common Stock		Additional	Accumulated Other		Total Stockholders'
	Number of Shares	Amount	Number of Shares	$0.0001 Par Value	Paid-In Capital	Comprehensive Income (Loss)	Accumulated Deficit	Equity (Deficit)
Balance at December 31, 2017	12,285,434	$ 128,531	626,613	$ 1	$ 7,201	$ (90)	$ (150,574)	$ (143,462)
Stock-based compensation expense	—	—	—	—	366	—	—	366
Exercise of stock options and vesting of early exercise shares	—	—	32,169	—	126	—	—	126
Net income	—	—	—	—	—	—	310	310
Balance at March 31, 2018	12,285,434	$ 128,531	658,782	$ 1	$ 7,693	$ (90)	$ (150,264)	$ (142,660)
Stock-based compensation expense	—	—	—	—	372	—	—	372
Exercise of stock options and vesting of early exercise shares	—	—	59,226	—	185	—	—	185
Net income	—	—	—	—	—	—	1,797	1,797
Balance at June 30, 2018	12,285,434	$ 128,531	718,008	$ 1	$ 8,250	$ (90)	$ (148,467)	$ (140,306)

See accompanying notes.

PRINCIPIA BIOPHARMA INC.
Condensed Consolidated Statements of Cash Flows
(Unaudited)
(In thousands)

	Six Months Ended June 30,	
	2019	**2018**
Operating activities:		
Net income (loss)	$ (6,572)	$ 2,107
Adjustments to reconcile net income (loss) to net cash used in operating activities:		
Change in fair value of convertible preferred stock warrant liability	—	509
Amortization of discount on marketable securities	(962)	—
Depreciation	835	107
Stock-based compensation	5,681	738
Deferred rent	220	—
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	1,608	(9,573)
Deferred revenue	(5,160)	(14,436)
Accounts payable	(52)	(160)
Accrued liabilities	1,918	(1,013)
Net cash used in operating activities	(2,484)	(21,721)
Investing activities:		
Purchases of property and equipment	(1,913)	(368)
Maturities of marketable securities	103,535	—
Purchases of marketable securities	(93,650)	(8,485)
Net cash provided by (used in) investing activities	7,972	(8,853)
Financing activities:		
Proceeds from issuances of common stock upon exercise of options and participation in employee stock purchase plan	1,014	311
Deferred IPO costs	—	(385)
Net cash provided by (used in) financing activities	1,014	(74)
Net increase (decrease) in cash, cash equivalents and restricted cash	6,502	(30,648)
Cash, cash equivalents and restricted cash at beginning of period	35,138	41,236
Cash, cash equivalents and restricted cash, at end of period	$ 41,640	$ 10,588
Supplemental disclosures of cash flow information		
Non cash tenant improvement allowance used for leasehold improvements	8,324	—
Purchases of property and equipment accrued but not yet paid	172	15
Deferred IPO costs accrued but not yet paid	—	886

See accompanying notes.

1. Organization

Description of Business

We, Principia Biopharma Inc. ("Principia"), are a late-stage biopharmaceutical company focused on developing novel therapies for immunology and oncology. We were incorporated on October 6, 2008, began operations in February 2011, and are headquartered in South San Francisco, California.

2. Significant Accounting Policies

Basis of Presentation

The accompanying interim condensed consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America ("U.S. GAAP") and include the accounts of Principia and our wholly-owned Australian subsidiary. All intercompany accounts, transactions and balances have been eliminated. Certain information and note disclosures normally included in the financial statements prepared in accordance with U.S. GAAP have been condensed or omitted pursuant to the applicable rules and regulations of the Securities and Exchange Commission ("SEC").

These interim condensed consolidated financial statements and related disclosures are unaudited, have been prepared on the same basis as the annual consolidated financial statements and, in the opinion of management, reflect all adjustments of a normal and recurring nature that are necessary for the fair presentation of our financial position and results of operations for the periods presented. The condensed consolidated balance sheets as of December 31, 2018 included herein were derived from audited consolidated financial statements as of that date. This quarterly report should be read in conjunction with our audited consolidated financial statements included in our Annual Report on Form 10-K filed with the SEC on March 19, 2019 ("2018 Annual Report").

Use of Estimates

The preparation of our financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, as well as related disclosure of contingent assets and liabilities. Significant estimates include amounts to determine the fair value of common stock-based awards, warrants, and other issuances, embedded derivatives, accruals for research and development costs and uncertain tax positions, and the estimated periods of performance used in the determination of collaboration revenues. We base our estimates on historical experience and on various other market specific and relevant assumptions that our management believes to be reasonable under the circumstances. Actual results could differ materially from our estimates.

Concentration of Credit Risk and Other Risks and Uncertainties

Financial instruments that potentially subject us to a significant concentration of credit risk consist primarily of cash, cash equivalents and marketable securities. The majority of our cash and cash equivalents is maintained with one financial institution in the United States. Deposits with this financial institution have exceeded and will continue to exceed federally insured limits. We have not experienced any losses on our cash deposits. Additionally, we have established guidelines regarding the diversification of our investments in approved instruments, their credit quality ratings and maturities. The guidelines are designed to preserve principal balances and provide liquidity. Cash, cash equivalents and marketable securities totaled $178.5 million and $180.6 million at June 30, 2019 and December 31, 2018, respectively.

We are subject to a number of risks similar to other early-stage biopharmaceutical companies, including, but not limited to, the need to obtain adequate additional funding, possible failure of current or future preclinical studies or clinical trials, our reliance on third parties or partners to conduct our clinical trials, the need to obtain regulatory and marketing approvals for our drug candidates or to rely on partners to do so, competitors developing new technological innovations, the need to successfully commercialize and gain market acceptance of our drug candidates, our right to develop and commercialize our drug candidates pursuant to the terms and conditions of the licenses granted to us, protection of proprietary technology, the ability to make or collect milestone, royalty or other payments due, or due to us, under any license or collaboration agreements, and the need to secure and maintain adequate manufacturing arrangements with third parties. If we do not successfully commercialize or partner any of our drug candidates, we will be unable to generate product revenue or achieve profitability.

Cash and Cash Equivalents

We consider all highly liquid financial instruments with original maturities of 90 days or less at the date of purchase to be cash equivalents. Cash equivalents are stated at fair value.

Marketable Securities

We carry marketable securities consisting primarily of money market funds, U.S. Treasury securities and obligations of government-sponsored enterprises and corporate bonds and commercial paper. Marketable securities with maturities greater than 90 days at the time of purchase and that mature less than one year from the consolidated balance sheet date are classified as short-term. Marketable securities with a maturity date greater than one year at each balance sheet date are classified as long-term. All of our marketable securities are considered available-for-sale and carried at estimated fair values on the consolidated balance sheets. Unrealized gains or losses are excluded from net income and reported in accumulated other comprehensive income (loss) as a separate component of stockholders' equity on the consolidated balance sheets. Realized gains and losses and declines in fair value judged to be other than temporary, if any, on marketable securities are included in other income (expense), net. The cost of securities sold is based on the specific-identification method. Interest earned on marketable securities is included in interest income. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts and such amortization and accretion are included as a component of interest income.

Restricted Cash

As of June 30, 2019 and December 31, 2018, we had $0.6 million in long-term restricted cash for a lease security deposit. This amount is separated from cash and cash equivalents on the condensed consolidated balance sheets.

Segments

We have one operating segment. Our chief operating decision maker, our President and Chief Executive Officer, manages our operations on a consolidated basis in assessing performance and allocating resources.

Leases

We enter into lease agreements for our laboratory and office facilities. These leases are classified as operating leases. Rent expense is recognized on a straight-line basis over the term of the lease. The difference between rent expense recognized and rental payments is recorded as deferred rent in the condensed consolidated balance sheets.

Lease incentives and allowance provided by our landlord for the construction of leasehold improvements are recorded as lease incentive obligations as the related construction costs are incurred, up to the maximum aggregate allowances. Lease incentive obligations are classified as a component of deferred rent and are amortized on a straight-line basis over the lease term as a reduction of rent expense.

Revenue Recognition

Effective January 1, 2019, we adopted Accounting Standards Codification, or ASC No. 2014-09, Revenue from Contracts with Customers, or ASC 606, using the modified retrospective approach. Under this approach, we recorded a cumulative adjustment to decrease accumulated deficit and deferred revenue by $0.4 million as of the adoption date. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods and services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract, determine those that are performance obligations and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

We have entered into licensing and collaboration agreements that are within the scope of ASC 606. In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under such licensing and collaboration agreements, we

perform the five-step model under ASC 606. As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract.

Licenses of Intellectual Property: If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenues from non-refundable, upfront fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promised goods or services, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, upfront fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Milestone Payments: At the inception of each arrangement that includes development, regulatory or commercial milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant reversal of cumulative revenue would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or that of our licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received or the underlying activity has been completed. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenue in the period of adjustment.

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

The impact of the adoption of Topic 606 on the accompanying condensed consolidated balance sheet as of January 1, 2019 was as follows (in thousands):

	December 31, 2018	Adjustments Due to ASC 606	January 1, 2019
Liabilities			
Deferred revenue	$ 5,616	$ (456)	$ 5,160
Stockholders' Equity			
Accumulated deficit	(132,407)	456	(131,951)

The impact of the adoption of ASC 606 on our unaudited condensed consolidated statement of operations for the three and six months ended June 30, 2019 was as follows (in thousands):

	Three Months Ended June 30, 2019		
	As Reported	Adjustments	Balance without ASC 606 Adoption
Revenue	$ 30,000	$ —	$ 30,000
Income (loss) from operations	6,049	—	6,049
Net income (loss)	7,115	—	7,115
Net income per share, basic	0.30	—	0.30
Net income per share, diluted	0.28	—	0.28

	Six Months Ended June 30, 2019		
	As Reported	Adjustments	Balance without ASC 606 Adoption
Revenue	$ 35,160	$ 456	$ 35,616
Income (loss) from operations	(8,821)	456	(8,365)
Net income (loss)	(6,572)	456	(6,116)
Net loss per share, basic and diluted	(0.28)	0.02	(0.26)

During the three and six months ended June 30, 2019, we did not recognize any revenue from performance obligations satisfied in previous periods.

Convertible Preferred Stock Warrants

In connection with the issuance of certain convertible notes in 2016 and 2017 (the "Notes"), we issued warrants to purchase our capital stock. Freestanding warrants to purchase our convertible preferred stock were recorded as a liability on our condensed consolidated balance sheets because the underlying shares of convertible preferred stock are contingently redeemable, which, therefore, may obligate us to transfer assets to settle those warrants. The warrants are subject to revaluation at each balance sheet date, with changes in fair value recognized as a component of other income, net, on the condensed consolidated statements of operations. During the three and six months ended June 30, 2018, other expense, net, included $0.2 million and $0.5 million, respectively, related to the change in fair value of the preferred stock warrant liability.

Upon the completion of our IPO in September 2018, all of our convertible preferred stock warrants were converted into warrants to purchase shares of common stock. We re-valued the convertible preferred stock warrants upon completion of our IPO and reclassified the estimated fair value of the warrants to additional paid in capital.

Comprehensive Income (Loss)

Comprehensive income (loss) is defined as the change in stockholders' equity (deficit) of a business enterprise during a period, resulting from transactions from non-owner sources, and consists primarily of unrealized gains or losses related to our available-for-sale marketable securities, which are carried at estimated fair values on the consolidated balance sheets.

Net Income (Loss) per Share

Basic net income (loss) per share attributable to common stockholders is calculated by dividing the net income (loss) attributable to common stockholders by the weighted-average number of shares of common stock outstanding for the period.

Diluted net income (loss) per share includes the effect of potentially dilutive securities, which include outstanding warrants and stock options if the effect of their inclusion would be dilutive. In periods of net loss, diluted net loss per share is the same as basic net loss per share as the inclusion of potentially dilutive securities in the calculation would be anti-dilutive.

We have issued securities other than common stock that participate in dividends to the extent declared ("Participating Securities"), and therefore utilize the two-class method to calculate net income (loss) per share. These Participating Securities include Series A, Series B-1, Series B-2, Series B-3 and Series C redeemable convertible preferred stock. The two-class method requires a portion of net income (loss) to be allocated to the Participating Securities to determine net income (loss) attributable to common stockholders. Net income (loss) attributable to common stockholders is equal to the net income (loss) less dividends paid on preferred stock with any remaining earnings allocated in accordance with the bylaws between the outstanding common and redeemable convertible preferred stock as of the end of each period. In September 2018, upon our IPO, all shares of convertible preferred stock were converted into equal number shares of common stock.

Recent Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board, or FASB, or other standard setting bodies and adopted by us as of the specified effective date. Unless otherwise discussed, the impact of recently issued standards that are not yet effective will not have a material impact on our condensed consolidated financial statements upon adoption. Under the Jumpstart Our Business Startups Act of 2012, as amended (the "JOBS Act"), we meet the definition of an emerging growth company, and have elected the extended transition period for complying with new or revised accounting standards pursuant to Section 107(b) of the JOBS Act.

Recently Adopted Accounting Standards Updates

In November 2016, the FASB issued accounting standard update ("ASU") 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash*. The ASU requires that the statements of cash flows explain the change during the period in the total of cash, cash equivalents, and amounts generally described as restricted cash or restricted cash equivalents. As a result, amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the consolidated statements of cash flows. The ASU is effective for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years with early adoption is permitted. We early adopted ASU 2016-18 during the fourth quarter of 2018 and the adoption did not have a material impact on our consolidated financial statements and related disclosures.

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers (Topic 606)*, as subsequently amended, which outlines a single comprehensive model for entities to use in accounting for revenue arising from contracts with customers and supersedes most recent current revenue recognition guidance, including industry-specific guidance. The core principle of the revenue model is that an entity recognizes revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services.

Entities have the option of applying either a full retrospective approach to all periods presented, or a modified approach that reflects differences prior to the date of adoption as an adjustment to equity. We adopted ASC No. 2014-09 on January 1, 2019 using the modified retrospective method of transition applied to contracts that were not completed at January 1, 2019. Therefore, comparative information will not be adjusted and the impact of the transition is reflected as an adjustment to the opening accumulated deficit. A completed contract is a contract for which all, or substantially all, of the revenue was recognized in accordance with revenue guidance in effect before the date of initial application. The new revenue recognition standard differs from the previous accounting standard in many respects, such as in the accounting for variable consideration and the measurement of progress toward completion of performance obligations.

Recently Issued Accounting Standards or Updates Not Yet Effective

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*. ASU 2016-02 requires an entity to recognize assets and liabilities arising from a lease for both financing and operating leases. The ASU will also require new qualitative and quantitative disclosures to help investors and other financial statement users better understand the amount, timing, and uncertainty of cash flows arising from leases. In July 2018, the FASB issued ASU No. 2018-11, *Leases (Topic 842)*: Targeted Improvements, permitting another transition method for ASU 2016-02, which allows the transition to the new lease standard by recognizing a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption. We have elected the extended transition period provided by the JOBS Act and accordingly ASU 2016-02 is effective for us for fiscal years beginning after December 15, 2019, and interim periods beginning after December 15, 2020. The ASU is expected to impact our financial statements as we have certain operating lease agreements under which we are the lessee. We are currently evaluating the impact of the adoption of this ASU and anticipate the recognition of additional assets and corresponding liabilities on our balance sheet related to leases.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement*. This ASU eliminates, modifies and adds disclosure requirements for fair value measurements. The amendments in this ASU are effective for fiscal years, and for interim periods within those fiscal years, beginning after December 15, 2019, with early adoption permitted. We are currently evaluating the effects of this ASU on our consolidated financial statements and related disclosures.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments.* The updated accounting guidance requires changes to the recognition of credit losses on financial instruments not accounted for at fair value through net income. The guidance is effective for interim and annual periods beginning after December 15, 2019. The guidance will be applied using a modified retrospective approach with the cumulative effect recognized as an adjustment to retained earnings. A prospective transition approach is required for debt securities that have recognized an other-than-temporary impairment prior to the effective date. We are currently evaluating the effects of this ASU on our consolidated financial statements and related disclosures.

3. Fair Value Measurements

Financial assets and liabilities are recorded at fair value. We determine fair value using the fair value hierarchy, which establishes three levels of inputs that may be used to measure fair value, as follows:

Level 1 inputs include quoted prices in active markets for identical assets or liabilities.

Level 2 inputs include observable inputs other than Level 1 inputs, such as quoted prices for similar assets or liabilities in active markets; quoted prices for identical or similar assets or liabilities in markets that are not active; and other inputs that are observable or can be corroborated by observable market data for substantially the full term of the asset or liability.

Level 3 inputs include unobservable inputs that are supported by little or no market activity and are significant to the fair value of the underlying asset or liability. Such inputs reflect our best estimate of what market participants would use in pricing the asset or liability at the reporting date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. Our assessment of the significance of a particular input to the fair value measurement in its entirety requires our management to make judgments and consider factors specific to the asset or liability.

Assets and liabilities measured at fair value on a recurring basis as of June 30, 2019 and December 31, 2018 were as follows (in thousands):

	June 30, 2019			
	Level 1	Level 2	Level 3	Total
Assets				
Cash equivalents				
Money market funds	$ 27,781	$ —	$ —	$ 27,781
Corporate commercial paper	8,980	—	—	8,980
Short-term marketable securities				
Corporate commercial paper	—	32,042	—	32,042
Corporate debt securities	—	64,438	—	64,438
Government- sponsored enterprise securities	—	32,012	—	32,012
Long-term marketable securities				
Government- sponsored enterprise securities	—	8,972	—	8,972
Total	$ 36,761	$ 137,464	$ —	$ 174,225

	December 31, 2018			
	Level 1	Level 2	Level 3	Total
Assets				
Cash equivalents				
Money market funds	$ 19,861	$ —	$ —	$ 19,861
Corporate commercial paper	—	7,465	—	7,465
Corporate debt securities	—	4,499	—	4,499
Short-term marketable securities				
Corporate commercial paper	—	36,180	—	36,180
Corporate debt securities	—	71,903	—	71,903
Government- sponsored enterprise securities	—	9,906	—	9,906
U.S. Treasury securities	—	24,447	—	24,447
Long-term marketable securities				
Corporate debt securities	—	3,712	—	3,712
Total	$ 19,861	$ 158,112	$ —	$ 177,973

The carrying amounts of accounts payable and accrued liabilities approximate their fair values due to their short-term maturities. Our Level 2 securities are valued using third-party pricing sources. The pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or

indirectly. There were no transfers of assets or liabilities between the fair value measurement levels during the six months ended June 30, 2019 and 2018.

4. Cash Equivalents and Marketable Securities

Cash equivalents and marketable securities consisted of the following as of June 30, 2019 and December 31, 2018 (in thousands):

	June 30, 2019			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash equivalents				
Money market funds	$ 27,781	$ —	$ —	$ 27,781
Corporate commercial paper	8,980	—	—	8,980
Total cash equivalents	36,761	—	—	36,761
Short-term marketable securities				
Corporate commercial paper	31,988	54	—	32,042
Corporate debt securities	64,286	153	(1)	64,438
Government-sponsored enterprise securities	32,006	6	—	32,012
Total short-term marketable securities	128,280	213	(1)	128,492
Long-term marketable securities				
Government-sponsored enterprise securities	8,982	—	(10)	8,972
Total long-term marketable securities	8,982	—	(10)	8,972
Total	$ 174,023	$ 213	$ (11)	$ 174,225

	December 31, 2018			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash equivalents				
Money market funds	$ 19,861	$ —	$ —	$ 19,861
Corporate commercial paper	7,466	—	(1)	7,465
Corporate debt securities	4,499	—	—	4,499
Total cash equivalents	31,826	—	(1)	31,825
Short-term marketable securities				
Corporate commercial paper	36,197	—	(17)	36,180
Corporate debt securities	71,920	8	(25)	71,903
Government-sponsored enterprise securities	9,911	—	(5)	9,906
U.S. Treasury securities	24,451	—	(4)	24,447
Total short-term marketable securities	142,479	8	(51)	142,436
Long-term marketable securities				
Corporate debt securities	3,706	6	—	3,712
Total long-term marketable securities	3,706	6	—	3,712
Total	$ 178,011	$ 14	$ (52)	$ 177,973

All our marketable securities are considered available-for-sale. There were no sales of available-for-sale marketable securities in any of the periods presented. The carrying value of marketable securities that were in unrealized loss positions totaled approximately $14.0 million as of June 30, 2019. We have determined that (i) we do not have the intent to sell any of these investments, and (ii) it is not more likely than not that we will be required to sell any of these investments before recovery of the entire amortized cost basis. We anticipate that we will recover the entire amortized cost basis of such securities and have determined there were no other-than-temporary impairments associated with any of these marketable securities before recovery of the entire amortized cost basis during the six months ended June 30, 2019. At June 30, 2019, the remaining contractual maturities of long-term marketable securities were less than two years.

5. Balance Sheet Components

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the condensed consolidated balance sheets that sum to the total of the amounts shown in the condensed consolidated statements of cash flows (in thousands):

	June 30, 2019	December 31, 2018	June 30, 2018	December 31, 2017
Cash and cash equivalents	$ 41,073	$ 34,489	$ 9,839	$ 41,054
Restricted cash, current	—	82	182	100
Restricted cash, non-current	567	567	567	82
Total	$ 41,640	$ 35,138	$ 10,588	$ 41,236

Property and equipment as of June 30, 2019 and December 31, 2018 consisted of the following (in thousands):

	June 30, 2019	December 31, 2018
Laboratory equipment	$ 1,973	$ 2,500
Computer equipment	289	508
Furniture and Fixtures	1,499	392
Leasehold improvements	8,324	420
	12,085	3,820
Less accumulated depreciation and amortization	(1,487)	(2,154)
Total	$ 10,598	$ 1,666

Prepaid expenses and other current assets as of June 30, 2019 and December 31, 2018 consisted of the following (in thousands):

	June 30, 2019	December 31, 2018
Other accounts receivable	$ 740	$ 2,104
Prepaid expenses	1,417	1,661
Total	$ 2,157	$ 3,765

6. License and Collaboration Agreements

Sanofi

In November 2017, we entered into a strategic collaboration agreement with Sanofi, or the Sanofi Agreement, for an exclusive license to PRN2246/SAR442168 and backup molecules for development in multiple sclerosis ("MS") and other central nervous system ("CNS") diseases. Under the Sanofi Agreement, we have completed the Phase 1 trials and Sanofi is taking on all further development activities. We and Sanofi each have been responsible for certain early development costs, and Sanofi is responsible for all further development and commercialization costs, subject to our Phase 3 option described below.

Sanofi has an exclusive license for PRN2246/SAR442168 and its backups for the CNS field, which includes indications of the central nervous system, retina and ophthalmic nerve. We have agreed not to develop other BTK inhibitors within the CNS field, and Sanofi has agreed not to develop PRN2246/SAR442168 or its backups for any indications outside the CNS field. In the event we cease all development and commercialization of our other BTK inhibitors or unilaterally decide to offer Sanofi a field expansion, Sanofi could expand its field upon a field expansion payment to us as well as potential milestone payments and royalties within the expanded field.

In December 2017, we received a $40.0 million upfront payment from Sanofi. In May 2018, we amended the Sanofi Agreement to include additional activities under the early development plan and to modify the definition of one of the milestone payments. Pursuant to the amendment, we received a $10.0 million payment in July 2018 for the completion of a major part of the Phase 1 trial. In August 2018, we received a $5.0 million payment for the successful completion of preclinical toxicology studies. In November 2018, we received $10.0 million in additional payments from Sanofi for successful development activities of PRN2246/SAR442168 related to the early development plan. In June 2019, we received a $30.0 million milestone payment from Sanofi for the initiation of the Phase 2b clinical trial of PRN2246/SAR442168.

Under the amended Sanofi Agreement, we may receive development, regulatory and commercial milestone payments of up to an aggregate of $765.0 million, as well as royalties up to the mid-teens. We have an option to fund a portion of Phase 3 development costs in return for, at our option, either a profit and loss sharing arrangement within the United States, or an additional worldwide royalty that would result in royalties up to the high-teens. The additional royalty option would only be available if we

develop PRN1008 for major enumerated indications overseen by the Division of Pulmonary, Allergy and Rheumatology Products of the U.S. Food and Drug Administration's (the "FDA") or if we experience a change in control involving certain Sanofi competitors. Royalties are subject to specified reductions and are payable, on a product-by-product and country-by-country basis until the later of the date that all of our patent rights that claim a composition of matter of such product expire in such country, the date of expiration of regulatory exclusivity for such product in such country, or the date that is ten years from the first commercial sale of such product in such country.

We identified the following performance obligations under the Sanofi Agreement: (i) granting a license of rights to PRN2246/SAR442168, (ii) transferring of technology (know-how) related to PRN2246/SAR442168, and (iii) providing research and development services related to our responsibilities under the early development plan. We concluded that the delivered license is not distinct at inception of the arrangement due to our proprietary expertise with respect to the licensed compound and related developmental participation under the agreement, which is required for Sanofi to fully realize the value from the delivered license. Therefore, we combined these performance obligations as one unit of accounting and recognized the $40.0 million upfront payment and an aggregate of $25.0 million milestone payments over the performance period under the Sanofi Agreement, which ended in December 2018.

On January 1, 2019, we adopted ASC 606 using the modified retrospective approach. The transaction price was determined to be $65.0 million, which includes the $40.0 million upfront payment we received from Sanofi in December 2017 and an aggregate of $25.0 million milestone payments received in 2018. All potential future milestones and other payments were considered constrained at the inception of the Sanofi Agreement since the Company could not conclude it is probable that a significant reversal in the amount recognized will not occur. Upon adoption of ASC 606, we also determined that variable considerations related to certain milestones not previously recognized were constrained because they were not probable, due to the inherent uncertainty related to the achievement of these milestones. In May 2019, we achieved a clinical development milestone and Sanofi was obligated to make a $30.0 million milestone payment to us. As the amount due for the clinical development milestone was no longer constrained, we increased the transaction price by $30.0 million from inception through June 30, 2019. As of June 30, 2019, we fully recognized the $30.0 million milestone payment to us as revenue as all performance obligations had been completed. We will re-evaluate the transaction price in each reporting period relating to potential future milestones as uncertain circumstances are resolved or other changes in events occur.

We concluded upon analysis that there is no adjustment necessary in revenue recognized through December 31, 2018 under ASC 606 for the Sanofi Agreement. All deliverables under ASC 605 and all performance obligations under ASC 606 had been completed as of June 30, 2019. For the three and six months ended June 30, 2019, we recognize $30.0 million in revenue, respectively, related to the Sanofi Agreement. For the three and six months ended June 30, 2018, we recognized approximately $11.5 million and $21.4 million in revenue, respectively, related to the Sanofi Agreement.

AbbVie

In June 2017, we entered into a collaboration agreement with AbbVie, or the AbbVie Agreement, to research and develop oral immunoproteasome inhibitors and received an upfront payment of $15.0 million. We identified the following performance obligations under the AbbVie Agreement: (i) granting a license of rights to certain licensed compounds to develop and commercialize oral immunoproteasome inhibitors, (ii) transferring of technology (know-how) related to the oral immunoproteasome inhibitors program, and (iii) providing research and development services during the two-year research period, which can be extended for up to six months. We determined that each of these performance obligations individually is not distinct, rather each one represents a component of a single performance obligation of the contract. Prior to the adoption of ASC 606, we concluded under ASC 605 that the delivered license did not have standalone value at the inception of the arrangement due to our proprietary expertise with respect to the licensed compounds and related ongoing research participation under the AbbVie Agreement, which is required for AbbVie to fully realize the value from the licensed compound. Therefore, the $15.0 million received related to this combined unit of accounting was being recognized as revenue ratably over the estimated performance period, which was estimated to continue through the fourth quarter of 2019.

On January 1, 2019, we adopted ASC 606 using the modified retrospective approach. Upon adoption, the fixed, non-refundable and non-creditable upfront payment of $15.0 million received in 2017 was determined to be the transaction price. Revenue is recognized based on a measurement of progress toward the completion of the performance obligation of providing research services for two years, which was subject to an extension for up to six months. In March 2019, we announced a mutual agreement with AbbVie to end our collaboration and to reacquire rights to the program. The measurement is calculated using an input-method based on research costs incurred by us during each reporting period compared to the total research costs projected to provide research services by us pursuant to the AbbVie Agreement. Such costs include external direct costs and internal direct labor consisting of the efforts of certain of our employees that dedicate their time providing research services pursuant to the AbbVie Agreement. Based on this methodology, we concluded that under ASC 606, approximately $9.8 million in revenue should be recognized through December 31, 2018, as compared to $9.4 million under ASC 605. We recorded a cumulative adjustment to decrease accumulated deficit and deferred revenue by $0.4 million as of the adoption date.

In March 2019, we and AbbVie agreed to conclude the collaboration and as of the date of termination, there were no further financial obligations between us. For the three and six months ended June 30, 2019, we recognized zero revenue and the remaining balance of the transaction price of $5.2 million in revenue, respectively, related to the AbbVie Agreement. For the three and six months ended June 30, 2018, we recognized approximately $1.5 million and $3.0 million in revenue, respectively, related to the AbbVie Agreement.

7. Commitments and Contingencies

Leases

Our corporate headquarters are located in South San Francisco, California. In April 2018, we signed a lease (the "Lease Agreement") for approximately 47,500 square feet of office, research and development and laboratory space with occupancy commencing on February 1, 2019 for a seven year period with an option to extend for another seven year period subject to certain conditions. Pursuant to the April 2018 Lease Agreement, we provided a letter of credit to the landlord for $0.6 million which is recorded as long-term restricted cash at June 30, 2019. The Lease Agreement allows for a landlord provided tenant improvement allowance of up to $7.1 million to be applied to the cost of construction of tenant improvements to the new leased premises. The Lease Agreement also provides, and we have utilized, an option through July 1, 2019 for an additional tenant improvement allowance of up to $1.2 million to the costs of tenant improvements. The additional tenant improvement allowance used in connection with this option is amortized and was added to monthly rent payments upon completion of the tenant improvements in May 2019. Reimbursable construction costs incurred will be recorded as a leasehold improvement with a corresponding lease incentive obligation, which is classified as a component of deferred rent. Amounts that will be reimbursed under the tenant improvement allowance will be recorded as deferred rent and amortized as a reduction to rent expense over the lease term. We utilized the aggregate amount of allowances available to us and have recorded $8.3 million of tenant improvement costs as leasehold improvements as of June 30, 2019.

We recognize rent expense on a straight-line basis over the non-cancellable lease term and record the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. Where leases contain escalation clauses, rent abatements, and/or concessions such as rent holidays and landlord or tenant incentives or allowances, we apply them in the determination of straight-line rent expense over the lease term. We recorded tenant improvement allowances as deferred rent and the associated expenditures as leasehold improvements. Leasehold improvements are being amortized over the shorter of their estimated useful life or the term of the lease. We do not assume renewals in our determination of the lease term unless renewals are deemed by management to be reasonably assured at lease inception. We have determined that our lease related to the Lease Agreement commenced on August 1, 2018, when we had right to use or control physical access to the new leased premises.

Future minimum lease payments for operating leases at June 30, 2019 are as follows (in thousands):

Year ended December 31,		
2019 (remaining 6 months)	$	1,502
2020		3,093
2021		3,193
2022		3,296
2023		3,403
2024 and beyond		7,447
Total	$	21,934

We recorded rent expense of $0.7 million and $1.4 million for the three and six months ended June 30, 2019, respectively, and $0.5 million and $0.9 million for the three and six months ended June 30, 2018, respectively.

Our previous lease, which expired on January 31, 2019, was for 30,000 square feet of office, research and development, and laboratory space in South San Francisco. It was subject to several amendments to secure additional space, sublease certain office and laboratory space and/or extend the lease term.

Indemnifications

We are required to recognize a liability for the fair value of any obligations we assume upon the issuance of a guarantee. We have certain agreements with licensors, licensees, collaborators and service providers that contain indemnification provisions. In such provisions, we typically agree to indemnify the licensor, licensee collaborator or service provider against certain types of third party claims. The maximum amount of the indemnifications is usually not limited. We accrue for known indemnification issues when a loss is probable and can be reasonably estimated. There were no accruals for expenses related to indemnification issues for any periods presented.

We indemnify each of our officers and directors for certain events or occurrences, subject to certain limitations, while the officer or director is or was serving at our request in such capacity, as permitted under Delaware law and in accordance with our certificate of incorporation, our bylaws and certain indemnification agreements between us and each of our directors and officers. The term of the indemnification period lasts as long as an officer or a director may be subject to any proceeding arising out of acts or omissions of such officer or director in such capacity. The maximum amount of potential future indemnification is unlimited; however, we currently hold director and officer liability insurance. This insurance allows the transfer of risk associated with our exposure and may enable us to recover a portion of any future amounts paid. We believe that the fair value of these indemnification obligations is minimal. Accordingly, we have not recognized any liabilities relating to these obligations for any period presented.

8. Stock-Based Compensation

The following table summarizes our stock option activity under our stock plans and related information:

	Options Outstanding	Weighted Average Exercise Price
Balance at December 31, 2018	2,998,590	$ 9.39
Options granted	1,247,125	$ 34.38
Options forfeited	(103,754)	$ 15.09
Options exercised	(17,603)	$ 6.64
Options repurchased	—	
Shares added to plans	—	
Balance at June 30, 2019	4,124,358	$ 16.81
Vested and expected to vest	4,124,358	$ 16.81
Exercisable as of June 30, 2019	2,428,297	$ 6.96

At June 30, 2019 and December 31, 2018, 29,460 shares and 33,882 shares, respectively, were subject to repurchase by us at the original exercise price in the event the optionee's employment is terminated either voluntarily or involuntarily. We classify cash received from the exercise of unvested options as a short term liability. Liabilities related to the early exercise of stock options were approximately $0.2 million as of June 30, 2019 and December 31, 2018, respectively, and were included in accrued liabilities on the condensed consolidated balance sheets. Amounts from liabilities are reclassified into common stock and additional paid-in capital as the shares vest, which is generally over 48 months.

The following table summarizes total stock-based compensation expense related to our 2018 Equity Incentive Plan, 2008 Equity Incentive Plan and 2018 Employee Stock Purchase Plan (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Research and development	$ 1,776	$ 179	$ 2,926	$ 341
General and administrative	1,700	188	2,755	392
Total	$ 3,476	$ 367	$ 5,681	$ 733

As of June 30, 2019, there was approximately $40.5 million of unamortized compensation cost related to stock option awards that is expected to be recognized as expense over a weighted-average period of approximately 3.3 years. The weighted-average remaining contractual term of options outstanding at June 30, 2019, was 8.0 years.

Our stock-based compensation expense for the three and six months ended June 30, 2019 includes approximately $0.7 million in expense related to modifications of stock options for members of our Board of Directors.

9. Net Income (Loss) per Share

Net income is allocated between our common stock and other participating securities based on their participation rights. Additionally, during the periods in which we have net income, the diluted net income per share has been computed using the weighted average number of shares of common stock outstanding and other dilutive securities. For the periods presented with a net loss herein, the computation of basic earnings per share using the two-class method is not applicable as the participating securities do not have contractual rights and obligations to share in our losses.

The following table presents a reconciliation of the numerators and denominators of the basic and diluted net income (loss) per share computations and the calculation of basic and diluted net income (loss) per share (in thousands, except share and per share data):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Numerator				
Net income (loss)	$ 7,115	$ 1,797	(6,572)	$ 2,107
Allocation of undistributed earnings to participating securities	—	(1,797)	—	(2,107)
Net income (loss) attributable to common stockholders	7,115	—	(6,572)	—
Denominator				
Weighted-average common shares outstanding, basic	23,927,172	681,616	23,896,788	656,129
Effect of dilutive shares:	1,864,929	731,312	—	852,455
Weighted-average shares outstanding used in per share calculation, diluted	25,792,101	1,412,928	23,896,788	1,508,584
Net income (loss) per share, basic	$ 0.30	$ —	$ (0.28)	$ —
Net income (loss) per share, diluted	$ 0.28	$ —	$ (0.28)	$ —

The following outstanding shares of common stock equivalents were excluded in the computation of diluted net income (loss) per share attributable to common stockholders, because their effect would have been antidilutive for the periods presented:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Employee stock purchase plan	11,326	—	43,745	—
Warrants to purchase capital stock	48,406	173,000	168,046	173,000
Common stock options issued and outstanding	2,390,056	1,323,262	4,124,358	1,202,118
Early exercised common stock subject to future vesting	29,460	21,835	29,460	21,835
Total	2,479,248	1,518,097	4,365,609	1,396,953

10. Income Taxes

We did not record a provision for income taxes for the three months ended June 30, 2019 and 2018 and for the six months ended June 30, 2018, because all of our taxable income will be fully offset by net operating losses generated in prior years. In addition, the deferred tax assets continue to be subject to a full valuation allowance.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our unaudited condensed consolidated financial statements and the notes thereto included in Part I, Item 1, of this Quarterly Report on Form 10-Q and with our audited financial statements and notes thereto for the year ended December 31, 2018, included in our Annual Report on Form 10-K, filed with the U.S. Securities and Exchange Commission ("SEC") on March 19, 2019.

Overview

We are a late-stage biopharmaceutical company dedicated to bringing transformative oral therapies to patients with significant unmet medical needs in immunology and oncology. Our proprietary Tailored Covalency® platform enables us to design and develop reversible covalent and irreversible covalent, small molecule inhibitors with potencies and selectivities that we believe will rival those of injectable biologics, but with the convenience of a pill. We have produced three new drug candidates from our platform, resulting in four clinical programs. In November 2018, we initiated a pivotal Phase 3 trial of PRN1008, a wholly owned Bruton's Tyrosine Kinase, or BTK, inhibitor for the treatment of pemphigus vulgaris (PV) and pemphigus foliaceus (PF) (referred to collectively as "pemphigus". We retain full, worldwide rights to PRN1008, PRN1371 and our oral immunoproteasome inhibitor program, and have established an ongoing collaboration with Sanofi for PRN2246/SAR442168.

Since commencing operations in 2011, we have devoted substantially all our resources to identifying and developing our drug candidates, including conducting preclinical studies and clinical trials and providing general and administrative support for these operations. Our clinical pipeline programs include PRN1008, a reversible covalent BTK inhibitor for the treatment of pemphigus; PRN1008 for the treatment of immune thrombocytopenic purpura, now known as immune thrombocytopenia, or ITP; PRN2246/SAR442168, an irreversible BTK inhibitor that was designed to cross the blood-brain barrier, for the treatment of multiple sclerosis, or MS, and other central nervous system, or CNS, disorders; and PRN1371, an irreversible inhibitor of Fibroblast Growth Factor Receptor, or FGFR, for the treatment of bladder cancer.

- Based on the interim results from our Phase 2 trial in pemphigus, we initiated a pivotal Phase 3 trial of PRN1008 in pemphigus in November 2018. In parallel, we initiated a Phase 2 trial of PRN1008 in ITP, and anticipate announcing topline data in the fourth quarter of 2019. We intend to assess one or more additional immunological indications for PRN1008 for future clinical development. We expect to commercialize PRN1008, if approved, by developing our own sales organization targeting dermatologists and hematologists at specialized centers in the United States.
- In November 2017, we entered an exclusive licensing agreement with Sanofi. We believe that this collaboration maximizes the potential of PRN2246/SAR442168 to address target indications affecting larger populations of patients with CNS diseases. We have completed our development efforts under the early development plan and Sanofi is responsible for further clinical development of this compound in patients suffering from MS. In the event that Sanofi informs us of their intended initiation of the first Phase 3 clinical trial for PRN2246/SAR442168, we will have a period of time to decide on exercising our option to fund a portion of the Phase 3 development costs in exchange for additional economic rights.
- We have initiated the expansion cohort of our Phase 1 trial of PRN1371 in patients with metastatic urothelial carcinoma having FGFR 1, 2, 3, or 4 genetic alterations and are planning another study for treatment of non-muscle invasive bladder cancer, an early bladder cancer, which has a high rate of FGFR expression.
- We are expanding our wholly owned pipeline by continuing to innovate and discover differentiated oral small molecules with the potential to be best-in-class, and we intend to keep our programs at the forefront of covalent inhibitor drug discovery by investing in new technologies that will broaden the target space of our Tailored Covalency platform. In addition, we plan to explore the new biology discovered with our oral immunoproteasome inhibitors and to select the optimal development path for these highly differentiated assets.
- As we have done with our collaboration with Sanofi, we plan to selectively use collaborations and partnerships as strategic tools to maximize the value of our drug candidates, particularly in indications with large target patient populations.

Since inception and through June 30, 2019, we have financed our operations primarily with proceeds totaling $299.5 million from our initial public offering ("IPO"), private placements of our convertible preferred stock and convertible notes and with payments from license and research collaborations. We received a $30.0 million milestone payment in 2019 and milestone payments totaling $25.0 million in 2018 from our collaboration agreement with Sanofi. In 2017, we received non-refundable upfront payments of $40.0 million and $15.0 million from our collaboration agreements with Sanofi and AbbVie, respectively.

In August 2018, we sold 3,474,668 shares of Series C convertible preferred stock at a price of $14.3898 per share for net proceeds of $49.8 million. On September 13, 2018, our Registration Statement on Form S-1 filed in connection with our IPO was declared effective by the SEC. In connection with our IPO, we issued and sold an aggregate of 7,187,500 shares of common stock, including 937,500 shares issued and sold pursuant to the underwriters' full exercise of their overallotment option to purchase additional shares, at an offering price to the public of $17.00 per share. Proceeds from the IPO, net of underwriting discounts and commissions, were $113.6 million. In connection with the completion of our IPO in September 2018, all then outstanding shares of convertible preferred stock were converted into 15,760,102 shares of common stock. In addition, warrants to purchase 12,285,434 shares of our convertible preferred stock were converted into warrants to purchase shares of common stock.

As of June 30, 2019, we held cash, cash equivalents and marketable securities totaling $178.5 million. We do not have any products for sale and have not generated any product revenue since our inception. As of June 30, 2019, all our revenue has been generated from the non-refundable upfront and milestone payments received from our collaboration agreements with Sanofi and AbbVie. For the six months ended June 30, 2019 and 2018, we recorded a net loss of $6.6 million and net income of $2.1 million, respectively. As of June 30, 2019, we have an accumulated deficit of $138.5 million, and we do not expect positive cash flows from operations for the foreseeable future. We expect to continue to incur significant expenses and net operating losses as we advance our clinical drug candidates and expand our pipeline, seek regulatory approval and, if successful, proceed to commercial launch activities. Furthermore, we expect to incur additional costs associated with operating as a public company. In addition, we do not yet have a sales organization or commercial infrastructure. Accordingly, we will incur significant expenses to develop a sales organization or commercial infrastructure in advance of generating any commercial product sales. As a result, we will need substantial additional capital to support our operating activities. We currently anticipate that we will seek to fund our operations through equity or debt financings or other sources, such as potential collaboration agreements with third parties. Adequate funding may not be available to us on acceptable terms, or at all. If sufficient funds on acceptable terms are not available when needed, we could be required to significantly reduce our operating expenses and delay, reduce the scope of or eliminate one or more of our development programs. Based on our planned operations, we believe our cash, cash equivalents and marketable securities at June 30, 2019 are sufficient to fund our operations for at least the next 12 months from the issuance date of these financial statements.

Sanofi Agreement

In November 2017, we entered into a strategic collaboration agreement with Sanofi, or the Sanofi Agreement, for an exclusive license to PRN2246/SAR442168 and backup molecules for development in MS and other CNS diseases. Under the Sanofi Agreement, we have completed the Phase 1 trials and Sanofi is taking on all further development activities. We and Sanofi are each responsible for certain early development costs, and Sanofi is responsible for all further development and commercialization costs, subject to our Phase 3 option described below.

Sanofi has an exclusive license for PRN2246/SAR442168 and its backups for the CNS field, which includes indications of the central nervous system, retina and ophthalmic nerve. We have agreed not to develop other BTK inhibitors within the CNS field, and Sanofi has agreed not to develop PRN2246/SAR442168 or its backups for any indications outside the CNS field. In the event we cease all development and commercialization of our other BTK inhibitors or unilaterally decide to offer Sanofi a field expansion, Sanofi could expand its field upon a field expansion payment to us, as well as potential milestones payments and royalties within the expanded field.

In December 2017, we received a $40.0 million upfront payment from Sanofi. In May 2018, we amended the Sanofi Agreement to include additional activities under the early development plan and to modify the definition of one of the milestone payments. Pursuant to the amendment, we received a $10.0 million payment in July 2018 for the completion of a major part of the Phase 1 trial. In August 2018, we received a $5.0 million payment for the successful completion of preclinical toxicology studies. In November 2018, we received $10.0 million in additional payments from Sanofi for successful development activities of PRN2246/SAR442168 related to the early development plan. In June 2019, we received a $30.0 million milestone payment from Sanofi for the initiation of Sanofi's Phase 2b clinical trial of PRN2246/SAR442168.

Under the amended Sanofi Agreement, we may receive development, regulatory and commercial milestone payments of up to an aggregate of $765.0 million, as well as royalties up to the mid-teens. We have an option to fund a portion of Phase 3 development costs in return for, at our option, either a profit and loss sharing arrangement within the United States, or an additional worldwide royalty that would result in royalties up to the high-teens. Only the additional royalty option would be available if we develop PRN1008 for major enumerated indications overseen by the FDA's Division of Pulmonary, Allergy and Rheumatology

Products or if we experience a change in control involving certain Sanofi competitors. Royalties are subject to specified reductions and are payable, on a product-by-product and country-by-country basis until the later of the date that all of our patent rights that claim a composition of matter of such product expire in such country, the date of expiration of regulatory exclusivity for such product in such country, or the date that is ten years from the first commercial sale of such product in such country.

We identified the following performance obligations under our Sanofi Agreement: (i) granting a license of rights to PRN2246/SAR442168, (ii) transferring of technology (know-how) related to PRN2246/SAR442168, and (iii) performance of research and development services related to our responsibilities under the early development plan. We concluded that the delivered license is not distinct at the inception of the arrangement due to our proprietary expertise with respect to the licensed compound and related developmental participation under the agreement, which is required for Sanofi to fully realize the value from the delivered license. Therefore, we combined these performance obligations as one unit of accounting and recognized the $40.0 million upfront payment and an aggregate of $25.0 million milestone payments over the performance period under the Sanofi Agreement, which ended in December 2018.

On January 1, 2019, we adopted ASC 606 using the modified retrospective approach. We concluded upon analysis that there is no adjustment necessary in revenue recognized through December 31, 2018 under ASC 606 for the Sanofi Agreement. All deliverables under ASC 605 and all performance obligations under ASC 606 have been completed as of December 31, 2018. In June 2019, we received a $30.0 million milestone payment from Sanofi for achieving a clinical development milestone and recognized the full payment as revenue.

AbbVie Agreement

In June 2017, we entered into a collaboration agreement with AbbVie, or the AbbVie Agreement, to research and develop oral immunoproteasome inhibitors and received an upfront payment of $15.0 million. We identified the following performance obligations under the AbbVie Agreement: (i) granting a license of rights to certain licensed compounds to develop and commercialize oral immunoproteasome inhibitors, (ii) transferring of technology (know-how) related to the oral immunoproteasome inhibitors program, and (iii) providing research and development services during the two-year research period, which was subject to an extension for up to six months. In March 2019, we announced a mutual agreement with AbbVie to end our collaboration and to reacquire rights to the program. We determined that each of these performance obligations individually is not distinct, rather each one represents a component of a single performance obligation of the contract. Prior to the adoption of ASC 606, we concluded under ASC 605 that the delivered license did not have standalone value at the inception of the arrangement due to our proprietary expertise with respect to the licensed compounds and related ongoing research participation under the AbbVie Agreement, which is required for AbbVie to fully realize the value from the licensed compound. Therefore, the $15.0 million received related to this combined unit of accounting was being recognized as revenue ratably over the estimated performance period, which was estimated to continue through the fourth quarter of 2019.

On January 1, 2019, we adopted ASC 606 using the modified retrospective approach. Upon adoption, the fixed non-refundable and non-creditable upfront payment of $15.0 million received in 2017 was determined to be the transaction price. Revenue is recognized based on a measurement of progress toward the completion of the performance obligation of providing research services for two years, which was subject to an extension for up to six months. The measurement is calculated using an input-method based on research costs incurred by us during each reporting period compared to the total projected research costs to provide research services by us pursuant to the AbbVie Agreement. Such costs include external direct costs and internal direct labor consisting of the efforts of certain of our employees that dedicate their time providing research services pursuant to the AbbVie Agreement. Based on this methodology, we concluded that under ASC 606, approximately $9.8 million in revenue should be recognized through December 31, 2018, as compared to $9.4 million under ASC 605. We recorded a cumulative adjustment to decrease accumulated deficit and deferred revenue by $0.4 million as of the adoption date.

In March 2019, we and AbbVie have agreed to conclude the collaboration and as of the date of termination, there were no further financial obligations between us. We recognized the remaining balance of the transaction price of $5.2 million in the first quarter of 2019.

Components of Operating Results

Revenue

To date, all our revenue has been generated from payments pursuant to our collaboration arrangements with Sanofi and AbbVie.

In connection with the Sanofi Agreement, we received a $40.0 million non-refundable upfront payment in December 2017, additional milestone payments of $25.0 million in 2018 for successful development activities under the early development plan, and a $30.0 million clinical development milestone payment from Sanofi in 2019. We adopted ASC 606 on January 1, 2019 and concluded that the delivered license was not distinct at the inception of the arrangement due to our proprietary expertise with respect to the licensed compound and related developmental participation under the agreement, which is required for Sanofi to fully realize the value from the delivered license. Therefore, the aggregate $65.0 million received, prior to December 31, 2018, related to this combined unit of accounting was recognized as revenue ratably over the performance period, which ended as of December 31, 2018. We further concluded that there is no adjustment to revenue recognized through December 31, 2018 under ASC 606 because all deliverables under ASC 605 and all performance obligations under ASC 606 have been completed as of December 31, 2018. We recognized $30.0 million in revenue from the Sanofi Agreement during the three and six months ended June 30, 2019. We recognized $11.5 million and $21.4 million in revenue from Sanofi during the three and six months ended June 30, 2018, respectively. There was no deferred revenue related to the Sanofi Agreement at June 30, 2019 and December 31, 2018.

In connection with the AbbVie Agreement, we received a $15.0 million non-refundable upfront payment in June 2017. Upon adoption of ASC 606 using the modified retrospective method, we concluded that the delivered license was not distinct at the inception of the arrangement due to our proprietary expertise with respect to the licensed compounds and related ongoing research participation under the AbbVie Agreement, which is required for AbbVie to fully realize the value from the licensed compound. Therefore, the $15.0 million received related to this combined unit of accounting is recognized as revenue over the estimated performance period, which as of December 31, 2018 was estimated to continue through the fourth quarter of 2019. Revenue related to AbbVie for the three and six months ended June 30, 2018 was approximately $1.5 million and $3.0 million, respectively. Deferred revenue related to the AbbVie Agreement was $5.6 million at December 31, 2018. On January 1, 2019, we recorded a $0.4 million decrease to our accumulated deficit resulting from the adoption of ASC 606 for the AbbVie Agreement. In March 2019, we announced a mutual agreement with AbbVie to end our collaboration and to reacquire rights to the program. We and AbbVie have agreed to conclude the collaboration effective March 2019 and there were no further financial obligations between us, as of the date of the termination. We recognized $5.2 million in revenue in March 2019, upon termination of the AbbVie Agreement.

Operating Expenses

We classify our operating expenses into two categories: research and development and general and administrative.

Research and Development

Our research and development expenses account for a significant portion of our operating expenses and relate to expenses incurred in connection with research and development activities, including the preclinical and clinical development of our drug candidates. These expenses primarily consist of preclinical and clinical expenses; payroll and personnel expenses, including stock-based compensation, for our research and development employees; consulting costs, laboratory supplies and facilities costs. We expense both internal and external research and development costs as they are incurred. Non-refundable advance payments for services that will be used or rendered for future research and development activities are recorded as prepaid expenses and recognized as an expense as the related services are performed.

Our external research and development expenses consist primarily of:

- expenses incurred with contract research organizations, investigative clinical trial sites and other vendors involved in conducting our clinical trials;
- expenses incurred with contract manufacturing organizations for process development, scale up, as well as manufacturing of drug substance and drug candidates;
- expenses incurred with third party vendors for performing preclinical testing on our behalf; and
- consulting fees and certain laboratory supply costs related to the execution of preclinical studies and clinical trials.

With respect to internal costs, several of our departments support multiple clinical programs, and we do not allocate those costs by clinical program. Internal research and development expenses consist primarily of personnel-related costs, facilities and infrastructure costs, certain laboratory supplies and non-capitalized equipment used for internal research and development activities.

We expect our research and development expenses to increase over the next several years as we continue to execute on our business strategy, advance our current programs and expand our research and development efforts, and pursue regulatory approvals of any of our drug candidates that successfully complete clinical trials.

General and Administrative

General and administrative expenses consist primarily of payroll and personnel related expenses, including stock-based compensation, for our personnel in finance, legal, human resources, business and corporate development and other administrative functions, professional consulting fees for legal and accounting services, costs related to our intellectual property and other allocated costs, such as facility expenses not otherwise allocated to research and development, and infrastructure costs.

We expect our general and administrative expenses to increase as a result of operating as a public company. Additional expenses include those related to compliance with the rules and regulations of the SEC and the Nasdaq Global Market, additional insurance expenses, investor relations activities and other administrative and professional services.

Other Income, Net

Other income, net, consists primarily of changes in fair value related to the outstanding convertible preferred stock warrant liability and the convertible notes redemption features liability.

Interest Income

Interest income is primarily related to interest earned on our marketable securities.

Results of Operations

Comparison of the Three Months Ended June 30, 2019 and 2018

The following table summarizes our results of operations for the three months ended June 30, 2019 and 2018 (dollars in thousands):

	Three Months Ended June 30,		Change	
	2019	2018	$	%
Revenue	$ 30,000	$ 12,987	$ 17,013	131%
Operating expenses:				
Research and development	18,718	8,894	9,824	110%
General and administrative	5,233	2,222	3,011	136%
Total operating expenses	23,951	11,116	12,835	115%
Income (loss) from operations	6,049	1,871	4,178	*
Other income (expense), net	(42)	(186)	144	-77%
Interest income	1,108	112	996	*
Net income (loss)	$ 7,115	$ 1,797	$ 5,318	*

* Percentage not meaningful

Revenue

Revenue for the three months ended June 30, 2019 consisted of a $30.0 million clinical development milestone payment received in connection with the Sanofi Agreement. Revenue for the three months ended June 30, 2018 was $13.0 million consisting of a portion of the upfront payments received in connection with the Sanofi Agreement and the AbbVie Agreement, as well as a portion of the payment from Sanofi for completing a major part of the Phase 1 trial in May 2018.

We recorded $30.0 million and approximately $11.5 million in revenue related to the Sanofi Agreement for the three months ended June 30, 2019 and 2018, respectively.

We recorded zero and approximately $1.5 million in revenue related to the AbbVie Agreement for the three months ended June 30, 2019 and 2018, respectively.

Research and Development Expenses

Research and development expenses were approximately $18.7 million for the three months ended June 30, 2019, an increase of $9.8 million, compared to approximately $8.9 million for the three months ended June 30, 2018. The increase was primarily driven by a $3.7 million increase in personnel related expenses, a $3.7 million increase in external PRN1008 program costs due to the initiation of a global Phase 3 trial in pemphigus in November 2018 and certain manufacturing campaigns to supply drug products for our PRN1008 clinical trials, and a $1.4 million increase in other unallocated research and development expenses, mainly facility costs related to our new office space. The increase in personnel related expenses is due to increased research and development headcount and increased stock-based compensation expenses attributed to a higher valuation of options granted in 2019.

The following table summarizes research and development expenses (in thousands):

	Three Months Ended June 30,	
	2019	2018
PRN1008 program external expenses	$ 7,854	$ 4,171
PRN1371 program external expenses	1,234	315
PRN2246 program external expenses	—	726
Preclinical external expenses(1)	1,077	311
Personnel related expenses(2)	6,087	2,315
Other unallocated research and development expenses	2,466	1,056
Total research and development expenses	$ 18,718	$ 8,894

(1) Preclinical external expenses include external research and development expenses for all of our preclinical programs. This includes the oral immunoproteasome program we reacquired the rights to from AbbVie in March 2019.

(2) Personnel related expenses include stock-based compensation expense of $1.8 million and $0.2 million for the three months ended June 30, 2019 and 2018, respectively. As our research and development personnel generally support several of our programs and a significant amount of our internal development activities broadly support all of our programs, we do not separately track or allocate our personnel related expenses by program.

General and Administrative Expenses

General and administrative expenses were $5.2 million for the three months ended June 30, 2019, an increase of $3.0 million, compared to $2.2 million for the three months ended June 30, 2018. The increase was primarily driven by a $2.6 million increase in personnel related expenses due to increased stock-based compensation attributable to higher valuation of options granted and increased headcount expenses.

Other Income (Expense), Net

Other expense, net, for the three months ended June 30, 2019 was insignificant compared to $0.2 million for the three months ended June 30, 2018.

Interest Income

Interest income for the three months ended June 30, 2019 and 2018 was $1.1 million and $0.1 million, respectively, and consists primarily of interest income earned on our cash, cash equivalents and marketable securities. The increase of $1.0 million is mainly due to higher balances of marketable securities in 2019 as compared to the same period in 2018.

Comparison of the Six Months Ended June 30, 2019 and 2018

The following table summarizes our results of operations for the six months ended June 30, 2019 and 2018 (dollars in thousands):

	Six Months Ended June 30,		Change	
	2019	2018	$	%
Revenue	$ 35,160	$ 24,436	$ 10,724	44%
Operating expenses:				
Research and development	34,241	17,655	16,586	94%
General and administrative	9,740	4,378	5,362	122%
Total operating expenses	43,981	22,033	21,948	100%
Income (loss) from operations	(8,821)	2,403	(11,224)	*
Other income (expense), net	(41)	(523)	482	-92%
Interest income	2,290	227	2,063	*
Net income (loss)	$ (6,572)	$ 2,107	$ (8,679)	*

Revenue

Revenue for the six months ended June 30, 2019 was $35.2 million consisting of a $30.0 million clinical development milestone payment received in connection with the Sanofi Agreement and a portion of the upfront payments received in connection with the AbbVie Agreement. Revenue for the six months ended June 30, 2018 was $24.4 million consisting of a portion of the upfront payments received in connection with the Sanofi Agreement and the AbbVie Agreement, as well as a portion of the payment from Sanofi for completing a major part of the Phase 1 trial in May 2018.

The clinical development milestone payment of $30.0 million received in 2019 under the Sanofi Agreement was recognized as revenue when earned in May 2019. The aggregate payments of $65.0 million received in 2017 and 2018 under the Sanofi Agreement were recognized ratably over the estimated performance period ended December 31, 2018, and we recorded approximately $21.4 million in revenue related to the Sanofi Agreement for the six months ended June 30, 2018.

The nonrefundable upfront payment under the AbbVie Agreement was recognized ratably over the estimated performance period, and we recorded approximately $5.2 million and $3.0 million in revenue related to the AbbVie Agreement for the six months ended June 30, 2019 and 2018, respectively.

Research and Development Expenses

Research and development expenses were $34.2 million for the six months ended June 30, 2019, an increase of $16.6 million, compared to $17.7 million for the six months ended June 30, 2018. The increase was primarily driven by a $6.7 million increase in personnel related expenses, a $6.3 million increase in external PRN1008 program costs due to the initiation of a global Phase 3 trial in pemphigus in November 2018 and the initiation of an ITP trial in December 2017, and a $2.4 million increase in other unallocated research and development expenses, mainly facility costs related to our move to our new office space in February 2019. The increase in personnel related expenses is due to increased research and development headcount and increased stock-based compensation expenses attributed to a higher valuation of options granted in 2019.

The following table summarizes research and development expenses (in thousands):

	Six Months Ended June 30,	
	2019	2018
PRN1008 program external expenses	$ 14,959	$ 8,681
PRN1371 program external expenses	1,881	752
PRN2246 program external expenses	8	1,422
Preclinical external expenses(1)	2,035	588
Personnel related expenses(2)	10,993	4,237
Other unallocated research and development expenses	4,365	1,975
Total research and development expenses	$ 34,241	$ 17,655

(1) Preclinical external expenses include external research and development expenses for all of our preclinical programs. This includes the oral immunoproteasome program we reacquired the rights to from AbbVie in March 2019.

(2) Personnel related expenses include stock-based compensation expense of $2.9 million and $0.3 million for the six months ended June 30, 2019 and 2018, respectively. As our research and development personnel generally support several of our programs and a significant amount of our internal development activities broadly support all of our programs, we do not separately track or allocate our personnel related expenses by program.

General and Administrative Expenses

General and administrative expenses were $9.7 million for the six months ended June 30, 2019, an increase of $5.3 million, compared to $4.4 million for the six months ended June 30, 2018. The increase was primarily driven by a $4.5 million increase of personnel related expenses due to increased stock-based compensation attributable to higher valuation of options granted and increased headcount expenses.

Other Income (Expense), Net

Other expense, net, for the six months ended June 30, 2019 was insignificant compared to $0.5 million for the six months ended June 30, 2018.

Interest Income

Interest income for the six months ended June 30, 2019 and 2018 was $2.3 million and $0.2 million, respectively, and consists primarily of interest income earned on our cash, cash equivalents and marketable securities. The increase of $2.1 million is mainly due to higher balances of marketable securities in 2019 as compared to the same period in 2018.

Liquidity and Capital Resources

To date, we have financed our operations primarily through our IPO, private placements of our convertible preferred stock and convertible notes and payments from license and research collaborations. In 2017, we entered into the Sanofi Agreement and the AbbVie Agreement, pursuant to which we received non-refundable upfront payments of $40.0 million and $15.0 million, respectively. From inception to date, we have received $299.5 million in aggregate proceeds through our IPO and private placements and an additional $110.0 million from license and research collaborations. As of June 30, 2019 and December 31, 2018, we held cash, cash equivalents and marketable securities totaling $178.5 million and $180.6 million respectively.

We do not have any products for sale and have not generated any product revenue since our inception. To date, all our revenue has been generated from payments received from our agreements with Sanofi and AbbVie. We have incurred significant operating losses since the commencement of our operations. As of June 30, 2019, we have an accumulated deficit of $138.5 million. We expect to continue to incur significant expenses as we advance our drug candidates and expand our pipeline through clinical development, the regulatory approval process and, if successful, commercial launch activities. If after reviewing the Phase 2 data, we elect to exercise our option to fund a portion of Phase 3 development under the Sanofi Agreement, we will be required to share in certain development costs. Furthermore, we expect to incur additional costs associated with operating as a public company.

We believe our cash, cash equivalents and marketable securities at June 30, 2019 are sufficient to fund our operations for at least the next 12 months from the issuance date of these financial statements.

We have based our projections of operating capital requirements on assumptions that may prove to be incorrect and we may use all of our available capital resources sooner than we expect. 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, rate of progress, results and costs of research and development activities, conducting preclinical studies, laboratory testing and clinical trials for our drug candidates;
- the number and scope of clinical programs we decide to pursue;
- the cost, timing and outcome of regulatory review of our drug candidates;
- the scope and cost of manufacturing development and commercial manufacturing activities;
- the timing and amount of milestone payments, if any, we receive under the Sanofi Agreement;

- our ability to maintain existing and establish new, strategic collaborations, licensing or other arrangements on favorable terms, if at all;
- the costs of preparing, filing, prosecuting, maintaining, defending and enforcing our intellectual property portfolio;
- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of our drug candidates;
- the costs associated with being a public company; and
- the costs associated with commercialization activities if any of our drug candidates are approved for sale.

See our "Risk Factors" elsewhere in this quarterly report for a description of additional risks associated with our substantial capital requirements.

Cash Flows

The following table summarizes cash flows for each of the periods presented below (in thousands):

	Six Months Ended June 30,	
	2019	2018
Cash used in operating activities	$ (2,484)	$ (21,721)
Cash provided by (used in) investing activities	7,972	(8,853)
Cash provided by (used in) financing activities	1,014	(74)
Net decrease in cash, cash equivalents and restricted cash	$ 6,502	$ (30,648)

Cash used in operating activities

During the six months ended June 30, 2019, cash used in operating activities was $2.5 million, which resulted from a net loss of $6.6 million adjusted for changes in operating assets and liabilities and non-cash charges. Non-cash charges included $5.7 million in stock-based compensation, $0.2 million in deferred rent and $0.8 million in depreciation and amortization, partially offset by $0.9 million from the amortization of discounts on marketable securities. Changes in operating assets and liabilities included a decrease of $5.2 million in deferred revenue, a decrease of $0.1 million in accounts payable, partially offset by a 1.9 million increase in accrued liabilities and a $1.6 million decrease in prepaid expenses and other assets.

During the six months ended June 30, 2018, cash used in operating activities was $21.7 million, which resulted from net income of $2.1 million adjusted for changes in operating assets and liabilities and non-cash charges. Changes in operating assets and liabilities included a decrease of $14.4 million in deferred revenue, an increase of $9.6 million in accounts receivable due to the amendment of the Sanofi Agreement in May 2018 and an increase of $0.5 million in long-term restricted cash and other assets. Non-cash charges included stock-based compensation of $0.7 million and a $0.5 million charge related to the change in fair value of the convertible preferred stock warrant liability.

Cash provided by (used in) investing activities

During the six months ended June 30, 2019, cash provided by investing activities was $8.0 million and is primarily the result of maturities in excess of purchases of marketable securities of $9.9 million offset by purchases of laboratory and computer equipment of $1.9 million.

During the six months ended June 30, 2018, cash used in investing activities was $8.9 million, consisting of $8.5 million for the purchases of marketable securities offset by $0.4 million for the purchase of laboratory and computer equipment.

Cash provided by (used in) financing activities

During the six months ended June 30, 2019 cash provided by financing activities was $1.0 million, primarily relating to the proceeds from the issuance of common stock upon exercise of options and participation in the employee stock purchase plan.

During the six months ended June 30, 2018, cash used in financing activities was $0.1 million, relating to the payment of deferred IPO costs, partially offset by proceeds from the issuance of common stock.

Off-Balance Sheet Arrangements

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

JOBS Act

The JOBS Act permits an "emerging growth company" such as ours to take advantage of an extended transition time to comply with new or revised accounting standards applicable to public companies. We have elected the extended transition period for complying with new or revised accounting standards pursuant to Section 107(b) of the JOBS Act, which extension runs 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 (i) the last day of our first fiscal year (a) following the fifth anniversary of the completion of our IPO, (b) in which we have total annual gross revenues of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates as of the end of our second fiscal quarter, or June 30th, exceeds $700.0 million, and (ii) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

Critical Accounting Policies, Significant Judgments and Use of Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States ("U.S. GAAP"). The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

A summary of our critical accounting policies, significant judgments and use of estimates is presented in Part II, Item 7 of our Annual Report on Form 10-K for the year ended December 31, 2018. On an ongoing basis, we evaluate our judgments and estimates considering changes in circumstances, facts and experience. Other than the adoption of Topic 606, as described below, there were no material changes to our critical accounting policies and estimates during the six months ended June 30, 2019.

Revenue Recognition

Effective January 1, 2019, we adopted Accounting Standards Codification ("ASC") 606 using the modified retrospective approach. Under this approach, we recorded a cumulative adjustment to decrease accumulated deficit and deferred revenue by $0.4 million as of the adoption date. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods and services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract, determine those that are performance obligations and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

We have entered into a licensing and collaboration agreements that are within the scope of ASC 606. In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under such licensing and collaboration agreements, we perform the five-step model under ASC 606. As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract.

Licenses of Intellectual Property: If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenues from non-refundable, upfront fees allocated to the

license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promised goods or services, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, upfront fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Milestone Payments: At the inception of each arrangement that includes development, regulatory and/or commercial milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant reversal of cumulative revenue would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or that of our licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received or the underlying activity has been completed. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenue in the period of adjustment.

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

Recent Accounting Pronouncements

See Note 2, Significant Accounting Policies, to our consolidated financial statements for recently issued accounting pronouncements, including the respective effective dates of adoption and effects on our results of operations and financial condition.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risks in the ordinary course of our business. These risks primarily relate to interest rate sensitivities. We had cash, cash equivalents and marketable securities of $178.5 million and $180.6 million as of June 30, 2019 and December 31, 2018, respectively, which consisted of bank deposits, money market funds, U.S. Treasury securities and government agency securities and corporate debt securities.

We have established guidelines regarding the diversification of our investments in approved instruments, their credit quality ratings and maturities. The primary objective of our investment activities is to preserve principal balances and provide liquidity. Because our investments are primarily short-term in duration, we believe that our exposure to interest rate risk is not significant. Based on our investment portfolio at June 30, 2019, a hypothetical 1% movement in market interest rates would not have a significant impact on the total value of our portfolio. We had no debt outstanding as of June 30, 2019.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We maintain “disclosure controls and procedures” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act that are designed to ensure that information required to be disclosed in the reports that 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 our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of June 30, 2019. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control Over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the period covered by this Quarterly Report on Form 10-Q that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Controls

Our management, including our Chief Executive Officer and Chief Financial Officer, believes that our disclosure controls and procedures and internal control over financial reporting are designed to provide reasonable assurance of achieving their objectives and are effective at the reasonable assurance level. However, our management does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, have been detected. These inherent limitations include the realities that judgments in decision making can be faulty, and that breakdowns can occur because of a simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by management override of the controls. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

From time to time, we may be a party to litigation and subject to claims incident to the ordinary course of business. Although the results of litigation and claims cannot be predicted with certainty, we currently believe that the final outcome of these ordinary course matters will not have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 1A. Risk Factors.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should consider and read carefully all of the risks and uncertainties described below, as well as other information included in this Quarterly Report on Form 10-Q, including our condensed consolidated financial statements and related notes before making an investment decision. The risks described below are not the only ones facing us. The occurrence of any of the following risks or additional risks and uncertainties not presently known to us or that we currently believe to be immaterial could materially and adversely affect our business, financial condition or results of operations. In such case, the trading price of our common stock could decline, and you may lose all or part of your original investment. This Quarterly Report on Form 10-Q also contains forward-looking statements and estimates that involve risks and uncertainties. These statements, like all statements in this report, speak only as of the date of this Quarterly Report on Form 10-Q (unless another date is indicated), and, except as required by law, we undertake no obligation to update or revise these statements in light of future developments. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of specific factors, including the risks and uncertainties described below.

Risks Related to Limited Operating History and Financial Position

We are a late-stage biopharmaceutical company with a limited operating history. We have never generated any revenue from product sales and may never be profitable.

We are a late-stage biopharmaceutical company focused on developing oral, small molecule drugs for the treatment of unmet medical needs in immunology and oncology. We have a limited operating history that may make it difficult to evaluate the success of our business to date and to assess our future viability. In addition, biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. Our operations have been limited to organizing and staffing our company, business planning, raising capital, identifying potential drug candidates, establishing licensing and partnering arrangements, undertaking various research and preclinical studies and conducting clinical trials of our drug candidates.

We have never generated any revenue from product sales and have incurred cumulative net losses since we commenced operations. For the six months ended June 30, 2019 and 2018, we recorded net loss of $6.6 million and net income of $2.1 million, respectively. As of June 30, 2019, we had an accumulated deficit of $138.5 million. We expect that it will be several years, if ever, before we have a drug candidate ready for commercialization. We expect to incur increasing levels of operating expenses, and continue to incur net operating losses, for the foreseeable future as we seek to advance our drug candidates. The net operating losses that we incur may fluctuate significantly from quarter to quarter and year to year.

To become and remain profitable, we must develop and eventually commercialize a product with significant product revenue. This will require us to be successful in a range of challenging activities, including, but not limited to:

- initiating and conducting the required preclinical studies and clinical trials of our current and future drug candidates;
- submitting applications for and obtaining marketing approval for these drug candidates;
- researching and discovering new drug candidates;
- establishing a new sales and marketing presence for, or entering into a collaboration with respect to the sales and marketing of, these drug candidates;
- manufacturing, marketing and selling products for which we may obtain marketing approval and satisfying any post-marketing regulatory requirements;
- entering into and maintaining successful collaborations with our strategic partners or future partners;

- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- implementing operational, financial and management systems and appropriate controls; and
- attracting, hiring and retaining additional administrative, clinical, regulatory and scientific personnel.

These challenging activities will increase our operating expenses substantially. We may never succeed in these activities and, even if we succeed in commercializing one or more of our drug candidates, we may never generate revenues that are significant or large enough to achieve profitability. In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown challenges. Because of these numerous risks and uncertainties, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to generate product revenues or achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis and we will continue to incur substantial research and development and other expenditures to develop and market additional drug candidates. Our failure to become and remain profitable could decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or 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 funding to finance our operations, complete the development and any commercialization of our drug candidates and evaluate future drug candidates. If we are unable to raise funding when needed, we may be forced to delay, reduce or eliminate our product development programs or other operations.

Since our inception, we have used substantial amounts of cash to fund our operations, and we expect our expenses to increase substantially in the foreseeable future. Developing our drug candidates and conducting clinical trials for the treatment of pemphigus, immune thrombocytopenia, or ITP, bladder cancer and any other indications that we may pursue in the future, as well as potentially funding a portion of the costs for Phase 3 clinical trials for treatment of multiple sclerosis, or MS, will require substantial amounts of capital. We will also require a significant additional amount of capital to commercialize any approved products. Accordingly, we expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate clinical trials of, and seek marketing approval for, our drug candidates. Our expenses could increase beyond expectations if the U.S. Food and Drug Administration, or FDA, or other regulatory authorities require us to perform preclinical, clinical and other studies in addition to those that we currently anticipate. In addition, if we obtain marketing approval for any of our drug candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Furthermore, we expect 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. Any such funding may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business. 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.

As of June 30, 2019, our cash, cash equivalents and marketable securities totaled $178.5 million. Based on our planned operations, we expect our existing cash, cash equivalents and marketable securities as of June 30, 2019, will enable us to fund our current planned operations for at least the next twelve months. In addition, other factors may arise causing us to need additional capital resources sooner than anticipated. We anticipate that we will need to raise substantial additional funds in the future to fund our operations. Our future capital requirements will depend on many factors, including, but not limited to:

- the scope, rate of progress, results and costs of research and development activities, conducting preclinical studies, laboratory testing and clinical trials for our drug candidates;
- the number and scope of clinical programs we decide to pursue;
- the cost, timing and outcome of regulatory review of our drug candidates;
- the scope and cost of development manufacturing and commercial manufacturing activities;
- the timing and amount of milestone payments, if any, we receive under the Sanofi Agreement;
- our ability to maintain existing and establish new, strategic collaborations, licensing or other arrangements on favorable terms, if at all;
- the costs of preparing, filing, prosecuting, maintaining, defending and enforcing our intellectual property portfolio;
- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of our drug candidates;

- the costs associated with being a public company; and
- the costs associated with commercialization activities if any of our drug candidates are approved for sale.

Adequate additional financing may not be available when we need it, on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts, or grant rights to develop and market drug candidates, such as PRN1008, that we would otherwise develop and market ourselves.

Risks Related to the Development and Commercialization of our Drug Candidates

Clinical drug development is a lengthy, expensive and uncertain process. The results of preclinical studies and early clinical trials are not always predictive of future results. Any drug candidate that we advance into clinical trials may not achieve favorable results in later clinical trials, if any, or receive marketing approval.

The research and development of drugs is an extremely risky industry. Only a small percentage of drug candidates that enter the development process ever receive marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any drug candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. Clinical testing is expensive and can take many years to complete, and its outcome is uncertain.

The results of preclinical studies and completed clinical trials are not necessarily predictive of future results, and our current drug candidates may not be further developed or have favorable results in later studies or trials. Clinical trial failure may result from a multitude of factors including, but not limited to, flaws in study design, dose selection, placebo effect, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits. As such, failure in clinical trials can occur at any stage of testing. A number of companies in the biopharmaceutical industry have suffered setbacks in the advancement of their drug candidates into later stage clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding results in earlier preclinical studies or clinical trials. Based upon negative or inconclusive results, we may decide, or regulatory authorities may require us, to conduct additional clinical trials or preclinical studies. In addition, data obtained from preclinical trials and clinical trials are susceptible to varying interpretations, and regulatory authorities may not interpret our data as favorably as we do, which may further delay, limit or prevent development efforts, clinical trials or marketing approval. Furthermore, as more competing drug candidates within a particular class of drugs proceed through clinical development to regulatory review and approval, the amount and type of clinical data that may be required by regulatory authorities may increase or change.

We currently have three drug candidates in clinical development, and their risk of failure is high. We are unable to predict if these drug candidates or any of our future drug candidates that advance into clinical trials will prove safe or effective in humans or will obtain marketing approval. Our lead drug candidate, PRN1008, has only been tested in a limited number of patients and healthy volunteers.

If we are unable to complete preclinical studies or clinical trials of current or future drug candidates, due to safety concerns, or if the results of these trials are not sufficient to convince regulatory authorities of their safety or efficacy, we will not be able to obtain marketing approval for commercialization. Even if we are able to obtain marketing approval for any of our drug candidates, those approvals may be for indications or dose levels that deviate from our desired approach or may contain other limitations that would adversely affect our ability to generate revenue from sales of those products. Additionally, patent rights are of limited duration, and patents protecting such drug candidates might expire before, or soon after, we obtain marketing approval leaving us open to competition from biosimilar or generic products. Moreover, if we are not able to differentiate our product against other approved products within the same class of drugs, or if any of the other circumstances described above occur, our business would be harmed and our ability to generate revenue from that class of drugs would be severely impaired.

Enrollment and retention of subjects in clinical trials is expensive and time consuming and could result in significant delays and additional costs in our product development activities, or in the failure of such activities.

We may encounter delays in enrolling, or be unable to enroll and retain, a sufficient number of subjects to complete any of our clinical trials. In addition, certain of our drug candidates are designed to treat orphan indications for which there exist limited patient populations, and we may have to compete for patients if competing molecules are also conducting trials, which could result in delays or failure in achieving enrollment of a sufficient number of patients to conduct our trials. Patient enrollment and retention in clinical trials is a significant factor in the timing of clinical trials and depends on many factors, including the size of the patient population required for analysis of the trial's primary endpoints, the nature of the trial protocol, our ability to recruit clinical trial investigators with the appropriate competencies and experience, the existing body of safety and efficacy data with respect to the drug candidate, the number and nature of competing products or drug candidates and ongoing clinical trials of competing drug candidates for the same

indication, the proximity of subjects to clinical trial sites, the eligibility criteria for the clinical trial and our ability to obtain and maintain subject consents.

Furthermore, any negative results that we may report in preclinical studies or clinical trials of our drug candidates may make it difficult or impossible to recruit and retain subjects in other clinical trials of that same drug candidate. Delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our drug candidates. Failures in planned subject enrollment or retention may result in increased costs or program delays and could render further development of drug candidates impossible.

As a company, we have never completed a Phase 3 program or obtained marketing approval for any drug candidate and we may be unable to successfully do so for any of our drug candidates.

We are currently conducting a Phase 3 trial of PRN1008 for pemphigus, a Phase 2 extension trial of PRN1008 in pemphigus, a Phase 2 trial of PRN1008 for ITP and a Phase 1 trial of PRN1371 for bladder cancer. We may need to conduct additional clinical trials before initiating any other future Phase 3 clinical trials. The conduct of Phase 3 clinical trials and the submission of a successful new drug application, or NDA, is a complicated process. As an organization, we have never successfully conducted a Phase 3 clinical trial and have limited experience in preparing, submitting and prosecuting regulatory filings, and have not submitted an NDA before. Consequently, even if our current and planned clinical trials are successful, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to an NDA submission and approval of our drug candidates. In addition, we expect to rely on Sanofi to conduct the Phase 3 trial of PRN2246/SAR442168 under the terms of our collaboration agreement. Failure to commence or complete, or delays in, our planned clinical trials would prevent us from or delay us in commercializing our drug candidates, and failure to successfully complete any of these activities in a timely manner for any of our drug candidates could have a material adverse impact on our business and financial performance.

Our Tailored Covalency platform is novel and unproven, and our strategy relies on discovering, developing and commercializing highly differentiated small molecules using this platform. We may be unable to identify biological targets that work well with our platform or discover and develop new small molecules utilizing our platform.

Our Tailored Covalency platform relies on our ability to successfully identify well-established biological targets that have been historically difficult to inhibit in an effective and safe manner, and subsequently relies on our ability to create drug candidates with relevant levels of potency and selectivity for these targets. This approach to drug discovery is unproven and may not yield any drug candidates viable for regulatory approval or commercial sale. All of our drug candidates are in various stages of development, and none of these candidates have been approved for commercial sale. We cannot assure you that we will be able to successfully identify relevant targets or develop new small molecules to build a pipeline of drug candidates, or that there are a significant number of relevant targets appropriate for our platform. Even if we are able to identify targets for our platform, our efforts to create drug candidates for such targets may not be successful. If our approach does not generate or result in drug candidates with improved features, including effectiveness and dosing convenience, relative to competitive products, or that are not differentiated from other drug candidates in development, either through their efficacy, safety, or toxicity profile or otherwise, our product development activities, business and prospects would be harmed. Furthermore, the covalent drug candidates we develop using our platform may have adverse effects that are unknown and would harm our prospects.

If clinical trials of our drug candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA or similar regulatory authorities outside the United States or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our drug candidates.

Before obtaining regulatory approval for the sale of our drug candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and the outcome is uncertain. Despite preclinical and early clinical trial data, any drug candidate can unexpectedly fail at any stage of further preclinical or clinical development. The historical failure rate for drug candidates is high. The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Even if our clinical trials are completed as planned, we cannot be certain that their results will support our proposed indications. In particular, we have conducted certain preclinical studies of our drug candidates PRN1008, PRN2246/SAR442168 and PRN1371, which are in various stages of clinical trials, and we do not know whether these drug candidates will perform in clinical trials as they have performed in preclinical studies. In addition, if our clinical results are not successful, we may terminate the clinical trials for a drug candidate and abandon any further research or studies of the drug candidate. Any delay in, or termination of, our clinical trials will delay and possibly preclude the filing of any NDAs with the FDA and, ultimately, our ability to commercialize our drug candidates and generate product revenues.

Serious adverse events, undesirable side effects or toxicities, or other unexpected properties of our drug candidates could limit the commercial potential of such drug candidates.

To date, we have tested our drug candidates in a limited number of patients and healthy volunteers. As we continue our development of these drug candidates and initiate additional preclinical studies or clinical trials of these or future drug candidates, if any serious adverse events, unacceptable levels of toxicity, undesirable side effects or unexpected characteristics may emerge, it could cause us to abandon these drug candidates or limit their development to more narrow uses, lower dose levels or subpopulations in which the serious adverse events, unacceptable levels of toxicity, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk/benefit perspective. For example, marketed Bruton's Tyrosine Kinase, or BTK, inhibitors have reported incidences of major hemorrhage, atrial fibrillation or thrombocytopenia, and we could observe such incidences in the future.

Even if our drug candidates initially show promise in early clinical trials, the side effects of drugs are frequently only detectable after they are tested in large Phase 3 clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. Sometimes, it can be difficult to determine if the serious adverse or unexpected side effects were caused by the drug candidate or another factor, especially in subjects who may suffer from other medical conditions and may be taking other medications. Regulatory authorities may draw different conclusions or require additional testing to confirm any such determination.

If serious adverse or unexpected side effects are identified during development and are determined to be attributable to or result from our drug candidate, we may be required to discontinue the development program or the regulatory authorities may refuse to approve the drug candidate. Drug-related side effects could also affect subject recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects.

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

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients, to enter into a risk evaluation and mitigation strategy, or REMS, or to compile a patient database;
- we could face litigation and be held liable for harm caused to patients; and
- our reputation may suffer.

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

If we are unable to commercialize our drug candidates, if approved, or if we experience significant delays in doing so, our business will be harmed.

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 our drug candidates, if approved. Even if we or our collaborators successfully develop and commercialize any of PRN1008, PRN2246/SAR442168 or PRN1371, we may not be successful in developing and commercializing our other drug candidates or other drug candidates we may develop, and our commercial opportunities may be limited. The success of our drug candidates will depend on many factors, including, but not limited to, the following:

- successful enrollment in, and completion of, clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity for our products;
- successfully launching commercial sales, if and when approved, whether alone or in collaboration with others;
- acceptance, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- a continued acceptable safety profile following approval; and

- enforcing and defending intellectual property rights and claims.

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 obtain approval for and commercialize our drug candidates, which would harm our business.

We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our drug candidates.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our drug candidates, including:

- regulatory authorities or institutional review boards or ethics committees, or IRBs or ECs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site or we may fail to reach a consensus with regulatory authorities on trial design;
- regulatory authorities in jurisdictions in which we seek to conduct clinical trials may differ from each other on our trial design, and it may be difficult or impossible to satisfy all such authorities with one approach;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different contract research organizations, or CROs, and trial sites;
- clinical trials of our drug candidates may produce negative or inconclusive results, and we may decide, or regulatory authorities may require us, to conduct additional clinical trials or abandon product development programs;
- number of patients required for clinical trials of our drug candidates may be larger than we anticipate;
- enrollment in our clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- changes to clinical trial protocols;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we might have to suspend or terminate clinical trials of our drug candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- regulatory authorities or IRBs may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our drug candidates may be greater than we anticipate, and we may lack adequate funding to continue one or more clinical trials;
- the supply or quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate;
- third-party clinical investigators may lose the licenses or permits necessary to perform our clinical trials, or not perform our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, good clinical practices, or GCP, or other regulatory requirements;
- third-party contract manufacturing organizations may lose licenses due to their failure to comply with good manufacturing practices, or GMP, or failing to satisfy inspection requirements;
- third-party vendors, such as laboratories, used by us, may fail to follow quality guidelines or otherwise lose their ability to perform functions for which we rely on them;
- our drug candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulatory authorities or institutional review boards to suspend or terminate the trials; and
- occurrence of serious adverse events in trials of the same class of agents conducted by other companies.

Regulatory delays are part of drug discovery, with the FDA issuing 540 clinical holds in 2017. We have experienced regulatory delays in the past and may experience such delays in the future. In the event of a delay, we work closely and collaboratively with the regulatory authority to address their concerns. In our case, the original investigational new drug applications, or INDs, for PRN1008 in

rheumatoid arthritis, or RA, and ITP were placed on clinical hold by the FDA due to concerns with a preclinical study finding. We conducted additional preclinical studies that investigated the relation of the finding to the gut/brain axis and reconfirmed that the finding was not adverse. The clinical holds were lifted, and PRN1008 now has three open INDs in the United States for each of PV, ITP and RA. No other regulatory authority imposed such delays on our PRN1008 program.

If we are required to conduct additional clinical trials or other testing of our drug candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our drug candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our drug candidates;
- not obtain marketing approval at all;
- obtain approval for indications, dosages or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements; or
- have the medicine removed from the market after obtaining marketing approval.

Product development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be amended or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our drug candidates, could allow our competitors to bring products to market before we do, and could impair our ability to successfully commercialize our drug candidates, if approved, any of which may harm our business and results of operations. In addition, many of the factors that cause, or lead to a delay in the commencement or completion of, clinical trials may also ultimately lead to termination or suspension of a clinical trial. Any of these occurrences may harm our business, financial condition and prospects significantly. Any termination of any clinical trial of our drug candidates will harm our commercial prospects and our ability to generate revenues.

The design or our execution of clinical trials may not support regulatory approval.

The design or execution of a clinical trial can determine whether its results will support regulatory approval and flaws in the design or execution of a clinical trial may not become apparent until the clinical trial is well advanced or completed. In some instances, there can be significant variability in safety or efficacy results between different trials of the same drug candidate due to numerous factors, including changes or variations in trial protocols, differences in size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We do not know whether any clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our drug candidates.

Further, the FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and in determining when or whether regulatory approval will be obtained for any of our drug candidates. Our drug candidates may not be approved even if they achieve their primary endpoints in current or future Phase 3 clinical trials or registration trials. For example, while the FDA generally requires two adequate and well-controlled Phase 3 trials to support a marketing application, we plan to pursue an application for PRN1008 for PV on the basis of a single pivotal Phase 3 trial. The FDA or other non-U.S. regulatory authorities may disagree with our trial design and our interpretation of data from preclinical studies and clinical trials, or our plans to support our marketing applications with a single pivotal trial, or may have divergent requirements for our trials or approval. In addition, any of these regulatory authorities may change requirements for the approval of a drug candidate even after reviewing and providing comments or advice on a protocol for a pivotal Phase 3 clinical trial that has the potential to result in FDA or other regulatory authorities' approvals. In addition, any of these regulatory authorities may also approve a drug candidate for fewer or more limited dose levels or indications than we request or may grant approval contingent on the performance of costly post-marketing clinical trials. The FDA or other non-U.S. regulatory authorities may not approve the labeling claims that we believe would be necessary or desirable for the successful commercialization of our drug candidates, if approved. Failure to successfully obtain regulatory approval could have a material adverse impact on our business and financial performance.

Certain of our current clinical trials are being conducted outside the United States, and the FDA may not accept data from trials conducted in foreign locations.

Certain current clinical trials of our drug candidates are being conducted outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to certain conditions imposed by

the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with ethical principles. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In general, the patient population for any clinical trials conducted outside of the United States must be representative of the population for whom we intend to label the product in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. Moreover, when studies are conducted only at sites outside of the United States, the FDA generally does not provide advance comment on the clinical protocols for the studies, and therefore there is an additional potential risk that the FDA could determine that the study design or protocol for a non-U.S. clinical trial was inadequate, which would likely require us to conduct additional clinical trials.

Conducting clinical trials outside the United States also exposes us to additional risks, including risks associated with:

- additional foreign regulatory requirements;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment and storage requirements;
- an inability to negotiate the terms of clinical trial agreements at arms' length in countries where a template agreement for such trials is required by law;
- cultural differences in medical practice and clinical research; and
- diminished protection of intellectual property in some countries.

We cannot assure you that the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from such clinical trials, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of our drug candidates.

Even if we receive marketing approval, we may not be able to successfully commercialize our drug candidates due to unfavorable pricing regulations or third-party coverage and reimbursement policies, which could make it difficult for us to sell our drug candidates profitably.

Obtaining coverage and reimbursement approval for a product from a third-party payor, including governmental healthcare programs such as Medicare and Medicaid, private health insurers, managed care organizations, and other third-party payors, is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of such product to the payor. There may be significant delays in obtaining such coverage and reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a product 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, and in some countries, we may lose eligibility for coverage even after obtaining it. Interim reimbursement levels for new products, 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 product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors, by any future laws limiting drug prices and by any future relaxation of laws that presently restrict imports of product from countries where they may be sold at lower prices than in the United States.

Additionally, coverage and reimbursement policies for drug products can differ significantly from payor to payor as there is no uniform policy of coverage and reimbursement for drug products among third-party payors in the United States. While third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, they also have their own methods and approval process apart from Medicare determinations. There may be significant delays in obtaining coverage and reimbursement as the process of determining coverage and reimbursement is often time-consuming and costly which will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage or adequate reimbursement will be obtained. It is difficult to predict at this time what government authorities and third-party payors will decide with respect to coverage and reimbursement for our drug products.

We cannot be sure that reimbursement will be available for any product that we commercialize and, if coverage and reimbursement are available, what the level of reimbursement will be. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with branded therapeutics and therapeutics administered under the supervision of a physician. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private

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.

We may not be able to obtain or maintain orphan drug designations or exclusivity for our drug candidates, which could limit the potential profitability of our drug candidates, if approved.

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 of 1983, the FDA may designate a drug as an orphan drug if it is a drug 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 it affects more than 200,000, there is no reasonable expectation that sales of the drug in the United States will be sufficient to offset the costs of developing and making the drug available in the United States. Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for an indication for which it receives the designation, then the drug is eligible for a seven-year period of marketing exclusivity during which the FDA may not approve another marketing application for the same drug for the same indication, except in limited circumstances, such as if a subsequent application demonstrates that its product is clinically superior. During an orphan drug's exclusivity period, however, competitors may receive approval for drugs with different active moieties for the same indication as the approved orphan drug, or for drugs with the same active moiety as the approved orphan drug, but for different indications. Orphan drug exclusivity could block the approval of one of our products for seven years if a competitor obtains approval for a drug with the same active moiety intended for the same indication before we do, unless we are able to demonstrate that grounds for withdrawal of the orphan drug exclusivity exist or that our product is clinically superior. Further, if a designated orphan drug receives marketing approval for an indication broader than the rare disease or condition for which it received orphan drug designation, it may not be entitled to exclusivity. For purposes of small molecule drugs, the FDA defines "same drug" as a drug that contains the same active moiety and is intended for the same use as the drug in question. A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan drug designation.

We have received orphan drug designation for PRN1008 from the FDA for the treatment of pemphigus vulgaris, or PV, and from the European Commission for the treatment of pemphigus. We have also received orphan drug designation for PRN1008 from the FDA for the treatment of ITP. We intend to pursue orphan drug designation for other future drug candidates as applicable. Obtaining orphan drug designations is important to our business strategy; however, obtaining an orphan drug designation can be difficult, and we may not be successful in doing so. Even if we were to obtain orphan drug designation for a drug candidate, we may not obtain orphan exclusivity, and any such exclusivity, if attained, may not effectively protect the drug from the competition of different drugs for the same condition, which could be approved during the exclusivity period. Additionally, after an orphan drug is approved, the FDA could subsequently approve another application for the same drug for the same indication if the FDA concludes that the later drug is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusive marketing rights in the United States also may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. The failure to obtain an orphan drug designation for any drug candidates we may develop, the inability to maintain that designation for the duration of the applicable period, or the inability to obtain or maintain orphan drug exclusivity could reduce our ability to make sufficient sales of the applicable drug candidate to balance our expenses incurred to develop it, which would have a negative impact on our operational results and financial condition.

Even if any of our drug candidates receives marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, hospitals, healthcare payors and others in the medical community necessary for commercial success.

If any of our drug candidates receives marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. For example, high-dose corticosteroids, or CS, can be used to treat pemphigus, and physicians may continue to rely on these treatments rather than adopt PRN1008 as a preferred treatment method, in part because CS are relatively inexpensive. The degree of market acceptance of our drug candidates, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- our ability to offer our medicines for sale at competitive prices relative to existing products for the same indication;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- sufficient third-party coverage and adequate reimbursement;

- pricing approvals and complexity of coverage and reimbursement; and
- the prevalence and severity of any side effects.

If some or all of our drug candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable.

We currently have no marketing and sales organization and have no experience as a company in commercializing products.

We have no sales, marketing or distribution capabilities or experience. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization, which would be expensive and time consuming, or outsource these functions to third parties. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our drug candidates if and when they are approved.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. 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 drug candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

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

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future medicines;
- the extent to which our products are approved for coverage or reimbursement;
- the lack of complementary medicines 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, marketing and distribution services, our product revenues or the profitability of these product revenues to us are likely to be lower than if we were to market and sell any medicines that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our drug candidates or may be unable to do so on terms that are favorable to us. In entering into third-party marketing or distribution arrangements, any revenue we receive will depend upon the efforts of the third parties and we cannot assure you that such third parties will establish adequate sales and distribution capabilities or devote the necessary resources and attention to sell and market our medicines effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our drug candidates.

Even if we obtain FDA approval of any of our drug candidates, we may never obtain approval or commercialize such products outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any drug candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining commercial approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our ability to realize the full market potential of our products will be harmed.

Risks Related to our Business Operations

We may expend our limited resources to pursue a particular drug candidate or indication and fail to capitalize on drug 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 must prioritize our research programs and will need to focus our drug candidates on the potential treatment of certain indications. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that may 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 drug 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 drug candidate, we may also relinquish valuable rights to that drug 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 drug candidate.

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

As of June 30, 2019, we had 83 full-time employees. As we advance our research and development programs and continue to operate as a public company, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical development, quality, regulatory affairs and, if any of our drug candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must:

- identify, recruit, integrate, maintain and motivate additional qualified personnel;
- manage our development efforts effectively, including the initiation and conduct of clinical trials for our drug candidates, both as monotherapy and in combination with other intra-portfolio drug candidates; and
- improve our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to develop, manufacture and commercialize our drug candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert financial and other resources, and a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.

We are highly dependent on the services of Martin Babler, who serves as our President and Chief Executive Officer, David M. Goldstein, who serves as our Chief Scientific Officer, and Ken Brameld, who serves as our Vice President of Drug Discovery. Although we have entered into employment agreements with them, they are not for a specific term and each of them may terminate their employment with us at any time, though we are not aware of any present intention of any of these individuals to leave us.

Our industry has experienced a high rate of turnover in recent years. Our ability to compete in the highly competitive biopharmaceuticals industry depends upon our ability to attract, retain and motivate highly skilled and experienced personnel with scientific, medical, regulatory, manufacturing and management skills and experience. We conduct our operations in the San Francisco Bay Area, a region that is home to many other biopharmaceutical companies as well as many academic and research institutions, 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 biopharmaceutical companies. Many of the other biopharmaceutical 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 drug candidates and to grow our business and operations as currently contemplated.

Our future growth may depend, in part, on our ability to operate in foreign markets, where we would be subject to additional regulatory requirements and other risks and uncertainties.

Our future profitability may depend, in part, on our ability to commercialize our drug candidates in foreign markets for which we may rely on collaboration with third parties. We are not permitted to market or promote any of our drug candidates before we receive marketing approval from the applicable regulatory authority in that foreign market, and we may never receive such marketing approval for any of our drug candidates. To obtain marketing approval in many foreign countries, we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our drug candidates, and we cannot predict success in these jurisdictions. If we obtain approval of our drug candidates and ultimately commercialize our drug candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for our drug candidates in foreign markets;
- our inability to directly control commercial activities because we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language or cultural barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- the existence of additional potentially relevant third-party intellectual property rights;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

A majority of patients for certain of our drug candidates are in Europe and if foreign sales of our drug candidates are adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs, our business and its financial operations will be harmed.

We face substantial competition, which may result in others discovering, developing or commercializing products more quickly or marketing them more successfully than us.

The development and commercialization of new drug products is highly competitive. 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, or are less expensive than any products that we may develop or that would render any products that we may develop obsolete or non-competitive. Our competitors already have drugs that apply to or treat the target indications that we are focused on, even if not oral, and our competitors also may obtain marketing approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. We also compete with alternative treatments, even if such treatments are more invasive or not as effective.

Other products, from AbbVie and AstraZeneca, that are in the same class as some of our drug candidates have already been approved in oncology. With respect to our BTK inhibitor programs in immunology, we are aware of several other companies that are or may be developing competing BTK inhibitor drug candidates, including AbbVie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Genentech, Gilead, Merck KGaA, Novartis, Taiho and Takeda. For our small molecule inhibitors of FGFR, we are aware of competing FGFR-inhibiting drug candidates being developed by a number of pharmaceutical and biotechnology companies. As more drug candidates within a particular class of drugs proceed through clinical development to regulatory review and approval, the amount and type of clinical data that may be required by regulatory authorities may increase or change. Consequently, the results of our clinical trials for drug candidates in that class will likely need to show a risk/benefit profile that is competitive with or more favorable than those products and drug candidates in order to obtain marketing approval or, if approved, a product label that is favorable for commercialization. If the risk/benefit profile is not competitive with those other products or drug candidates, we may have developed a product that is not commercially viable, that we are not able to sell profitably or that is unable to achieve favorable pricing or reimbursement. In such circumstances, our future product revenue and financial condition would be adversely affected.

Many of our competitors listed above have longer operating histories and significantly greater financial resources and expertise in research and development, manufacturing, preclinical studies, 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 and management personnel, establishing clinical trial sites and enrolling patients for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

The key competitive factors affecting the success of all of our programs are likely to be the efficacy, safety, convenience, cost and availability of reimbursement for drug candidates arising from such programs. If we are not successful in developing, commercializing and achieving higher levels of reimbursement than our competitors, we will not be able to compete against them and our business would be harmed.

Our internal information technology systems, or those of our third-party CROs or other contractors or consultants, may fail or suffer security breaches, loss or leakage of data, and other disruptions, which could potentially expose 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, integrity and availability 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 contractors who have access to our confidential information.

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 and other contractors and consultants are potentially vulnerable to breakdown or other damage or service interruptions, system malfunctions, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, 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, privacy and availability of information), which may compromise our system infrastructure or lead to unauthorized or inappropriate use or disclosure of our confidential information. To the extent that any such incident were to result in a loss of, or damage to, our data or applications, or inappropriate use or disclosure of confidential or proprietary information, we could incur liability and reputational damage and the further development and commercialization of our drug candidates could be delayed. Even the perception that such an incident has occurred could harm our reputation and our business.

While to our knowledge we have not experienced any such system failure, accident or security breach to date, 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 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, it could result in a material disruption of our programs and the development of our drug candidates could be delayed. In addition, the loss of clinical trial data for our drug 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 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.

The 2017 comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Internal Revenue Code of 1986, as amended. The legislation, among other things, contained significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year

taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, reduction of the Orphan Drug Credit from 50% to 25% of eligible clinical costs and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the federal tax law changes is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the federal tax law changes. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

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 for the tax year ended December 31, 2017 and prior tax years will carry forward to offset future taxable income, if any, until such unused losses expire. Unused losses generated after December 31, 2017 will not expire and may be carried forward indefinitely but will be only deductible to the extent of 80% of current year taxable income in any given year. In addition, both our current and our future unused losses and certain other tax attributes may be subject to limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if we undergo an "ownership change," generally defined as a greater than 50 percentage point change (by value) in our equity ownership by certain stockholders over a rolling three-year period. As a result, our pre-2018 net operating loss carryforwards may expire prior to being used, our net operating loss carryforwards generated in 2018 and thereafter will be subject to a percentage limitation and, if we undergo an ownership change, our ability to use all of our pre-change net operating loss carryforwards, or NOLs, 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. As a result, even if we attain profitability, we may be unable to use all or a material portion of our NOLs and other tax attributes, which could adversely affect our future cash flows.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in certain U.S. states and territories. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including passage of the 2017 federal income tax legislation, changes in the mix of our profitability from state to state, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

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

We do not carry insurance for all categories of risk that our business may encounter. For example, we do not carry earthquake insurance. In the event of a major earthquake in our region, our business could suffer significant and uninsured damage and loss. Some of the policies we currently maintain include general liability, property, auto, workers' compensation, products liability and directors' and officers' insurance policies. Our insurance is expensive and we do not know if we will be able to maintain existing insurance with adequate levels of coverage. Our insurance policies contain exclusions that may apply to our risks. Some risks may not be insurable on commercially reasonable terms, or at all. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our cash position and results of operations.

Risks Related to our Reliance on Third Parties for Clinical Testing and Manufacturing

We 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 or fail to meet expected deadlines, our development programs may be delayed or subject to increased costs, each of which may have an adverse effect on our business and prospects.

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. As a result, we are and expect to remain dependent on third parties to conduct our ongoing, and any future, clinical trials of our drug candidates, or any other drug candidates we may develop. 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, we will not be able to control all aspects of their activities. Nevertheless, we are responsible for ensuring that each of our trials 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 GCP requirements, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, Australian Therapeutic Goods Administration and comparable foreign regulatory authorities for all of our drug 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 or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with product produced under current good manufacturing practices, or cGMP, regulations. Our failure 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. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If any of these third parties fails to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, otherwise performs in a substandard manner, or terminates its engagement with us, the timelines for our development programs may be extended or delayed or our development activities may be suspended or terminated. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in such clinical trials unless we are able to transfer those subjects to another qualified clinical trial site, which may be difficult or impossible. In addition, clinical trial investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA or any comparable foreign regulatory authority concludes that the financial relationship may have affected the interpretation of the trial results, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any marketing application we submit to the FDA or any comparable foreign regulatory authority. Any such delay or rejection could prevent us from commercializing our drug candidates.

We contract with third parties for the manufacture and supply of drug candidates for use in preclinical testing and clinical trials, which supply may become limited or interrupted or may not be of satisfactory quality and quantity.

We do not have any manufacturing facilities. We produce in our laboratory relatively small quantities of compounds for evaluation in our research programs. We rely, and expect to continue to rely, on third parties for the manufacture of our drug candidates for preclinical and clinical testing, as well as for commercial manufacture if any of our drug candidates are approved. We do not have any long-term contractual arrangements with manufacturers and instead rely on third parties to manufacture our drug candidates on a purchase-order basis. We currently have limited manufacturing arrangements, and we cannot be certain that we will be able to establish redundancy in manufacturers for our drug candidates, which could lead to reliance on a limited number of manufacturers for one or more of our drug candidates. This reliance increases the risk that we will not have sufficient quantities of our drug candidates or products, if approved, or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

Furthermore, all entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for our drug candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in clinical trials must be manufactured in accordance with cGMP requirements. These regulations govern manufacturing processes and procedures, including record keeping, and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants, or to inadvertent changes in the properties or stability of our drug candidates that may not be detectable in final product testing. In mid-February 2019, a third-party manufacturer of the active pharmaceutical ingredient, or API, of our drug product PRN1008 informed us that a mechanical failure at its facility may have compromised a batch of our API. We are engaged in ongoing discussions with the manufacturer related to this batch. We are not dependent on this batch to supply our ongoing clinical trials of PRN1008. However, we may suffer economic losses related to this incident, including but not limited to amounts advanced to this manufacturer related to this API batch, the costs of the necessary starting materials and intermediates that were produced or procured elsewhere prior to being sent to this manufacturer for API production, and costs of replacement starting materials and intermediates. Our previously filed insurance claim for such losses has been denied.

We or our contract manufacturers must supply all necessary documentation in support of an NDA on a timely basis and must adhere to the FDA's good laboratory practice, or GLP, regulations and cGMP regulations enforced by the FDA through its facilities inspection program. Comparable foreign regulatory authorities may require compliance with similar requirements. The facilities and quality systems of our third-party contractor manufacturers must pass a pre-approval inspection for compliance with the applicable regulations as a condition of marketing approval of our drug candidates. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMP regulations.

In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on a timely basis or on commercially reasonable terms, if at all. In particular, any replacement of our manufacturers could require significant effort and expertise because there may be a limited number of qualified replacements. In some cases, the technical skills or technology required to manufacture our drug candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our drug candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop drug candidates in a timely manner or within budget.

Our, or a third party's, failure to execute on our manufacturing requirements, or to do so on commercially reasonable terms and comply with cGMP could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of our drug candidates under development;
- delay in submitting regulatory applications, or receiving marketing approvals, for our drug candidates;
- loss of the cooperation of an existing or future collaborator;
- subjecting third-party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities;
- economic loss resulting from starting materials, intermediates, API or drug product that cannot be used in clinical trials or for other purposes;
- requirements to cease development or to recall batches of our drug candidates; and
- in the event of approval to market and commercialize our drug candidates, an inability to meet commercial demands for our product or any other future drug candidates.

We, or our third-party manufacturers, may be unable to successfully scale-up the manufacturing process for our drug candidates to provide sufficient quality and quantity, which would delay or prevent us from conducting clinical trials, developing our drug candidates and commercializing our drugs.

In order to conduct clinical trials of our drug candidates or commercialize our drugs, we will need to manufacture them in large quantities. We, or our manufacturing partners, may be unable to successfully increase the manufacturing capacity for any of our drug candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If we or our manufacturing partners are unable to successfully scale up the manufacture of our drug candidates in sufficient quality and quantity, the development, testing and clinical trials of that drug candidate may be delayed or become infeasible, and marketing approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business.

Existing or changes in methods of drug candidate manufacturing or formulation may result in additional costs or delays.

As drug candidates progress through preclinical to clinical-stage trials to marketing approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize yield, manufacturing batch size, minimize costs and achieve consistent quality and results. Such changes carry the risk that they will not achieve these intended objectives. For example, although we have data regarding PRN1008's long-term stability, PRN1008 is being developed as an amorphous solid, and in the event the solid crystallizes unexpectedly, the drug candidate or the drug product may not be useable or its effectiveness may be altered requiring an interruption or delay to ongoing clinical development due to a need to demonstrate bioequivalent performance of drug candidate or drug product. Any of these changes could cause our drug candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our drug candidates or jeopardize our ability to commercialize our drug candidates and generate any revenue.

Our employees, clinical trial investigators, CROs, 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, 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 laws and 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) laws and regulations in the United States and abroad relating to data privacy and security, fraud and abuse, government price reporting, transparency reporting requirements, and healthcare laws and regulations in the United States and abroad, (iv) laws that require the true, complete and accurate reporting of financial information or data, or (v) insider trading laws. 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 an insider trading policy, 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, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, imprisonment, integrity oversight and reporting requirements, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations.

Risks Related to our Licensing and Other Strategic Agreements

We may not realize the benefits of any collaborations or strategic alliances that we have entered into or may enter into in the future for the development and commercialization of our drug candidates.

The development, manufacture and potential commercialization of our drug candidates will require substantial additional capital to fund expenses. We have entered into collaboration and license agreements with multiple licensees and in the future may seek and form additional strategic alliances, or create joint ventures or collaborations or enter into acquisitions or additional licensing arrangements with third parties that we believe will help to accelerate or augment our development and commercialization efforts with respect to our drug candidates and any future drug candidates that we may develop. These transactions can entail numerous operational and financial risks, and we cannot be certain that we will achieve the financial and other benefits that led us to enter into such arrangements. When we collaborate with a third party for development and commercialization of a drug candidate, we relinquish some or all of the control over, as well as a portion of potential financial benefits of, the future success of that drug candidate to the third party.

We are party to a license agreement, or the Sanofi Agreement, that we entered into with Genzyme Corporation, a wholly owned subsidiary of Sanofi, for an exclusive license to PRN2246/SAR442168 and backup molecules for development in relapsing and progressive MS and other diseases of the central nervous system, or CNS. This agreement provides us with a strategic development and commercialization partner for our drug candidate PRN2246/SAR442168. Under the Sanofi Agreement, we are entitled to receive development, regulatory and commercial milestones that could total up to an aggregate of $765.0 million, as well as tiered royalties up to the mid-teens. We hold an option to fund a portion of Phase 3 development costs in return for, at our discretion, either a profit and loss sharing arrangement within the United States, or an additional worldwide royalty that would result in rates up to the high-teens. Only the additional royalty option would be available if we develop PRN1008 for major enumerated indications overseen by the FDA's Division of Pulmonary, Allergy and Rheumatology Products or if we experience a change of control involving certain Sanofi competitors. If Sanofi is delayed in its development efforts or fails to adequately commercialize PRN2246/SAR442168 following regulatory approval, or fails to pursue PRN2246/SAR442168 in all key markets, our receipt of such payments could be delayed or adversely impacted. If Sanofi elects to terminate the agreement or cease its development of PRN2246/SAR442168, we would not receive the full financial benefit of our agreement and may be required to seek another commercial partner for PRN2246/SAR442168.

We may, in the future, decide to collaborate with other pharmaceutical companies for the development and potential commercialization of our other drug candidates in the United States or other countries or territories of the world. We will face significant competition in seeking appropriate collaborators. We may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our drug candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our drug candidates as having the requisite potential to demonstrate safety and efficacy. If and when we collaborate with a third party for development and commercialization of a drug candidate, we can expect to relinquish some or all of the control over the future success of that drug candidate to the third party. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the following:

- the design or results of clinical trials;
- the likelihood of approval by the FDA or comparable foreign regulatory authorities;

- the potential market for the drug candidate;
- the costs and complexities of manufacturing and delivering such drug candidate to patients;
- the potential of competing products;
- the existence of uncertainty with respect to our ownership of technology or other rights, which can exist if there is a challenge to such ownership without regard to the merits of the challenge; and
- industry and market conditions generally.

The collaborator may also consider alternative drug candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our drug candidate, or may decide alone or together with us to terminate a collaboration. In March 2019, we announced a mutual agreement with AbbVie to end our collaboration and for us to reacquire rights to the program, and we will be able to absorb the costs of researching and advancing immunoproteasome inhibitors into the clinic. We may also be restricted under any license agreements from entering into agreements on certain terms or at all with potential collaborators. For example, we are restricted under our existing collaboration agreements from additional licenses in specified fields. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators and changes to the strategies of the combined company. As a result, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, or a collaboration is terminated, we may have to curtail the development of such drug candidate, reduce or delay one or more of our other development programs, delay the potential commercialization or reduce the scope of any planned sales or marketing activities for such drug candidate, or increase our expenditures and undertake development, manufacturing or commercialization activities at our own expense. If we elect to increase our expenditures to fund development, manufacturing or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our drug candidates or bring them to market and generate product revenue. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our drug candidates or bring them to market and generate product sales revenue, which would harm our business prospects, financial condition and results of operations.

We may wish to acquire rights to future assets through acquisitions, in-licensing or other collaborations in the future, but may not realize the benefits of any such arrangements.

We may in the future seek and form strategic alliances, create joint ventures or collaborations or enter into acquisitions or additional licensing arrangements with third parties for products or technologies that we believe will complement or augment our development and commercialization.

These transactions can 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 manage a collaboration or develop acquired products, drug candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business. As a result, if we enter into collaboration agreements, strategic partnerships or license new products, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business.

We also cannot be certain that, following a strategic or in-licensing transaction, we will achieve the revenue or specific net income that justifies such transaction or such other benefits that led us to enter into the arrangement. Failure to realize the benefits of any collaborations or strategic alliances may further cause us to curtail the development of a drug candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any planned sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense.

Risks Related to our Intellectual Property

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

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our drug candidates and research programs. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel discoveries and technologies that are important to our business. We have certain issued composition of matter patents for compounds, pharmaceutical compositions, formulations and process patents for uses and methods of treatment and processes for making compounds in the United States and other countries, we have certain patent applications pending, and we may seek additional patents in the future. Our pending and future patent applications may not result in patents being issued which protect our drug candidates or their intended uses or which effectively prevent others from commercializing competitive technologies, products or drug candidates.

Obtaining and enforcing patents is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications, or maintain and/or enforce patents that may issue based on our patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development results before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach these agreements and disclose such results before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation, resulting in court decisions, including Supreme Court decisions, that increase uncertainties as to the ability to enforce patent rights in the future. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa.

Further, we may not be aware of all third-party intellectual property rights potentially relating to our drug candidates or their intended uses, and as a result the impact of such third-party intellectual property rights upon the patentability of our own patents and patent applications, as well as the impact of such third-party intellectual property upon our freedom to operate, is highly uncertain. 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. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. 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 U.S. Patent and Trademark Office, or become involved in post-grant review procedures, oppositions, derivations, reexaminations or *inter partes* review proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such challenges may result in loss of exclusivity or in 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. In addition, given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

If we fail to comply with our obligations in our intellectual property licenses from third parties, we could lose license rights that are important to our business.

We are a party to an intellectual property license agreement with The Regents of the University of California, or Regents, under which Regents has granted to us an exclusive license, with the right to grant sublicenses under Regents' patent rights relating to our Tailored Covalency platform, to make, use, sell, offer for sale, and import products and services and practice methods covered by such patent rights in the United States and in other countries where Regents may lawfully grant such a license and in all fields of use, and we may enter into additional license agreements in the future. Our existing license agreements impose, and we expect that our future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, our licensors may have the right to reduce the scope of our rights or terminate these agreements, in which event we may not be able to develop and market any product that is covered by these agreements and would adversely impact our existing collaboration agreements under which we have sublicensed such rights. Termination of this license for failure to comply with such obligations or for other reasons, or reduction or elimination of our licensed rights under it or any other license, may result in our having to negotiate new or reinstated licenses on less favorable terms or our not having sufficient intellectual property rights to operate our business. The occurrence of such events could materially harm our business and financial condition.

The risks described elsewhere pertaining to our intellectual property rights also apply to the intellectual property rights that we in-license, and any failure by us or our licensors to obtain, maintain, defend and enforce these rights could have a material adverse effect on our business. In some cases we do not have control over the prosecution, maintenance or enforcement of the patents that we license, and may not have sufficient ability to provide input into the patent prosecution, maintenance and defense process with respect to such patents, and our licensors may fail to take the steps that we believe are necessary or desirable in order to obtain, maintain, defend and enforce the licensed patents.

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

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

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with will likely expect to be granted rights to publish data arising out of such collaboration and any joint research and development programs may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

We may rely on trade secret and proprietary know-how which can be difficult to trace and enforce and, if we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and drug candidates, we also rely on trade secrets, particularly with respect to our Tailored Covalency platform, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. Elements of our drug candidates, including processes for their preparation and manufacture, may involve proprietary know-how, information, or technology that is not covered by patents, and thus for these aspects we may consider trade secrets and know-how to be our primary intellectual property. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

Trade secrets and know-how can be difficult to protect. We require our employees to enter into written employment agreements containing provisions of confidentiality and obligations to assign to us any inventions generated in the course of their employment. We and any third parties with whom we may, in the future, share facilities with, will enter into written agreements that include confidentiality and intellectual property obligations to protect each party's property, potential trade secrets, proprietary know-how, and information. We further seek to protect our potential trade secrets, proprietary know-how, and information in part, by entering into non-disclosure and confidentiality agreements with parties who are given access to them, such as our corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. Despite these efforts, we cannot ensure that these agreements will provide adequate protection for our trade secrets, know-how or other proprietary information, and any of these parties may breach the agreements 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 inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, 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 them 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 competitive position would be harmed.

To the extent that consultants, contractors, and collaborators or key employees apply technological information independently developed by them or by others to our drug candidates, disputes may arise as to the proprietary rights in such information, which may not be resolved in our favor. With our consultants, contractors, outside scientific collaborators, and key employees who work with our

confidential and proprietary technologies, we enter into agreements that typically include invention assignment obligations. However, these consultants, contractors, collaborators, and key employees may terminate their relationship with us, and we cannot preclude them indefinitely from dealing with our competitors. If our trade secrets become known to competitors with greater experience and financial resources, the competitors may copy or use our trade secrets and other proprietary information in the advancement of their products, methods or technologies.

In the future, we may need to obtain additional licenses of third-party technology that may not be available to us or are available only on commercially unreasonable terms, and which may cause us to operate our business in a more costly or otherwise adverse manner that was not anticipated.

From time to time we may be required to license technology from additional third parties to further develop or commercialize our drug candidates. Should we be required to obtain licenses to any third-party technology, including any such patents required to manufacture, use or sell our drug candidates, such licenses may not be available to us on commercially reasonable terms, or at all. The inability to obtain any third-party license required to develop or commercialize any of our drug candidates could cause us to abandon any related efforts, which could seriously harm our business and operations.

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

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

The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. We may incorrectly determine that our products are not covered by a third party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. In addition, because patent applications can take many years to issue, there may be currently pending applications unknown to us that may later result in issued patents upon which our drug candidates may infringe. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our drug candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

In addition, we are aware of an issued U.S. patent owned by Pharmacyclics, Inc., which was acquired by AbbVie, with certain claims directed to an inhibited tyrosine kinase comprising an irreversible BTK inhibitor having a covalent bond to a cysteine residue of a BTK. We are also aware of other issued U.S. patents owned by Pharmacyclics with certain claims directed to compounds having a certain structure which includes a Michael acceptor moiety or formulations thereof. We are also aware that counterparts to those U.S. patents have issued and/or are pending in Australia, Canada, China, Europe, Japan, the United States and elsewhere. Pharmacyclics or a third party may assert that the sale of our BTK inhibitor drug candidates infringes one or more of these or other patents. Although we believe that the claims of these patents relevant to our BTK inhibitor drug candidates (PRN1008 and PRN2246/SAR442168) would likely be held invalid, we cannot provide any assurances that a court or an administrative agency would agree with our assessment. We have not attempted to obtain a license to these patents. If we decide to seek a license to these patents, we cannot guarantee that we would be able to obtain such a license on commercially reasonable terms, or at all, which could materially and adversely affect our business.

We cannot ensure that patent rights relating to inventions described and claimed in our pending patent applications will issue or that patents based on our patent applications will not be challenged and rendered invalid and/or unenforceable.

We have pending U.S. and foreign patent applications in our portfolio, however, we cannot predict:

- if and when patents may issue based on our patent applications;
- the scope of protection of any patent issuing based on our patent applications;
- whether the claims of any patent issuing based on our patent applications will provide protection against competitors;
- whether or not third parties will find ways to invalidate or circumvent our patent rights;
- whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications;

- whether we will need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose; and
- whether the patent applications that we own or in-license will result in issued patents with claims that cover our drug candidates or uses thereof in the United States or in other foreign countries.

We cannot be certain that the claims in our pending patent applications directed to our drug candidates and/or technologies will be considered patentable by the U.S. Patent and Trademark Office, or USPTO, or by patent offices in foreign countries. One aspect of the determination of patentability of our inventions depends on the scope and content of the "prior art," information that was or is deemed available to a person of skill in the relevant art prior to the priority date of the claimed invention. There may be prior art of which we are not aware that may affect the patentability of our patent claims or, if issued, affect the validity or enforceability of a patent claim. The examination process may require us to narrow our claims, which may limit the scope of patent protection that we may obtain. Even if the patents are issued based on our patent applications, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, patents in our portfolio may not adequately exclude third parties from practicing relevant technology or prevent others from designing around our claims. If the breadth or strength of our intellectual property position with respect to our drug candidates is threatened, it could dissuade companies from collaborating with us to develop and threaten our ability to commercialize our drug candidates. In the event of litigation or administrative proceedings, we cannot be certain that the claims in any of our issued patents will be considered valid by courts in the United States or foreign countries.

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

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

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

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

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

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our drug candidates without infringing the intellectual property and other proprietary rights of third parties. Third parties may allege that we have infringed or misappropriated their intellectual property. Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and, even if resolved in our favor, is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the market price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the

resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

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 rights with respect to our product candidates. Third parties may assert infringement claims against us based on existing or future intellectual property rights. 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 use. 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 drug candidates, products or methods 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 able to do this. Proving invalidity may be difficult. For example, in the United States, proving invalidity in court requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on our business and operations. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing drug 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 drug 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 a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our drug candidates, force us to cease some of our business operations, or require substantial investment and/or time to alter our products, processes, methods, or other technologies, all of which could 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.

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

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. In some cases, it may be difficult or impossible to detect third-party infringement or misappropriation of our intellectual property rights. Even if we detect such infringement or misappropriation, to counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. 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 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. 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, we cannot assure you 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.

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

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

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

We could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other confidential information of former employers or competitors. Although we try to ensure that our employees and consultants do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may become subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor.

While we may litigate to defend ourselves against these claims, even if we are successful, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our drug candidates, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition.

We may not be able to protect our intellectual property rights throughout the world.

Patents are of national or regional effect, and filing, prosecuting and defending patents on all of our drug candidates throughout the world would be prohibitively expensive. As such, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Further, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. In addition, certain developing countries, including China and India, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors and licensees may have limited remedies if patents are infringed or if we or our licensors or licensees are compelled to grant a license to a third party, which could diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical 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. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act (the Leahy-Smith Act), signed into law on September 16, 2011, could increase those uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. The Leahy-Smith Act includes a number of significant changes to 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. These include allowing 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. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements 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. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent

applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

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. 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 would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

Periodic maintenance fees, renewal fees, annuities fees and various other governmental fees on patents and/or patent applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent and/or patent application. The USPTO and various foreign governmental patent agencies also require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of 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. If we fail to maintain the patents and patent applications covering our drug candidates, our competitive and financial position would be adversely affected.

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

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our drug candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Patent terms may be inadequate to protect our competitive position on our drug candidates for an adequate amount of time.

Patent rights are of limited duration. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such drug candidates are commercialized. Even if patents covering our drug candidates are obtained, once the patent life has expired for a product, we may be open to competition from biosimilar or generic products. A patent term extension based on regulatory delay may be available in the United States. However, only a single patent can be extended for each marketing approval, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the patent term extension does not extend to the full scope of the claim, but instead only to the scope of the product as approved. Laws governing analogous patent term extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced.

Risks Related to our Industry

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

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

- delay or termination of clinical trials;
- decreased demand for any drug candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial subjects;
- initiation of investigations by regulatory authorities;
- significant costs to defend the related litigation and diversion of management's time and our resources;
- substantial monetary awards to study subjects or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage as our drug candidates advance through clinical trials and if we successfully commercialize any products. 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.

Failure to comply with existing or future health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal fines or penalties), private litigation, other liabilities, and/or adverse publicity. Compliance or the failure to comply with such laws and regulations could increase the costs of our products and services, could limit their use or adoption, and could otherwise negatively affect our operating results and business.

Regulation of data processing is evolving as federal, state, and foreign governments continue to adopt new, or modify existing, laws and regulations addressing data privacy and security, and the collection, use, disclosure and cross-border transfer of data. We and any collaborators may be subject to current, new, or modified 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 the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH). Depending on the facts and circumstances, we could be subject to significant civil, criminal, and administrative liabilities or 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.

In addition, in June 2018, California enacted the California Consumer Privacy Act of 2018, or CCPA, which takes effect on January 1, 2020. The CCPA gives California residents the right to access and require deletion of their personal information, the right to opt out of certain personal information sharing, and the right to detailed information about how their personal information is collected, used and shared. The CCPA provides civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Although the CCPA includes exemptions for certain clinical trials data, the law may increase our compliance costs and potential liability with respect to other personal information we collect about California residents. The CCPA has prompted a wave of proposals for new federal and state privacy legislation that, if passed, could increase our potential liability, increase our compliance costs and adversely affect our business. Several foreign jurisdictions, including the European Union (EU), its member states, the United Kingdom, Japan and Australia, among others, have adopted legislation and regulations that increase or change the requirements governing the collection, use, disclosure and transfer of the personal information of individuals in these jurisdictions. These laws and regulations are complex and change frequently, at times due to changes in political climate, and existing laws and regulations are subject to different and conflicting interpretations, which adds to the complexity of processing personal data from these jurisdictions. Additionally, certain countries have passed or are considering passing laws that require local data residency and/or restrict the international transfer of data. These laws have the potential to increase costs of compliance, risks of noncompliance and penalties for noncompliance.

Certain international data protection laws, including the EU's General Data Protection Regulation (GDPR) and EU member state implementing legislation, apply to health-related and other personal information of individuals in the EU. These laws impose strict obligations on the ability to process health-related and other personal information of individuals in the EU, including in relation to collection, use, disclosure and cross-border transfer of that information. These include several requirements relating to the consent of the individuals to whom the personal information relates, the information that companies must provide to individuals about how they collect, use and disclose personal information, individual rights to access and delete their personal information, notification of data breaches to authorities and affected individuals, and the security and confidentiality of the personal data. The GDPR prohibits the transfer of personal data to countries outside of the European Economic Area (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 other countries, including the United States, they are subject to legal challenges and uncertainty about compliance with EU data protection laws remains. Such mechanisms may not be available or applicable with respect to the personal data processing activities necessary to research, develop, and market our products and services. For example, ongoing legal challenges in Europe to the mechanisms allowing companies to transfer personal data across national borders could result in further limitations on the ability to engage in cross-border data transfers, particularly if governments are unable or unwilling to reach new or maintain existing agreements that support such transfers. The GDPR allows EU member states to make additional laws and regulations further limiting the processing of genetic, biometric, health data, or other personal data. Failure to comply with these laws, where applicable, can result in the imposition of significant regulatory fines and penalties of up to the greater of €20 million or 4% of annual global turnover (revenue).

Further, the United Kingdom's vote in favor of exiting the EU (often referred to as "Brexit") has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear whether the United Kingdom will enact data protection legislation equivalent to the GDPR and how data transfers to and from the United Kingdom will be regulated.

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 these laws and regulations could result in government enforcement actions (which could include significant civil, criminal or administrative penalties, fines or sanctions), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, 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 related to security or data privacy, 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.

Changes in healthcare law and implementing regulations, as well as changes in healthcare policy, may impact our business in ways that we cannot currently predict, and may have a significant adverse effect on our business and results of operations.

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of drug candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any drug candidates for which we obtain marketing approval. Among policy makers and payors in the United States and elsewhere, including in the European Union, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the Affordable Care Act, substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The Affordable Care Act, among other things: (i) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and expanded rebate liability from fee-for-service Medicaid utilization to include the utilization of Medicaid managed care organizations as well; (ii) established a branded prescription drug fee that pharmaceutical manufacturers of branded prescription drugs must pay to the federal government; (iii) expanded the list of covered entities eligible to participate in the 340B drug pricing program by adding new entities to the program; (iv) established a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; (v) extended manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations; (vi) expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability; (vii) established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and (viii) established a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the Affordable Care Act. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the Affordable Care Act or otherwise circumvent some of the requirements for health insurance mandated by the Affordable Care Act. Additionally, CMS promulgated regulations in 2018 that will give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the Affordable Care Act for plans sold through such marketplaces. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. The Tax Cuts and Jobs Act of 2017, or Tax Act, included a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Affordable Care Act-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Bipartisan Budget Act of 2018, or the BBA, among other things, amends the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In July 2018, CMS published a final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS

uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the Affordable Care Act will impact the Affordable Care Act and our business. We continue to evaluate the Affordable Care Act and its possible repeal and replacement, as it remains uncertain the extent to which any such changes may impact our business or financial condition.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year pursuant to the Budget Control Act of 2011 and subsequent laws, which began in 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027 unless additional Congressional action is taken. New laws may result in additional reductions in Medicare and other healthcare funding, which may adversely affect customer demand and affordability for our products and, accordingly, the results of our financial operations. Additional changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, which will first affect physician payment in 2019. At this time, it is unclear how the introduction of the Medicare quality payment program will impact overall physician reimbursement.

Also, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contained further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services, or HHS, has already started the process of soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. On January 31, 2019, the HHS Office of Inspector General, proposed modifications to the federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations. Although a number of these and other proposals may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, since 2016, Vermont requires certain manufacturer identified by the state to justify their price increases.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 ("Right to Try Act") was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

We expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs, once marketing approval is obtained.

In the European Union, coverage and reimbursement status of any drug candidates for which we obtain regulatory approval are provided for by the national laws of EU Member States. The requirements may differ across the EU Member States. Also at national

level, actions have been taken to enact transparency laws regarding payments between pharmaceutical companies and health care professionals.

We may be subject to applicable fraud and abuse, transparency, government price reporting, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

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

- The federal Anti-Kickback Statute, which prohibits any person or entity from, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of an item or service reimbursable, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. The term "remuneration" has been broadly interpreted to include anything of value. The federal Anti-Kickback Statute has also been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, formulary managers, and others on the other hand. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution.
- Federal civil and criminal false claims laws and civil monetary penalty laws, such as the False Claims Act, or FCA, which imposes significant penalties and can be enforced by private citizens, on behalf of the government, through civil qui tam actions, prohibits individuals or entities from, among other things, knowingly presenting, or causing to be presented, false, fictitious or fraudulent claims for payment of federal funds, and knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to avoid, decrease or conceal an obligation to pay money to the federal government. For example, pharmaceutical companies have been prosecuted under the FCA in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal health care programs for the product. In addition, a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. In addition, manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims.
- HIPAA, among other things, imposes criminal liability for executing or attempting to execute a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and creates federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry in connection with the delivery of or payment for healthcare benefits, items or services.
- HIPAA, as amended by HITECH, and their implementing regulations, which imposes privacy, security and breach reporting obligations with respect to individually identifiable health information upon entities subject to the law, such as health plans, healthcare clearinghouses and certain healthcare providers and their respective business associates that perform services for them that involve individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in U.S. federal courts to enforce HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.
- Federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.
- The federal transparency requirements under the Physician Payments Sunshine Act, created under the Affordable Care Act, which requires, among other things, certain manufacturers of drugs, devices, biologics and medical supplies reimbursed under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to CMS information related to payments and other transfers of value provided to physicians and teaching hospitals and physician ownership and investment interests, including such ownership and investment interests held by a physician's immediate family members.

- State and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws, that may impose similar or more prohibitive restrictions, and may apply to items or services reimbursed by any non-governmental third-party payors, including private insurers.
- State and foreign laws that require pharmaceutical companies to implement compliance programs, comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or to track and report gifts, compensation and other remuneration provided to physicians and other health care providers, state laws that require the reporting of information related to drug pricing, state and local laws that require the registration of pharmaceutical sales representatives and other federal, state and foreign laws that govern the privacy and security of health information or personally identifiable information in certain circumstances, including state health information privacy and data breach notification laws which govern the collection, use, disclosure, and protection of health-related and other personal information, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus requiring additional compliance efforts.

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

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Responding to investigations can be time-and resource-consuming and can divert management's attention from the business. Any such investigation or settlement could increase our costs or otherwise have an adverse effect on our business.

Ensuring that our business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. If our operations are found to be in violation of any of these laws or any other current or future governmental laws and 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, contractual damages, reputational harm, diminished profits and future earnings, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could substantially disrupt our 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 or administrative sanctions, including exclusions from government funded healthcare programs.

We are subject to certain U.S. and 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, or, collectively, Trade Laws, prohibit, among other things, companies and their employees, agents, clinical research organizations, 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 Trade 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.

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

We, and the third parties with whom we share our facilities, are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Each of our operations involve the use of hazardous and flammable materials, including chemicals and

biological and radioactive materials. Each of 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. We could be held liable for any resulting damages in the event of contamination or injury resulting from the use of hazardous materials by us or the third parties with whom we share our facilities, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, 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 may impair our research and development. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We currently take advantage of a Research and Development Tax Incentive program in Australia, which could be amended or changed.

We were eligible to receive a financial incentive from the Australian government as part of its Research and Development Tax Incentive program, or R&D Tax Incentive program, and received a $0.5 million R&D tax credit for the year ended December 31, 2017. The R&D Tax Incentive program is one of the key elements of the Australian government's support for Australia's innovation system and, if eligible, provides the recipient with a 43.5% refundable tax offset for research and development activities in Australia. There have been recent proposals to change the structure of the innovation and research and development funding landscape in Australia, which may impact the research and development tax incentive receivable for the 2018 financial year and beyond. There can be no assurance that we will qualify and be eligible for such incentives or that the Australian government will continue to provide incentives, offset, grants and rebates on similar terms or at all. We were not eligible for this tax credit for the year ended December 31, 2018.

Risks Related to Ownership of our Common Stock

The stock price of our common stock has been and is likely to continue to be volatile or may decline regardless of our operating performance and you could lose all or part of your investment.

The market price of our common stock has been volatile and is likely to continue to be volatile in response to numerous factors, many of which are beyond our control, including:

- results of clinical trials of PRN1008, PRN2246/SAR442168, PRN1371 and any other future drug candidates or those of our competitors, including public misperception of our trial results;
- overall performance of the equity markets;
- our operating performance and the performance of other similar companies;
- changes in our projected operating results that we provide to the public, our failure to meet these projections or changes in recommendations by securities analysts that elect to follow our common stock;
- regulatory or legal developments in the United States and other countries;
- the level of expenses related to PRN1008, PRN2246/SAR442168, PRN1371 and any other future drug candidates or clinical development programs;
- announcements of acquisitions, strategic alliances or significant agreements by us or by our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- the results of our efforts to discover, develop, acquire or in-license additional drug candidates;
- recruitment or departure of key personnel;
- our inability to obtain or delays in obtaining adequate drug supply for any approved drug or inability to do so at acceptable prices;
- significant lawsuits, including patent or stockholder litigation;

- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- the economy as a whole and market conditions in our industry;
- trading activity by a limited number of stockholders who together beneficially own a majority of our outstanding common stock;
- the expiration of market standoff or contractual lock-up agreements;
- the size of our market float; and
- investors' general perception of us and our business.

In addition, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many biopharmaceutical companies. Stock prices of many biopharmaceutical companies have fluctuated in a manner unrelated or disproportionate to the operating performance of those companies. In the past, stockholders have filed securities class action litigation following periods of market volatility. If we were to become involved in securities litigation, it could subject us to substantial costs, divert resources and the attention of management from our business and adversely affect our business.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. Our operating results may fluctuate due to a variety of factors, many of which are outside of our control and may be difficult to predict. As a result, comparing our operating results on a period-to-period basis may not be meaningful. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

We will have broad discretion in the use of our cash and cash equivalents and may not use them effectively.

We cannot specify with any certainty the particular uses of our cash and cash equivalents, but we currently expect such uses will include our ongoing clinical development of PRN1008 and PRN1371, our ongoing preclinical development of our other drug candidates and our other research and development activities. We will have broad discretion in the application of our cash and cash equivalents, which we may spend or invest in a way with which our stockholders disagree. The failure by our management to apply these funds effectively could adversely affect our business and financial condition. Pending their use, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value. These investments may not yield a favorable return to our investors.

Our failure to meet the continued listing requirements of the Nasdaq Global Select Market could result in a delisting of our common stock.

If we fail to satisfy the continued listing requirements of the Nasdaq Global Select Market, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement or prevent future non-compliance with Nasdaq's listing requirements.

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

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

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;

- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- not being required to hold a non-binding advisory vote on executive compensation or obtain stockholder approval of any golden parachute payments not previously approved.

Further, the JOBS Act permits an "emerging growth company" such as us to take advantage of an extended transition time to comply with new or revised accounting standards applicable to public companies. We have elected to use the extended transition period for complying with new or revised accounting standards applicable to public companies. Specifically, we have elected the extended transition period for complying with new or revised accounting standards pursuant to Section 107(b) of the JOBS Act 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 cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following September 18, 2023, (b) in which we have total annual gross revenue of at least $1.07 billion or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could result in sanctions or other penalties that would harm our business.

As a result of being a public company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, the Sarbanes-Oxley Act of 2002 and the rules and regulations of the Nasdaq Global Select Market. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal controls over financial reporting. Commencing with our fiscal year ending December 31, 2019, we must perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. This will require that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. We have never been required to test our internal controls within a specified period and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner.

We may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all 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 Nasdaq, the SEC or other regulatory authorities.

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. If few securities analysts commence coverage of us, or if industry analysts cease coverage of us, the trading price for our common stock would be negatively affected. If one or more of the analysts who cover us downgrade our common stock or publish inaccurate or unfavorable research about our business, our common stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our common stock could decrease, which might cause our common stock price and trading volume to decline.

We do not intend to pay dividends for the foreseeable future.

We have never declared nor paid cash dividends on our capital stock. We currently intend to retain any future earnings to finance the operation and expansion of our business, and we do not expect to declare or pay any dividends in the foreseeable future. Consequently, stockholders must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any future gains on their investment.

The concentration of our stock ownership will likely limit your ability to influence corporate matters, including the ability to influence the outcome of director elections and other matters requiring stockholder approval.

Based upon shares outstanding as of June 30, 2019, our executive officers, directors and the holders of more than 5% of our outstanding common stock, in the aggregate, beneficially owned approximately 69% of our common stock. As a result, these stockholders, acting together, will have significant influence over all matters that require approval by our stockholders, including the election of directors and approval of significant corporate transactions. Corporate actions might be taken even if other stockholders oppose them. This concentration of ownership might also have the effect of delaying or preventing a change of control of our company that other stockholders may view as beneficial.

Delaware law and provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make a merger, tender offer or proxy contest difficult, thereby depressing the trading price of our common stock.

Our status as a Delaware corporation and the anti-takeover provisions of the Delaware General Corporation Law may discourage, delay or prevent a change in control by prohibiting us from engaging in a business combination with an interested stockholder for a period of three years after the person becomes an interested stockholder, even if a change of control would be beneficial to our existing stockholders. In addition, our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may make the acquisition of our company more difficult, including the following:

- a classified board of directors with three-year staggered terms, which could delay the ability of stockholders to change the membership of a majority of our board of directors;
- the ability of our board of directors to issue shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of our board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by a majority vote of our entire board of directors, the chairman of our board of directors or our chief executive officer, which could delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors;
- the requirement for the affirmative vote of holders of at least two-thirds of the voting power of all of the then-outstanding shares of the voting stock, voting together as a single class, to amend the provisions of our amended and restated certificate of incorporation relating to the management of our business or our amended and restated bylaws, which may inhibit the ability of an acquiror to effect such amendments to facilitate an unsolicited takeover attempt; and
- advance notice procedures with which stockholders must comply to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

In addition, as a Delaware corporation, we are subject to Section 203 of the Delaware General Corporation Law. These provisions may prohibit large stockholders, in particular those owning 15% or more of our outstanding voting stock, from merging or combining with us for a certain period of time. A Delaware corporation may opt out of this provision by express provision in its original certificate of incorporation or by amendment to its certificate of incorporation or bylaws approved by its stockholders. However, we have not opted out of this provision.

These and other provisions in our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by our then-current board of directors, including delay or impede a merger, tender offer, or proxy contest involving

our company. The existence of these provisions could negatively affect the price of our common stock and limit opportunities for you to realize value in a corporate transaction.

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

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware 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 Delaware General Corporation Law, our certificate of incorporation or our bylaws or any action asserting a claim against us that is governed by the internal affairs doctrine. 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 our directors, officers or other employees and may discourage these types of lawsuits. Alternatively, if a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions.

Our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, referred to as the Federal Forum Provision. However, as disclosed in our Current Report on Form 8-K filed with the SEC on April 22, 2019, in light of the Sciabacucchi decision issued by the Delaware Court of Chancery in December 2018, finding that provisions similar to the Federal Forum Provision are not valid under Delaware law, we do not currently intend to enforce the Federal Forum Provision unless the Sciabacucchi decision is appealed and the Delaware Supreme Court reverses the decision. If the Delaware Supreme Court affirms the Delaware Chancery Court's decision, we intend to seek approval by our stockholders to amend the amended and restated certificate of incorporation at our next regularly-scheduled annual meeting of stockholders to remove the invalid provision.

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

(a) Recent Sales of Unregistered Equity Securities

On April 8, 2019, we issued 20,860 shares of common stock to the holder of one of our outstanding warrants upon that holder's exercise pursuant to a cashless exercise provision. The warrants had an exercise price of $8.99 per share. The shares of common stock were issued by us in reliance on Section 4(a)(2) of the Securities Act of 1933, as amended.

(b) Use of Proceeds from the IPO

There has been no material change in the planned use of the IPO proceeds as described in our final prospectus filed with the SEC on September 17, 2018 pursuant to Rule 424(b)(4) of the Securities Act

(b) Issuer Purchases of Equity Securities

None.

Item 3. Defaults Upon Senior Securities.

Not applicable.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

None.

Item 6. Exhibits.

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of the Company (incorporated herein by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-38653), filed with the SEC on September 18, 2018).
3.2	Amended and Restated Bylaws of the Company (incorporated herein by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K (File No. 001-38653), filed with the SEC on September 18, 2018).
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.
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.
32.1*	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Furnished herewith and not deemed to be "filed" for purposes of Section 18 of the Exchange Act, and shall not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Company Name

Date: August 8, 2019

By: /s/ Martin Babler

Martin Babler
Chief Executive Officer and Director
(Principal Executive Officer)

Date: August 8, 2019

By: /s/ Christopher Y. Chai

Christopher Y. Chai
Chief Financial Officer
(Principal Financial and Accounting Officer)

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, Martin Babler, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Principia Biopharma Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) 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) 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

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

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

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

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

Date: August 8, 2019

By: /s/ Martin Babler

Martin Babler
President and 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, Christopher Y. Chai, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Principia Biopharma Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) 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) 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

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

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

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

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

Date: August 8, 2019

By: /s/ Christopher Y. Chai

Christopher Y. Chai
Chief Financial Officer
(Principal Financial and Accounting 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

In connection with the Quarterly Report of Principia Biopharma Inc. (the "Company") on Form 10-Q for the period ending June 30, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Martin Babler, Chief Executive Officer of the Company, and Christopher Chai, Chief Financial Officer of the Company, each hereby certifies that, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; 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: August 8, 2019

By: /s/ Martin Babler
Martin Babler
President and Chief Executive Officer
(Principal Executive Officer)

By: /s/ Christopher Y. Chai
Christopher Y. Chai
Chief Financial Officer
(Principal Financial and Accounting Officer)